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The manuscript must have separate documents for the following written in English

1. Cover letter.
2. Research Article/Case Review/Original Research/Review Article file termed Main document.
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1. Cover Letter

A cover letter is a letter addressed to the Editor-in-Chief of the Journal of The Research Society of SKNMC stating why the article should be considered for publication in the journal. It should have the following components:

Abstract:

An abstract is a brief summary of a research article, review, Case report, or any in-depth analysis of a particular subject and is often used to help the reader quickly ascertain the paper's purpose. A well written abstract is informative and completely self-explanatory, briefly presents the topic, states the scope of the experiments, indicates significant data, and points out major findings and conclusions. The abstract should not exceed word limit of 300 for review & original article & 150 for case report, case series Instead of abbreviations, standard nomenclature should be used. The preferable format should accommodate a description of the study background, methods, results and conclusion.

Reviews, Original Articles, Research Articles must include a structured abstract and only include material appearing in the main body of the manuscript. Case Reports/ Case series/Letter to editor should come with a regular abstract.

2. Main Document.

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Original Articles, Research Articles : It should comprise of i) Introduction ii) Material and Methods, iii) Results, iv) Discussion, v) Conclusion, vi) References.

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should be written in Vancouver style. Name of Authors (Max 6 followed by et al, if more). Name of the article. Name of journal year of publication ;Issue: Page number. The citations should in round brackets after fullstop : References should be in range of minimum 6 to maximum 30.

Word Limit :

3000 words including references.

Font :

Times New Roman, 12 size, single spacing.

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EDITORIAL

Mind –Body Medicine In Conventional Healthcare System : A Need of The Hour

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"The natural healing force within each one of us is the greatest force in getting well" Hippocrates

A worldwide rise in non communicable diseases (NCD's) and concurrent emergence of COVID -19 pandemic in past two years has imposed unprecedented pressure on healthcare. Additionally the understanding of associated background inflammation in NCD's and limitations of the pharmacotherapy to effectively control them, once again call for moving beyond conventional pharmacotherapy. It is in this context that the need for incorporating Mind- Body medicine into conventional western medical management system is growing and receiving considerable global attention among the healthcare community.

A **Mind Body Medicine** approach to medicine recognizes the influence of thought, feeling and belief on health and illness, as well as the effect of health and illness on attitude and thoughts of an individual. Mind-body medicine focuses on providing health care that involves behavioural and lifestyle interventions on **an equal footing** with traditional medical interventions.

Historical perspective

There have been two opposing philosophical views dominating western medicine at different point of time namely mind-body interaction and mind body dualism. Hippocrates, the father of western medicine, believed that health is dependent on a balance between the body, mind, and environment, and that disease is caused by imbalances between them. However, thinkers of Mind –body dualism believed that health depended solely upon the physical mechanisms of the body. That is, a person is made up only of physical and chemical reactions that can be measured and manipulated scientifically. The scientific version of this mind-body split can be traced back to seventeenth century French philosopher Rene Descartes whose thinking added to development of science methodology to a great deal but was considered by many as a strong proponent of mind –body dualism. It has taken three centuries for mainstream medicine; begin to accept that the mind plays a major role in health and disease. It was Walter B. Cannon an American Physiologist who underlines the importance of mind-body interaction in his theory of **"Flight-and-Fight Response."** The sympathetic division of autonomic nervous system (fastest bi-directional "**Neuro-anatomical**" brain- body link) mediates this response to perceived threat. Later, it was Hans Selye (1956) who through his General Adaptation Syndrome theory highlighted the role of yet another brain- body link, the hypothalamo-pituitary –

adrenal axis (HPA axis – **Endocrine link**) in modulation of physiological response to a stressful situation. The fight-and- flight response is recognized as the first stage of the general adaptation syndrome. In the year1964 George F. Solomon(University of California in Los Angeles) and his research team coined the term "psychoimmunology" after demonstrating through series of experiments that mental state affects body immunity and vice versa. Thereafter in 1975, Robert Ader and Nicholas Cohen, at the University of Rochester, with their classic conditioning of immune function, demonstrated impact of mental and emotional cues on immune system and subsequently coined the term "psychoneuroimmunology. In the same period during 1970s, Hugo Besedovsky, Adriana del Rey and Ernst Sorkin, working in Switzerland reported multi-directional immune-neuro-endocrine interactions. The collective research of theses researchers led the foundation of new discipline popularly known as **Psycho-Neuro-Immuno- Endocrinology (PNIE)** that features moment -to -moment bi-directional interaction between mind and body. **The PNIE constitutes the theoretical foundation of Mind- Body Medicine.**

In context of NCD's it is the "**Neuroadrenergic theory of hypertension**" proposed by Grassi which states that, it is the progressive increase in sympathetic overdrive which affect the course of disease (from its inception to complication), further reflects inseparable connect between body and mind in illness.

Acute care model of modern medicine and Mind –Body Approach : Global Scenario

The acute care model of modern medicine is a mechanistic model of disease and treatment is based on a dualistic dichotomy of body and mind. The insistence is on diagnostic symptom-oriented interview, extensive laboratory investigations, imaging studies etc. to diagnose specific diseases. The corresponding treatment model places a heavy reliance on pharmacology. Although most physicians acknowledge the importance of life-stress, diet, and exercise, these factors are largely addressed when conventional therapeutic strategies fail. Psychological specialists are regarded as secondary and tertiary caregivers, to be utilized when the primary care physician has been unable to provide relief, or when no physical cause can be identified for a disorder. In many cases the patient's condition becomes more severe and chronic before such a referral takes place, and less amenable to behavioral intervention. Many times the patients with NCD's and functional disorders by choice opt for alternative and complementary medicine intervention either alone or with conventional pharmacotherapy. Usually in such scenario the treating physicians and alternative therapists are unaware of interventions that patients receive from both modalities. As a result of lack of integration between two therapies, the potential treatment benefit is reduced. Separation between two interventions is due to a lack of understanding and a lack of common scientific language between two therapies.

However scientific evidences of basic mechanism of action and clinical significance of mind body approach generated in past few decades have improved our understanding of mind-body techniques and strengthen the bridge between various treatment modalities. The evidence of **"Relaxation Response"** (reduced metabolism, rate of breathing, heart rate, and brain activity) **during meditation** (a mind-body technique) was shown by Dr Herbert Benson (founder of Benson-Henry Institute for Mind Body Medicine 2006, has been integrating the field of mind/body medicine into Massachusetts General Hospital's clinical care, research and training programs). Similarly "**Reversal of heart disease"** through behavioural

and dietary interventions along with conventional pharmacotherapy was scientifically demonstrated by Dr Dean Ornish. Scientific work by Richard Davidson (professor of psychology and psychiatry at the University of Wisconsin–Madison as well as founder and chair of the Centre for Healthy Minds) who showed the changes in physiological states and Neuroplasticity with practice of meditation assessed by MRI, positron emission tomography, electroencephalography and modern genetic and epigenetic methods is a classic examples of evidence –based mind body approach. These evidences boosted the inclusion of mind-body practices not just as an adjuvant/ alternative but as a part of mainstream medical treatment of NCD's in some of the premier medical institutes globally.

In India though our traditional knowledge and wisdom is always a proponent of mind-body interaction, however integration of mind-body approach in routine mainstream clinical practice is still in its infancy. Isolated initiatives to integrate mind-body medicine with mainstream medicine have been attempted recently in some of India's premier medical institutes like NIMHANS (National Institute of Mental Health and Neurosciences- Bangalore), Post Graduate Institute of Medical Education & Research (PGIMER) Chandigarh and AIIMS (All India Institute of Medical Sciences). However inclusion of mind-body medicine in undergraduate and post graduate medical curriculum is still a farfetched goal.

Mind-body medicine in NCD's : Outcome Benefits

Growing evidences from various studies has shown outcome benefits of mind-body interventions in various medical disorders viz. metabolic syndrome, type II diabetes, complications of diabetes, cardio-vascular diseases, hypertension, cancers and autoimmune conditions and psychological conditions like depression, anxiety, somatization disorder, and undifferentiated complaints of Psycho-physiological disorder, Post-traumatic conditions and Insomnia etc.

Fundamentals of Mind-Body Medicine

Along with conventional diagnose oriented interview and investigations, Mind-body medicine includes behavioral and psychosocial assessments and interventions among the **first line of interventions.**

1. Team approach in mind-body medicine

The mind-body medicine approach requires a partnership among specialists in the medical and mental specialties, including physicians, nurse and psychologists, as well as mind/body specialists, such as biofeedback practitioners, chiropractors (a practitioner of the system of complementary medicine based on the diagnosis and manipulative treatment of misalignments of the joints), nutritionists, and yoga teachers. **The result is an integrated team of caregivers who address mind and body in each health care visit.**

2. Active participation of patient in treatment

The **patient is given an active role** from the beginning in developing a treatment plan, and takes more responsibility for directing the psychosocial and lifestyle aspects of that plan. **Mind-body medicine emphasizes patient education and patient self-management as integral parts of clinical practice, from the first day of treatment initiation.**

3. Mind –body Techniques

Traditional Mind-Body technique in India includes practice of Ashtang Yoga (Yam, Niyam, Asana, Pranayama, Pratyahara, Dharana, Dhyan and Samadhi), Buddhist Meditation, Vipasyana etc. Other eastern traditional techniques are mindfulness meditation, Qi Gong etc. Western mind body techniques include movement to express thoughts/feelings, Visualization techniques, Guided Imagery, Mindful eating, Biofeedback, Progressive muscle relaxation, listening to music,

enjoying nature etc.

Along with mind –body techniques appropriate inputs from Western Psychotherapy viz. Cognitive Behaviour Therapy (CBT), Psychodynamic Therapy, Dialectical Behavior Therapy (DBT), Humanistic/Experiential Therapy are integral part of mind-body medicine.

These techniques improve **Self Awareness** at physical, emotional and cognitive level (better connect with oneself), **Attention process** (Focused v/s Generalized default state**)** and **Optimization of Behavioural Response (Action).**

The emphasis in mind –body approach is on providing freedom to choose the mind-body practice that the patient likes, rather than forcing the patient to do specific type of practice.

4. Importance of biofeedback for monitoring progress with mind body intervention

Biofeedback is the process of gaining greater awareness of many physiological functions of one's own body, by using electronic or other instruments, and with a goal of being able to manipulate the body's systems at will)

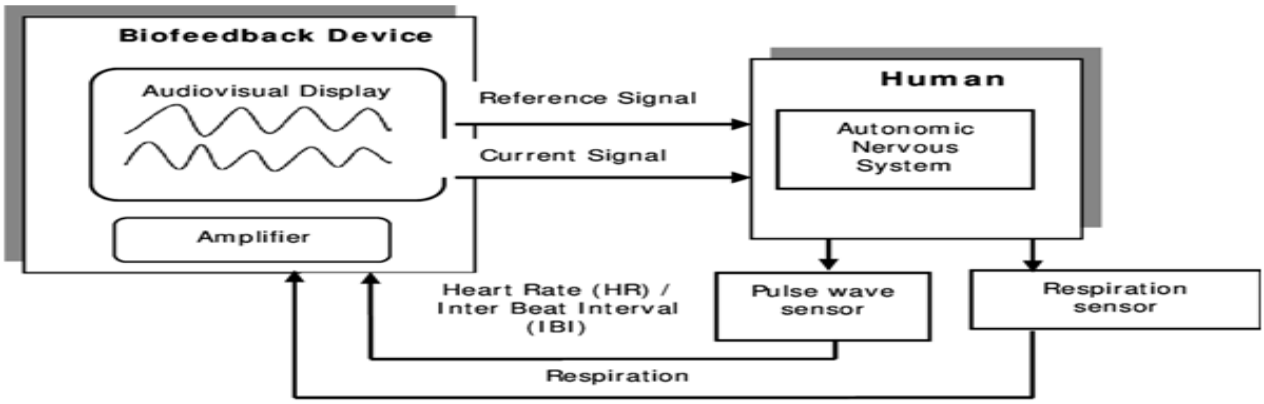

Figure 1 : *Bio feedback General Schematic representation (Bio sensors – Display of physiological parameters – Cognitive or behavioural modulation by patient – Affecting Physiological Parameters – Change in physiological parameter again captured and displayed by bio feedback machine)*

Physiological parameters used in Biofeedback

Electromyograph, Galvanic Skin Response, Temperature, Heart Rate Variability, Capnometry, Photoplethysmogram, Pneumograph, Electroencephelograph, Rheoencephelograh, Hemoencephelograph

5. Individualized Treatment (Tailor made) as against to generalized treatment approach

It is not just the pharmacotherapy but fine tuning of mind-body practices as per the need of patients is the key for better treatment outcomes. Assessment of patients both at the level of physical and psychological is crucial for designing tailor made treatment plan.

Road ahead: Though every physician understands the importance of mind-body interaction, in health and illness, however its genuine implementation in real world clinical settings is highly challenging in terms of availability of trained personnel, co-ordination among different mind-body healthcare givers, availability of such clinical setups etc. The change in healthcare system from conventional pharmacotherapy to integrated mind-body medicine requires a **strong will** to change healthcare policy, undergraduate and postgraduate academics/ curriculum and practice in clinical settings. **"Collective thoughts can bring changes in the existing paradigms".**

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Original Article

Post COVID-19 Rhino-Orbital-Cerebral Mucormycosis – A Morbid Epidemic in Pandemic

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Abstract

Alarming rise in no. of cases of rhino-orbital-cerebral mucormycosis (ROCM) is noted in post COID19 infection in India. Diabetes mellitus (DM) is a discrete risk factor for the severity of COVID-19 and mucormycosis. The widespread use of corticosteroids in the management of COVID-19 appears to increase mucormycosis. The data was collected by a systematic literature search in the electronic database of PubMed until 15 June 2021. A prospective observational study was undertaken at a rural tertiary care hospital in western Maharashtra, India, over a period of 2 months, from 15 April to 15 June 2021 all patients with invasive mucormycosis of the paranasal sinuses who presented to the ENT department were included in the study. Results of the study showed 26(87%) of the patients were diabetic; All 30 (100%) patients had used steroids during the management of their coronavirus-associated illness. All 30 (100%) patients underwent surgical debridement. 4(13%) patients died due to systemic complications out of these 3(75%) of them had an intracranial extension. This is a preliminary report, further evaluation of results of management of ROCM is required.

Keywords

Mucormycosis, COVID19, ROCM, Diabetes mellitus.

Introduction

Thousands of cases of mucormycosis have been reported in the wake of India's second wave of COVID-19 cases, bringing worldwide attention to this deadly life-threatening disease. Mucormycosis or zygomycosis is an aggressive, opportunistic, and devastating fungal infection

caused by saprophytic fungi of the mucoraceae family. The Spores are ubiquitous (soil, decaying organic matter). The incubation period is about one to two weeks through the exact period is not known [1]. It enters the human body directly through cut or open wounds, or by inhalation or ingestion route. Mucormycosis is a rapidly progressive disorder. The angioinvasive nature of fungus causes tissue necrosis. So delay in identification & management leads to high morbidity & mortality. Mucormycosis is rare in healthy individuals but predisposing factors are immunocompromised individuals, uncontrolled diabetes mellitus, prolonged use of broad-spectrum antibiotics, transplant recipients, malignancy. The reason for a sudden sharp increase in post COVID19 cases in India is not entirely clear; however, it is likely to have resulted from a combination of factors. Such factors include widespread use (and misuse) of steroids, even for mild COVID-19; poorly controlled diabetes, which is unmasked or exacerbated by COVID-19 itself; and, possibly, mucosal damage from the virus. Additional hypotheses that need investigation include factors related to the host, pathogen (heightened prevalence and virulence of Mucorales strains in India), or the antecedent COVID19 infection.

Mucormycosis involving the nose, paranasal sinuses, orbit, the central nervous system is called Rhino-orbital-cerebral mucormycosis (ROCM). It also can affect lungs (pulmonary mucormycosis), gastrointestinal tract, skin, heart, bones and joints, kidney, mediastinum, disseminated mucormycosis. The most commonly seen presentation is ROCM.

Clinically, ROCM can present with symptoms of sinusitis and symptoms similar to complicated sinusitis, such as nasal blockage, crusting, proptosis, facial pain and oedema, ptosis, chemosis, and even ophthalmoplegia, diplopia, diminished vision, loss of vision with general symptoms like headache and low-grade fever, malaise & lethargy and various neurological signs and symptoms of the intracranial extension [2, 3]. Maxillary symptoms like toothache, loosening of maxillary teeth, palatal involvement, lesions over the palate.

A black eschar is often seen in the nasal cavity or over the hard palate region but is not characteristic [4, 5]. Without early diagnosis and treatment, there may be a rapid progression of the disease, with reported mortality rates due to intra-orbital and intracranial complications such as cavernous sinus thrombosis, osteomyelitis, disseminated infection, and death of 50–80 %. [6]. Diagnosis is made by radiological investigations and biopsy apart from routine investigations. MRI (PNS, Orbit, and Brain) gadolinium-enhanced is important to know the extent of the disease, biopsy to confirm the presence of fungus. Histological features include mycotic infiltration of blood vessels, vasculitis with thrombosis, tissue infarction, haemorrhage and acute neutrophil infiltrate [7].

Even after reaching a diagnosis, management is challenging. Aggressive Surgical debridement of infected and necrotic tissue is essential to give the patient any chance of survival; however, this can lead to visual loss, severe disfigurement, or both. Many patients cannot access or afford effective antifungal therapy, which comprises another important pillar of management. [8] The mainstay of antifungal treatment is amphotericin B, a nephrotoxic polyene antifungal in use since 1958. Liposomal formulations are preferred because of reduced toxicity. The alternative drugs, such as posaconazole and isavuconazole, are far to reach for much of the world due to cost and availability. To ascertain control over the situation quick measures were taken by government authorities by setting up special task forces, arranging separate wards in hospitals for the management of mucormycosis cases, management guidelines and protocols are prepared and issued, and procuring the drugs required for treatment. Management guidelines for ROCM in COVID19 patients given

by the Indian Academy of Otorhinolaryngology &Head and Neck Surgery (IAOHNS) are as follow- Consultation with physician/ophthalmologist, maxillofacial /endocrinologist/pulmonologist, Control of diabetes & diabetic ketoacidosis, taper steroids and discontinue gradually, Discontinue other immunomodulating drugs.

The first line of Management

Surgical& Medical management.

Surgical Management includes Aggressive adjunctive surgical debridement of devitalized tissue as per extension - endoscopic sinus surgery for drainage of sinuses /Removal of palate/ Removal of orbital contents/ exenteration. Followed by Amphotericin nasal washes or cavity is soaked with Amphotericin B.

Medical Management - Liposomal Amphotericin B(L-AmB)Dose for Rhino-orbital is 5 mg/kg/day, for Cerebral involvement is - 10 mg/kg/day. Diluted in 200 cc of 5% dextrose over 2-3hours infusion for 3-6weeks

The second line of Management

Is considered in case of failure of the first-line treatment, renal failure and toxicity to amphotericin.

Posaconazole is the drug of choice Dose 300mg twice a day on the first day, followed by 300mg once a day.Check Posaconazole trough level after 7 days of therapy & avoid interacting drugs.Delayed-release tablets preferred over oral suspension.

Isavuconazole -recommended dose is 200mg three times a day for two days, followed by 200 mg once a day.

Over the past few months, our institute, a tertiary care teaching hospital, has seen a sudden rise in cases of mucormycosis, with much of the emergency operating theatres being occupied Although prevalent worldwide, mucormycosis is much more common in India: even before the COVID-19 pandemic, the incidence of mucormycosis in India was as much as 80 times higher than the global average. [9]

Materials and methods

The extent of the current epidemic is difficult to overemphasize. According to an official statement by the Ministry of Health of Govt. of India, on May 25, 2021, alone, there were reported to be over 11 700 patients receiving care for mucormycosis. [10] A prospective observational study was undertaken at a rural tertiary care hospital in western Maharashtra, India, over a period of 2 months, from 15 April to 15 June 2021. All patients with invasive mucormycosis of the paranasal sinuses who presented to the ENT department, and who were either recovered from COVID-19 or RTPCR positive were included in the study. The patient's detailed presentation, imaging findings, comorbidities, management, and follow-up information were obtained, recorded, and analyzed. All patients were operated upon, keeping complete surgical debridement as the aim, along with intravenous amphotericin B administration. To obtain worldwide data a systematic literature search was conducted in the electronic database of PubMed until 15 June 2021. Details of all the reported cases of mucormycosis (both confirmed and suspected) in people with COVID-19 so far, were retrieved. The collected data and our data were analysed.

Results

In our study, A total of 30 suspected patients presented; 22(73%) of these were male and 08(27%) were female. 11(36%) of these patients were RTPCR positive at the time of presentation but had been infected for more than 14 days; the remaining 19(56%) had been infected earlier and

had recovered. All patients (100%) had a primary disease infection involving the Ethmoid group of sinus air cells. The maxillary sinus was affected in 28(93%) of 30 cases. Sphenoid 3(10%) and frontal 1(3%) involvement were less common. 23(77%) patients had bilateral involvement while 7(23%) had unilateral disease. Of the 30 patients, 13(43%) had involvement of the orbit at the time of presentation; 4 had vision loss. All these 4 patients underwent orbital exenteration. The rest of these patients received intra-orbital amphotericin B treatment. Intracranial involvement was seen in 3(10%) cases. The classical black eschar on the hard palate and inferior/middle turbinate was observed in 7(23%) patients. 26(87%) of the patients were diabetic; 15 of these had uncontrolled blood sugar levels with haemoglobin A1c levels higher than 6.5 per cent, and the remaining 11 patients had controlled diabetes. 6(20%) patients had hypertension; all of these were diabetic. 2 patients were in ketoacidosis at the time of presentation. All 30 (100%) patients had received steroids during the management of their COVID19. All 30 (100%) patients required surgical endoscopic debridement of involved paranasal sinuses.16 (53%) were needed maxillofacial surgical intervention. 25 (83%) out of 30 patients were positive for mucormycosis on histopathology. Rest 5 showed aspergillosis and inflammatory changes. 4(13%) patients died due to subsequent systemic complications. 3(75%) of them had an intracranial extension.

Case reports of 101 cases of post COVID19 mucormycosis are reported word wide (including confirmed [95/101] and suspected [6/101]) in people with confirmed (RT-PCR diagnosis) were retrieved [11]. Largely, 82 cases (81.2%) of mucormycosis in patients with COVID-19 were reported from India, followed by 9 cases (8.9%) from the USA and 3 cases (3.1%) from Iran. Only 19 (18.8%) cases as of now were reported from other parts of the world. Data from this study showed mucormycosis was predominantly seen in males (78.9%), both in people who were active (59.4%) or recovered (40.6%) from COVID-19. Hyperglycemia at presentation (due to pre-existing DM or new-onset hyperglycemia or new-onset diabetes or diabetic ketoacidosis [DKA]) was the single most important risk factor observed in a majority of cases (83.3%) of Mucormycosis in people with COVID-19, followed by malignancy (3.0%). Pre-existing DM accounted for 80% of cases, while concomitant DKA was present in nearly 15% of people with mucormycosis and COVID-19. History of corticosteroid intake for the treatment of COVID-19 was present in 76.3% of cases, followed by remdesivir (20.6%) and tocilizumab (4.1%). The commonest organ involved with mucormycosis was the nose and paranasal sinus (88.9%), followed by rhino-orbital (56.7%) and ROCM type (22.2%). Overall mortality was noted in 30.7% of the cases.

Discussion

Globally, the prevalence of mucormycosis varied from 0.005 to 1.7 per million population, while its prevalence is nearly 80 times higher (0.14 per 1000) in India compared to developed countries, in a recent estimate of the year 2019-2020 [8,9,12]. In other words, India has the highest cases of mucormycosis in the world. Notwithstanding, India is already having the second largest population with diabetes mellitus (DM) [13]. Importantly, DM has been the most common risk factor linked with mucormycosis in India, although haematological malignancies and organ transplant takes the lead in Europe and the USA [12]. Nonetheless, DM remains the leading risk factor associated with mucormycosis globally, with an overall mortality of 46% [14]. Indeed, the presence of DM was an independent risk factor in a large 2018 meta-analysis of 851 cases of rarely occurring mucormycosis, and the most common species isolated was Rhizopus (48%) [14]. While

long-term use of corticosteroids has often been associated with several opportunistic fungal infections including aspergillosis and mucormycosis, even a short course of corticosteroids has recently been reported to link with mucormycosis especially in people with DM. A cumulative prednisone dose of greater than 600 mg or a total methyl prednisone dose of 2-7 g given during the month before, predisposes immunocompromised people to mucormycosis [15]. There are few case reports of mucormycosis resulting from even a short course (5–14 days) of steroid therapy, especially in people with DM [16]. Surprisingly, 46% of the patients had received corticosteroids within the month before the diagnosis of mucormycosis in the European Confederation of Medical Mycology study [17]. White et al. studied 135 adults with Covid-19 infection and reported an incidence of 26.7 percent for invasive fungal infections [18]. Song et al. studied the association between Covid-19 and invasive fungal sinusitis in April 2020, and concluded that a large number of patients affected by or recovered from Covid-19 are at increased risk for the development of invasive fungal diseases, and gave a management algorithm for such Cases [19]. In a 2019 nationwide multi-center study of 388 confirmed or suspected cases of mucormycosis in India prior to COVID-19, Prakash et al found that 18% had DKA and 57% of patients had uncontrolled DM [9]. Similarly, in data of 465 cases of mucormycosis without COVID-19 in India, Patel et al [20] has shown that rhino orbital presentation was the most common (67.7%), followed by pulmonary (13.3%) and cutaneous type (10.5%). The predisposing factors associated with mucormycosis in Indians include DM (73.5%), malignancy (9.0%), and organ transplantation (7.7%) [20]. The presence of DM significantly increases the odds of contracting ROCM by 7.5-fold as shown in a prospective Indian study, prior to the COVID-19 pandemic [21]. In a recent systematic review conducted until April 9, 2021, by John et al [22] that reported the findings of 41 confirmed mucormycosis cases in people with COVID-19, DM was reported in 93% of cases, while 88% were receiving corticosteroids. These findings are consistent with our findings of an even larger case series of 101 mucormycosis cases (95 confirmed and 6 suspected) in Covid-19, where 80% of cases had DM, and more than two-third (76.3%) received a course of corticosteroids.

Conclusion

Management of post-covid19 ROCM is challenging. The standard protocol for the management is primarily reversal of risk factors, like judicious use of steroids, good glycemic control, Early diagnosis and management by Aggressive surgical debridement and intravenous antifungal medication such as Amphotericin B along with treatment of comorbidities. Further evaluation of the results of these measures will give us more insight into the management of rhino-orbital-cerebral mucormycosis.

Conflict of Interest

The authors declare no conflicts of interest.

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A Review Article

Liquid Biopsy – Future of Diagnostic Pathology

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Abstract

In recent years, there has been an increase in knowledge of cancer, accompanied by a technological development that gives rise to medical oncology. An instrument that allows the implementation of individualized therapeutic strategies is a liquid biopsy. Its high potential as a tool for screening and early detection, the possibility of assessing the patient's condition after diagnosis and relapse, as well as the effectiveness of real-time treatments in different types of cancer. The elements that compose the liquid biopsy are circulating tumour cells, circulating tumour nucleic acids, free of cells or contained in exosomes, microvesicle and platelets.

List of abbreviations appearing in this paper

Abbreviations	*Full forms*
cfDNA	Dell Free DNA
CNVs	Copy Number Variation
CRT	Chemo Radiotherapy
CTC's	Circulating Tumor Cells
ctDNA	Circulating Tumor DNA
LB	Liquid Biopsy

Introduction

The biopsy is obtaining tissue samples from a lesion for detecting a pathological process. Traditionally, a biopsy could be classified as a needle biopsy, incisional and excisional biopsy. Taking a tissue biopsy is thus generally an invasive procedure. (1)

Isolation of these tumour-derived components from peripheral blood and their genomic or proteomic assessment represents a new diagnostic tool that has been called 'liquid biopsy' (Franco Silvestris) (2)

What is Liquid Biopsy? (3)(4)

Tumours release a variety of biomolecules into the bloodstream that can be collected via a blood test, separated from the plasma, and studied. Liquid biopsies are often used alongside surgical biopsies in the diagnosis and treatment of cancer

What are the components of liquid biopsy?

The components of LB mainly refers to the analysis of CTC, cell-free circulating nucleic acids, includes ctDNA, ct RNA, exosomes, microvesicles and platelets. (5)

What are the different samples used for the study? (6)(7)(8)

Now organ wise study of LB shows various other samples also can be used for study and diagnosis. Endometrial aspiration samples, semen, urine, ascetic fluid, cerebrospinal fluid (CSF), Endometrial aspiration, bone marrow aspiration can be used in the study.

What are the Uses of liquid biopsy in Pathology? (9)(2)(10)(11)(12)(13)(14)

We can use liquid biopsy for the study of RNA and protein expression, DNA and chromosomal abnormalities, Amplification, deletions, Translocations, Point mutations.

Table No. 1- Applications of Different components of LB

Cancer derived molecules/ cell	*Applications*
Circulating Tumor cell (CTC)(15)	1. Cancer monitoring by quantification 2. Detection of MRD (Minimal Residual disease)
Tumor derived cell free DNA	1. Screening of gastric and colorectal cancers by detection of methylated cell free DNA is serum 2. Screening of EBV associated cancers 3. Detection of mutation in tumour – derived cell free DNA for treatment selection 4. Tracking progression and evolution of cancers
mi RNA/ exosomes	Plasma or serum mi RNA for detection of cancers
Extra cellular vesicles	Detection of tumour- derived extra cellular vesicles by surface markers in serum of colorectal cancer patient

What are the advantages of liquid biopsy over routine surgical tissue biopsy? (5)(16)

Table No. 2 - Differences between LB & Tissue Biopsy (surgical Biopsy)

Liquid biopsy	*Tissue biopsy*
Minimally invasive	Invasive
Shorter time procedure	Longer time procedure
Lower cost for sample obtained	Higher cost for sample processing
More complete tumor molecular information	Molecular information limited to constraint areas
Compatible with tumor monitoring during surveillance / treatment	Not compatible with tumor monitoring during surveillance / treatment

Other advantages (2)

- Helps to understand the spatial and temporal heterogeneity of cancer
- Usually small 6-10 ml of blood
- Early detection of cancer & genotyping of mutation
- Real-time monitoring for treat met response and resistance could be performed by repeated analysis.

What are the disadvantages of Liquid biopsy? (2)(7)(17)

- Lack of standardization of the techniques
- Sufficient clinical and technical validation is not yet attained, that is required for the routine clinical implementation
- In some cancers (e. g., lung cancers), the diagnosis and subtyping cannot be done by liquid biopsy and can be established by only histology

CTC

What is mean by CTC? (18)(17)(19)

CTCs are intact tumour cells shed from both primary tumour sites and metastatic sites into the circulatory system. CTCs were first described by Thomas Ashworth in 1869. CTCs are shed from either primary or secondary tumour sites . They migrate into the circulatory system and are responsible for the development of distant metastases. CTCs are extremely rare, occurring at a frequency as low as 1 CTC per 10^6–10^7 leukocytes, with even lower numbers in early-stage diseases.

The phenotypic and genotypic characteristics of CTCs can change during cancer by microenvironmental and therapeutic selective pressures. As CTCs counts run in parallel with the tumour burden of the disease, they serve to be a more accurate method for the real-time monitoring of cancers than many other commonly used soluble biomarkers.

CTC isolation and detection from the sample -

CTC are having certain properties which makes them different from leukocytes and blood cells.

Important are Antigen expression, Size – 20-30 micro m, Mechanical Plasticity, Dielectric mobility . Based on these properties two different strategies are implicated they are 1) Enrichment and 2) isolation methods.

In Enrichment method we can use either Physical or Biological or Both properties. In case of isolation method, all used technologies are molecular based, like Flow cytomtery, DEPArray etc. So for detection of CTC sample needs to first go through the Enrichment method followed by isolation method. The explanation of each subtype of the method is beyond the scope of this article.

ctDNA

What is ctDNA? (24)(2)

ctDNA- DNA is released irrespective of the cell of origin, it is typically referred to as cfDNA

ctDNA. - DNA released specifically by the cancerous cells, is referred to as ctDNA.

The first experimental evidence of cell-free DNA (cfDNA) in the blood was reported by Mandel and Metais in 1948.

Potential origins of ctDNA:

1. **Apoptotic or necrotic tumour cells,**
2. **Tumour cells**
3. **CTCs**

Samples used for ctDNA analysis (25)(21)

- ctDNA can be isolated from plasma, serum, ascites, breast milk, lymphatic and peritoneal fluids, bone marrow aspirates, urine, prostatic fluid, peritoneal lavage, sputum, cerebrospinal fluid, gastric juice, and biliary and stool samples. ctDNA has a very short half-life of 15 minutes to 16 hours. A blood sample can be collected in an EDTA tube but plasma has to be isolated and stored at -80 0C within 1 hr. It is stable in plasma at -80 0C. The amount of ct DNA in serum is 2-24 times higher than in plasma.

Identification (22) (5)

Circulating tumour DNA (ctDNA) is part of the cfDNA deriving from the tumour mass. The easiest way to identify the ctDNA is to investigate the presence of somatic driver mutations, which, by definition, can be exclusively found on the tumour.

The rate of ctDNA shedding into the circulation depends on the location, size, and vascularity of the tumour. In cancer patients, ctDNA represents only a small proportion of total cfDNA (varies from less than 0. 1% to over 10%).

Methods for ctDNA detection and analysis (26) (25)

Two main approaches are utilized for the detection of ctDNA - a targeted, and an untargeted approach. The targeted approach can detect previously determined genetic mutations, where as in case of untargeted approach we don't need prior knowledge.

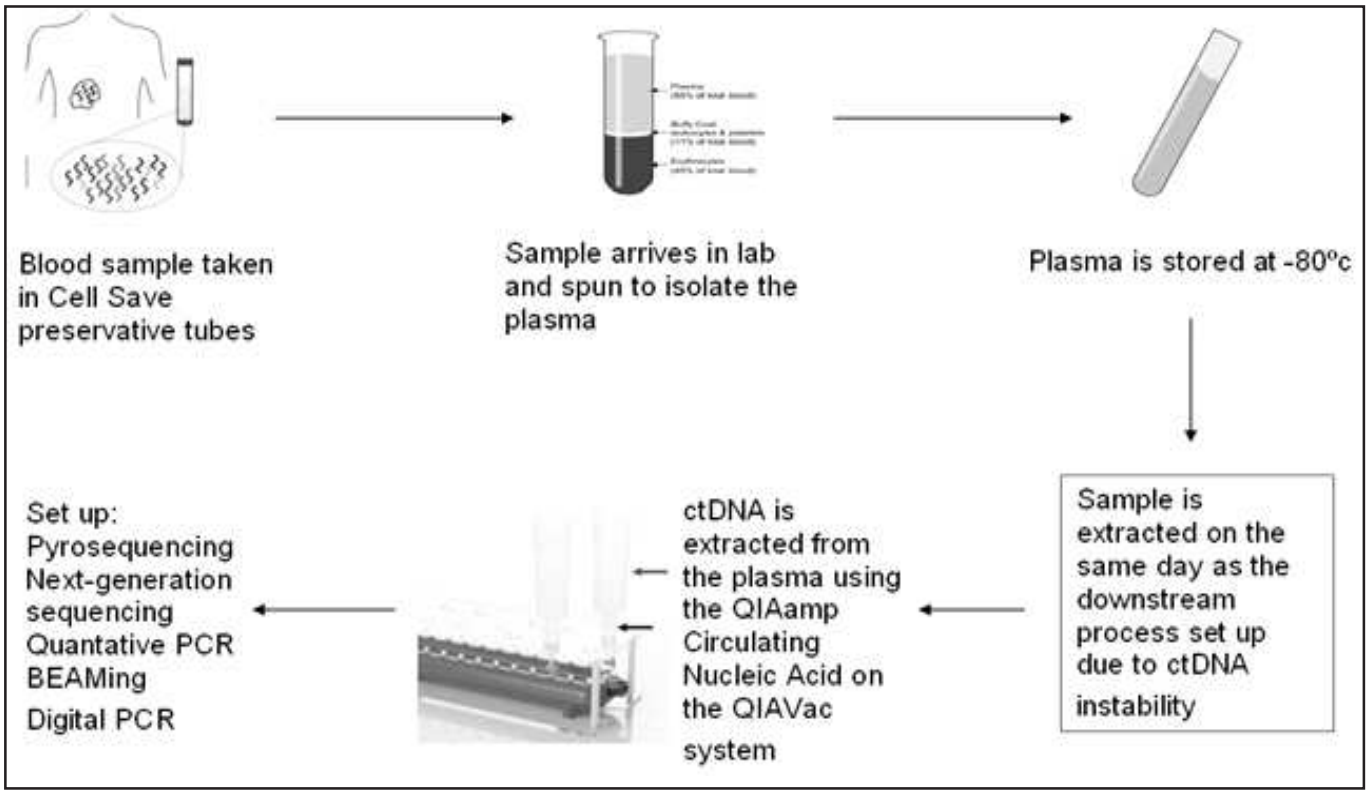

Fig- 1 – Explains how ctDNA sample is collected and processed through various steps. Exosomes **(27)(28)(29)**

Exosomes are nano-sized extracellular vesicles (40–100 nm) released by cells and detectable in most body fluid. First reported in 1983 by Pan and Johnstone while culturing sheep reticulocytes at McGill University. The content of exosomes is dependent on the cell of origin and can be transferred into adjacent or distant recipient cells.

What is the type of sample required for the isolation of Exosomes? (20)(30)

An abundant number of exosomes is released by tumour cells in comparison with non-tumorigenic cells, found in most body fluids, such as blood, serum, urine, cerebral spinal fluid, and even breast milk.

Methods to detect and isolate Exosomes

Two crucial points must be controlled to achieve a good quality in exosomes sample preparations: (1) the appropriate collection/ storage of the body fluid samples and (2) the purity of the isolated exosomes.

Main Techniques for isolation of exosomes (27) (28)(31)

1. Differential centrifugation/ultra-centrifugation with/without a sucrose gradient/cushion;
2. Size exclusion chromatography (SEC) method where a solution of molecules is separated based on the component's size, not molecular weight.

Differential ultracentrifugation is the current gold standard for exosomes isolation

Current utility of LB in cancer (2) (32)

These are some examples where currently LB is used and useful in detecting and monitoring Cancer cells and treatment.

Table No. 3 - Use OF LB in Cancers

Sl. No.	*Cancer Type Genes*
1 Colorectal Cancer	KRAS, BRAF, TP53, APC, CEA, SEPT9
2. Breast Cancer	HER2, BRCA1
3. Lung Cancer	KRAS, EGFR, BRAF, ERBB2, PIK3CA, ALK, ROS1, RET, HER2, MET, TP53, CTNNB1, PTEN, CDKN2A, ARID1A
4. Hepatocellular Cancer	MET, CDK6, EGFR, MYC, BRAF, RAF1, FGFR1, CCNE1, PIK3CA, ERBB2/HER2
5. Gastric Cancer	MUC1, CK19, HER2 TERT, CEA

Table No. 4 - Current Strengths and Limitations of Major Liquid Biopsy Targets(14)

	CTC	**ctDNA**	**EXOSOME**
Detection Principles	1. Label-dependent methods 2. Label-independent methods	1. Targeted approaches 2. Untargeted approaches	1. Immune affinity based methods 2. Biophysical property-based approaches
Chara-cteristics	+Can perform studies on morphology and gene profile+Immune checkpoint markers on CTCs allowing immunotherapeutic studies	+Short half-life +Able to detect genetic mutations	+Short half-life+Can analyze variety of molecular cargo (e. g., miRNA, metabolites) "Lack of standardization for detection and isolation
Biofluid Concentration	Very Low	Variable/Moderate	High
Detection in biofluids	Blood	Blood, Saliva	Blood, Saliva, Urine, Sweat
Sensitivity	Low	Variable	Higher
Specificity	Variable	Moderate	Low

Challenges and Deficiencies in LB- (2)(33)(34)(35)(36)

Liquid biopsy has emerged as a revolutionary technology that is providing new perspectives and dimensions to the field of medical oncology. Liquid biopsy plasma ctDNA has approximately 86 per cent chance of positive detection across all solid tumour types. It is a promising biomarker in advanced/metastasis cancer disease. However, a negative liquid biopsy test result may not indicate an absence of tumour oncogene. So here a tissue biopsy analysis is recommended and is still considered to be the "gold standard" for diagnosis and treatment choice for diseases of genetic involvement such as cancer. However, they are associated with inherent deficiencies such as:

- Limited accessibility of tumour tissue during tissue biopsy increases the chance of false-negative results
- Lack of information regarding spatial and temporal heterogeneity of the tumour.

Is LB technology is far away? (37)(33)(38)(32)

No, it's not far away. Many foreign companies are already in market and plying a pivotal role.

In the Indian scenario, many cancer institutes's are already adopting this technology and using it as a weapon against cancer. The most noted are ACTRECT Tata hospital, Rajiv Gandhi Cancer Institute New Delhi, Apollo Hospital. Roche's has launched their pan India plan for LB in 2016 only. In Pune also, Oncodiscover is an upcoming startup and doing well at affordable charges. The market is very big and it's growing day by day.

Conclusion

LB is at the dawn of a new era of cancer "theranostics", being a non-invasive addition to SB. LB is capable of generating valuable cancer information almost in real-time that can be used to reveal the genetic features of individual tumours, thus improving early detection, prognostication, and monitoring treatment responses and eventual resistance.

Conflict of interest

Author declares no conflict of interest

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Review Article

Use of Laboratory Animals in Biomedical Research

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Abstract :

Virtually every major medical advance of the last century has depended upon research with animals. Animals have served as surrogates in the investigation of human diseases and have yielded valuable data in the process of discovering new ways to treat, cure or prevent them. Animal experimentation is an essential component of biomedical and behavioralresearch. As in the past, investigators are using animals to learn about the most widespread diseases of the age, including heart disease and cancer, as well as to gain basic knowledge in genetics, physiology, and other life sciences. Animals are also needed to combat new diseases, of which acquired immune deficiency syndrome (AIDS) is currently the most prominent example. At the same time, behavioral researchers are drawing on animal studies to learn more about such major causes of human suffering as mental illness, drug addiction, etc. use of animals in biomedical and behavioral research has greatly increased scientific knowledge and has had enormous benefits for human health.

Introduction :

The use of animals in biomedical research has been recommended for perfecting and validating existing procedures(1-4) developing new materials (5-7)and understanding the various physiological and pathological processes (8-10)because there are no in vitro models capable of fully mimicking the complexity of the human organism. Animals are biologically similar to humans. In fact, mice share more than 98% DNA with us. Animals are susceptible many of the same health problems as humans- cancer, diabetes, heart diseases etc. with a shorter life cycle than humans, animal models can be studied throughout their whole life span

and across several generations, a critical element in understanding how a disease processes and how it interacts with a whole, living biological system (11). Small Laboratory animals such as Mice, Rats, Rabbits, guinea pigs etc have long been used as models to improve our understanding of several human maladies. The primary goal of developing animal models for research is to create an experimental system in which the conditions occurring in humans are phenocopied as accurately as possible in the laboratory animal (12). Various animals are used in medical research.

Rodents play an invaluable role in biomedical research. Approximately 95% of the laboratory animals are mice and rats[11]. Reducing reliance on higher – order species, rodents have become the animal model of choice for biomedical researchers because their physiology and genetic makeup closely resembles that of human. Despite certain differences between the rodents and humans, the similarities are strong enough to give researchers an enormously powerful and versatile mammalian system in which to investigate human diseases.

Mice

Mice have been used as research subjects for studies ranging from biology to psychology to engineering. They are used to model Human diseases for the purpose of finding treatments or cures. Some of the disease model includes; hypertension, diabetes, cataracts, obesity, seizures, respiratory problems, deafness, Parkinson's disease, Alzheimer's disease, various cancers, cystic fibrosis and AIDS, heart diseases, muscular dystrophy and spinal cord injuries. They are used in behavioral, sensory, aging, nutrition and genetic studies. (13)

Rat

Rats have prevalence within biomedical research second only to humans and they share 90% of the genome with humans. Almost all disease-linked human genes we currently know of have equivalent genes within the rat genome, making them a suitable research tool. The rat has allowed us to build up an incredible wealth of knowledge about basic biology and complex physiological interactions, and has served as a model of human disease and learning, much of which has been translated to greater knowledge about humans.

The rat has allowed us to build up an incredible wealth of knowledge about basic biology and complex physiological interactions, and has served as a model of human disease and learning, much of which has been translated to greater knowledge about humans.

Well-established strains of rat are used to study a number of human diseases such as:

- obesity and diabetes
- cancer
- cardiovascular disease (including high blood pressure and heart failure)
- neurological diseases (such as Parkinson's disease)
- Inflammatory and immune mediated diseases (such as certain types of kidney disease and multiple sclerosis). (14)

G. Pigs

Guinea pigs have been used as experimental animals for centuries; hence 'guinea pig' for a human experimental subject. Guinea pigs have contributed to 23 Nobel prizes for medicine with studies leading to the discovery of Vitamin C, the tuberculosis bacterium, and adrenaline, as well as the development of vaccines for diphtheria and tuberculosis, replacement heart valves, blood transfusion, kidney dialysis, antibiotics, anticoagulants and asthma medicines. Today, guinea pigs are still widely used in medical research, particularly in the study of respiratory, nervous and immune systems.

The four main areas that guinea pigs are used

in research today are(15):

- Allergies and respiratory diseases
- Nutritional research
- Hearing
- Safety testing

Rabbits

The rabbit was the first animal model used in several immunological studies and was crucial, for example for the development of rabies vaccine by Louis Pasteur in 1881(16).

The rabbit is actively used as a laboratory model for several non - infectious conditions, including atherosclerosis (17, 18), intestinal immunity(19), reproduction (20), lupus (21), arthritis (22), cancer(23) and Alzheimer's disease. (24) Rabbits are also carriers or reservoirs of several pathogens that can cause zoonotic diseases. (12)

The rabbit has also been increasingly used during the last two decades as a reliable animal model for many infectious diseases of viral, bacterial and parasitic origin. (12)

Rabbits are commonly used for toxicity and safety testing of substances such as drugs, chemicals and medical devices. They are used in skin and eye irritation studies

Hamsters

They are readily available, reproduce easily and are relatively free of spontaneous diseases yet susceptible to many induced viral disease. They are used for studies of obesity, induced carcinogenesis, prostatic diseases, toxicity, infectious diseases, dental caries, chronic bronchitis, teratogenesis. (25)

Gerbil

These rodents are larger than mice but smaller than rats. They have been used as experimental models in a number of areas of biomedical research. They are excellent subjects for laboratory animal research as they are susceptible to bacterial, viral and parasitic pathogens that affect humans. They have unique characteristics which make them appropriate for a number of animal models. Classically gerbils have been used in research involving stroke, parasitology, infectious diseases, epilepsy, brain developmentand behaviour and hearing. (26)

Cats

Although there has been a steady decline in absolute numbers in research since 1980, cats are still important models in neurosciences, cardiovascular studies, consequences of aging, and certain inherited diseases and in the study of infectious diseases. (27)

Dogs

Used for studies related to cardiology, endocrinology, orthopedics, prosthetic devices, surgical techniques, pharmacokinetics and product safety. They also play an important role in many studies related to cosmetic (as they have very sensitive skin). (28)

Fish

The most important aquatic species used in research are the zebra fish. 70% of human genes are found in Zebra. They have two eyes, a mouth, brain, spinal cord, intestine, pancreas, liver, bile ducts, kidney, esophagus, heart, ear, nose, muscle, blood, bone, cartilage and teeth. Many of the genes and critical pathways that are required to grow these features are highly conserved between humans and zebrafish. Thus, any type of disease that causes changes in these body parts in humans could theoretically be modeled in zebrafish(28). As they have all the main organs involved in the process of metabolism they can be used to studyseveral human metabolic disorders such as nonalcoholic fatty liver disease, type 2 diabetes mellitus, dyslipidemia and other hepatic diseases. (29)They are moreover well suited for embryonic studies because of their relatively transparent body

during the larval development stage.

Some interesting facts (29)

- Rodents do not vomit as they lack vomiting center.
- Rats do not have tonsils or a gall bladder; they are particularly suitable for the study of physiology of liver since following partial hepatectomy as the organ regenerates almost completely in a course of a week.
- A 24 hour rat is said to be physiologically similar to a 6 month old infant!
- Guinea pigs having sensitive cochlea are suitable for hearing experiments.
- Guinea pig is the only laboratory animal that requires exogenous Vitamin C; it is used in the study of Ascorbic acid metabolism.
- Hamsters have a cheek pouch makes the animal model for research in the field of Immunology. The pouch can be pulled under anesthesia and can be observed. The pouch in the everted position can be used as a site for the implantation of auto, homo, or hetero grafts.

Figure 1 - Animal in Published Research

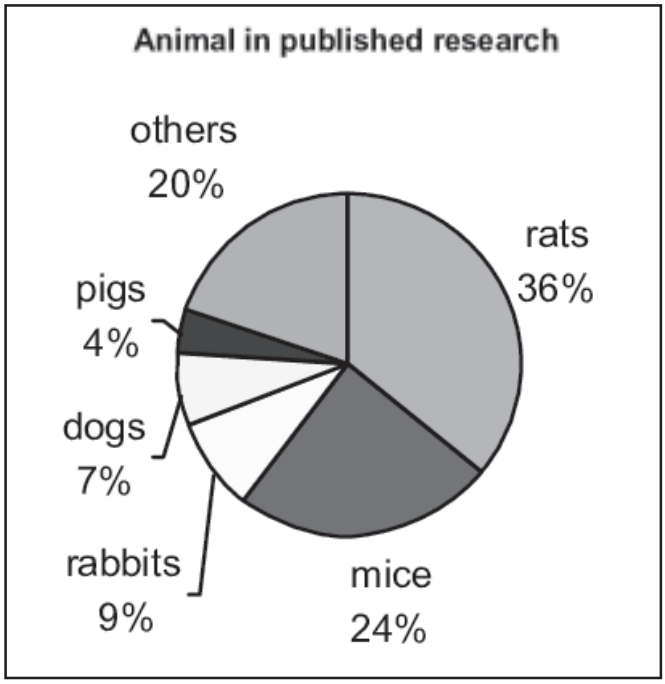
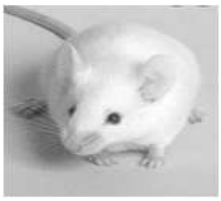
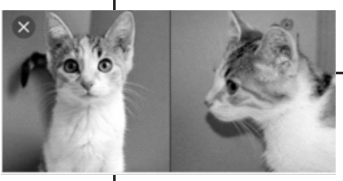


Table 1 – Biological and Physiological Data of Common Laboratory Animals (29)

PARAMETER	MICE	RAT	GUNIEA PIG	RABBIT	HAMSTER	
					GOLDEN	CHINESE
Typical Adult weight (g)	20-40	250	800	1500-5000	80-90	35-40
Average life span (years)	1. 5-2. 5	2-3	3-5	4-6	2-3	2-3
Average age suitable for experiment (months)	0. 75	1. 5	3	6	1	1
Breeding habits (1 male to number of females)	3	5	6	1	1	1
Average litter size	6-12	8-10	3-4	6-8	5-7	4-5
Number of litters per year	8-10	6	4	4	-	7
Heart rate	330-780	300-500	260-400	130-300	318-412	-
Blood volume (% B. W.)	7-9	6-7	6-12	4-8	6-9	-

Table: 2 At a glance (30)

SPECIES	USE IN BIOMEDICAL RESEARCH	IMAGE
MICE	Acute Toxicity Studies, Teratogenicity Studies, Cancer, diabetes, ageing, atherosclerosis, immunological disease, autoimmune disorders, neurological disorders, endocrine diseases	
RAT	Behavior, Pharmacology, Physiology, Neurosciences Immunogenetics, transplantation Cancer risk assessment, Cardiovascular diseases and ageing	
GUINEA PIG	Diagnostic tests, enteric Amoebiasis, Hypersensitivity, immune response, anaphylactic shock, encephalomyelitis, tuberculosis and Ascorbic acid metabolism	
RABBIT	Pyrogen testing, toxic effects of cosmetics, Production of Antibodies and antiserums	
	Field of stroke, epilepsy, auditory studies parasite and bacterial infections, lipid metabolism and heart diseases.	
HAMSTERS	Good model for Physiology, pathogenesis of Duchene's dystrophy, Tissue implants – tumors / grafts, in vitro and in vivo diagnostic techniques	
CAT	Behavioral studies, cardiovascular studies, nerve impulse transmission, neurophamacology, Chromosomal abnormality studies.	
DOG	Cardiovascular research, diabetes mellitus, ulcerative colitis, open heart surgery, organ transplantation, CNS, safety pharmacology and toxicology.	



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Case Report

COVID 19 with Myocardial Ischemia

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Abstract

Covid 19 is inflammatory state which may present with cardiovascular consequences such as new onset angina, myocardial infarction or worsening of previously existing disease . Patients with acute infection are known to have increased inflammatory, prothrombotic and procoagulant responses. Myocardial injury can happen irrespective of nature of elevation of inflammatory markers and it is associated with very high risk of arrythmias and death, hence very high suspicion is required during and after covid course of patient and proactive monitoring is required for cardiovascular complications.

Introduction

Covid 19 Infected patients have varied presenting symptoms like chest pain, palpitation, breathlessness are some of them, which can lead to serious cardiac event. Being watchful for symptoms as well as regular investigations such as ECG, cardiac enzymes, 2D ECHO, NT pro BNP can be helpful in early diagnosis and better treatment. There are several reasons for these condition such as cytokine storm related inflammatory changes, SARS–COVattachment to Angiotensin converting enzyme 2 receptors, inflammatory damage to endothelium ofblood vessels, reduced oxygen drive leading heart muscle damage. (1)Another Postulate was covid virus inhabitancy and replication in cardiac myocytes lead to viral myocarditis which further caused cardiac dysfunction. (2) Regular ECG monitoring and Follow-up is necessary in patients recovered from covid.

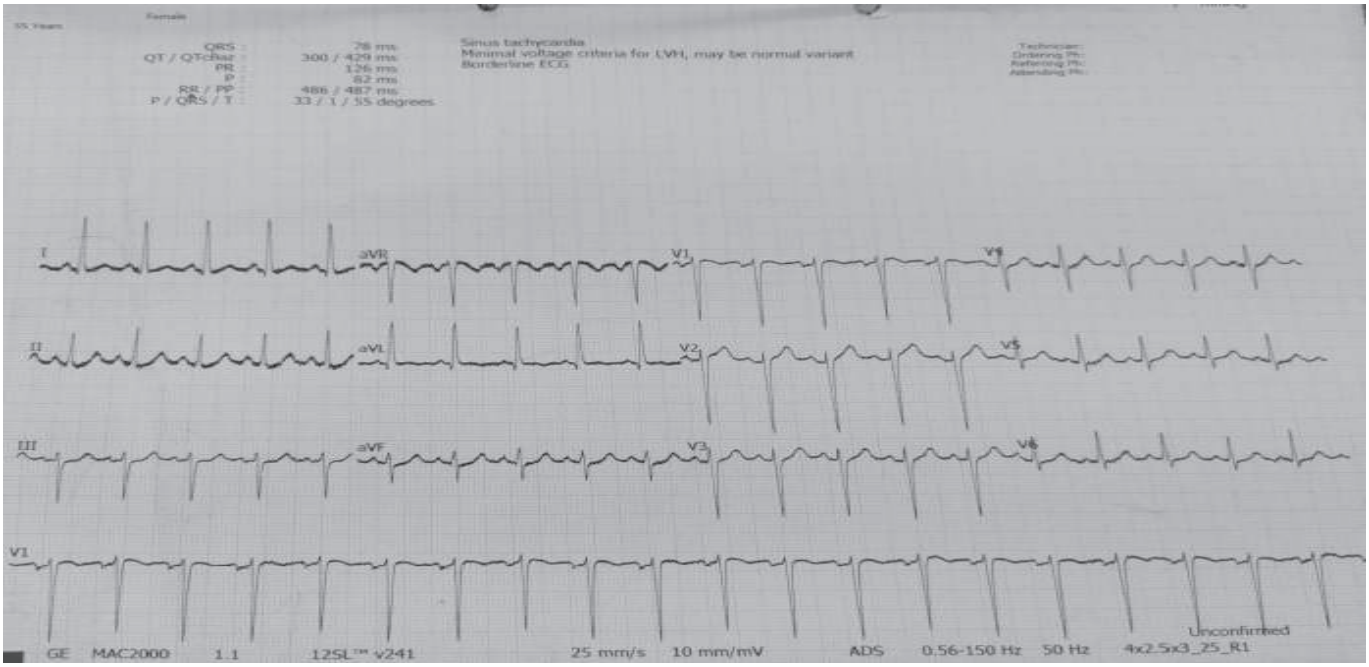
We present known case of covid 19 who developed ECG changes during hospitalization.

Case Report

55 year old Female patient with Covid 19 Pneumonia (RTPCR covid test confirmed 17 days ago prior to admission) with comorbidities of Diabetes Mellitus and Hypertension was admitted to our hospital with complaints of severe breathlessness at rest associated with cough and generalized weakness. Patient had already received 6 doses of injection Remdesvir and 1 dose of bevacizumab. At time of admission patient had no history of chest pain, palpitation, recent fever, cold etc. On clinical examination, Pulse 116/minute normal volume regular rhythm without radio-radial delay, Blood pressure was 140/90 mm of mercury taken onright brachial artery in supine position, respiratory rate 26 cycles / minute abdominothoracic breathing with use of accessory muscles of respiration, oxygen saturation was 95% with Non Re-Breather Mask at 15 L/Minute. Patient was started on symptomatic treatment along with injectable anticoagulant and steroids. Investigations were done which are

Parameter (Reference range)	Observed Value	Parameter (Reference range)	Observed Value	Parameter (Reference range)	Observed Value
HB (12-15 gm/dl)	13. 7	Total Bilirubin (0. 2 - 1. 3 mg/dl)	0. 8	Cholesterol (150-200mg/dl)	262
WBC ($4000-11000/mm^3$)	11720	Direct Bilirubin (0 - 0. 6 mg/dl)	0. 2	Triglycerides (50-150 mg/dl)	495
Platelet ($1. 5-4. 5lac/mm^3$)	3, 36, 000	SGOT (14-59 U/L)	18	HDL (40-60 mg/dl)	36
N/L Ratio	8. 5	SGPT (0-35 U/L)	24	Serum calcium (8. 4-10 mg/dl)	8. 1
PT (Seconds) / INR	17. 9/1. 3	ALP (38 -126 U/L)	127	Serum Protein (6. 3-8. 2 gm/dl)	5. 9
D Dimer (0 – 0. 5 ug/ml)	0. 70	HbA1c (< 5. 7 %)	8. 9	Serum Albumin (3. 5-5 gm/dl)	3. 2
CRP (<10 mg/l)	40. 2				
Ferritin (11. 1- 264 ng/ml)	511	Urea (15-43 mg/dl)	19	ABG	
		Creatinine (0. 5-1. 3mg/dl)	0. 4	pH	7. 43
CPK MB (3-16 IU/L)	16–>30	Sodium (137-145mmol/L)	138	pCO2	42. 1
CPK total (30-170 IU/L)	29–>60	Potassium (3. 5-5. 1mmol/L)	4. 6	pO2	69. 7
Serum LDH (120-246 U/L)	320–>446	Chloride (98-107mmol/L)	94	HCO3	28. 6

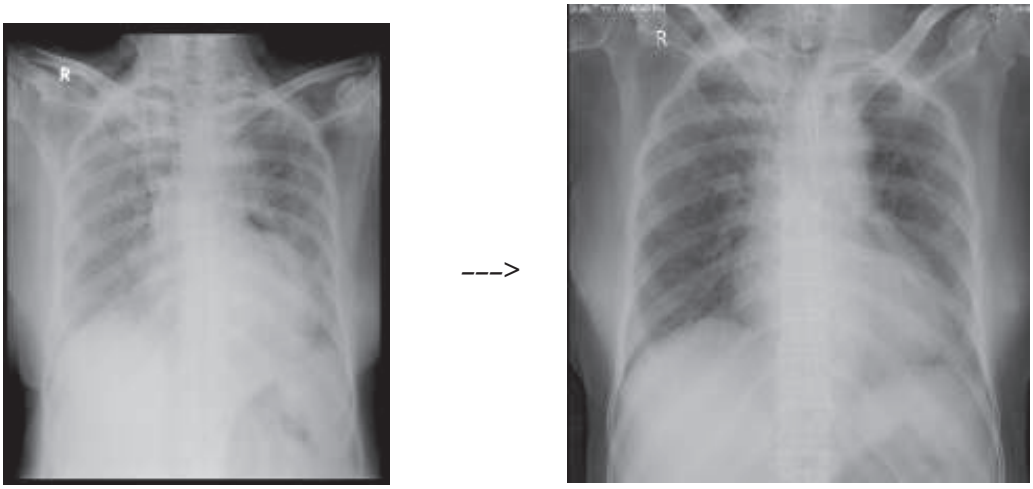
Figure 1. ECG (on admission)



ECG (on admission) Suggestive of sinus tachycardia with regular rhytm with Left Axis deviation

Baseline 2D ECHO was suggestive of anterior wall akinesia with ejection fraction of 35%, Grade 1 diastolic dysfunctoon, mild tricuspid regurgitation and mild pulmonary hypertension

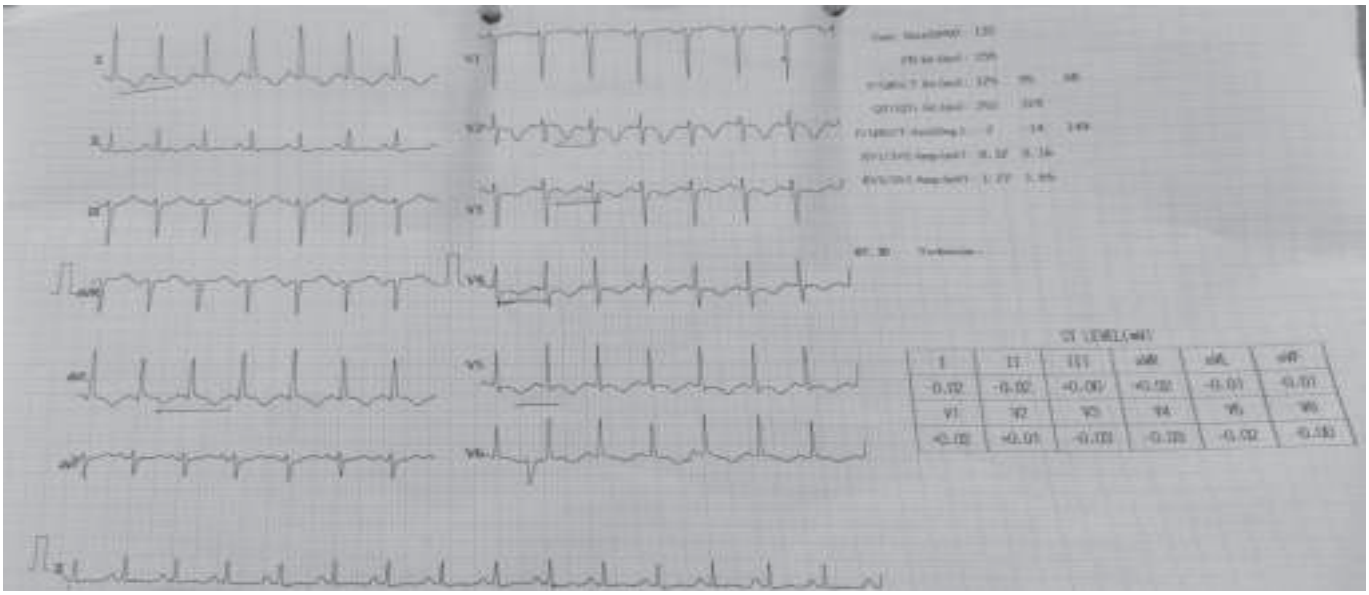
Figure 2 – CXR



CXR – Suggestive of right side midzone and lowerzone and left side lower zone haziness suggestive pneumonitis

On Day 3 of admission, Patient had desaturation with breathlessness and profuse sweating and was put on Non Invasive ventilator, maintaining 96 % oxygen saturation without any chest pain or pedal oedema. Covid Awake repositioning protocol was started. Serial ECG monitoring was done.

Figure 3. ECG



ECG suggestive of sinus tachycardia with regular rhythm with T wave inversion in Lead I, aVL and chest leads V1-V6 Suggestive of Extensive ischemic changes in Anterolateral wall with poor R wave progression

Cardiac enzymes CPK MB was elevated (30IU/L) with repeat 2D ECHO suggestive of Ejection Fraction 25% with Global Left Ventricular hypokinesia with mildly dilated Left ventricle and Mild Pulmonary Hypertension

Patient was planned for coronary angiography after cardiology consultation ; but couldn't be evaluated further as patient was requiring Non invasive ventilation. LMWH (low molecular weight heparin) therapy which was already started, was continued along with aspirin. No further events were noted.

Discussion

Patients with Covid Infection or those recovered from covid may have persistent symptoms such as palpitation, dyspnoea and chest pain and long term complications of myocarditis, myocardial fibrosis or scarring, arrhythmias. There is increased cardiometabolic demand, increased incidences of thromboembolic events due to hypercoagulability which may lead to myocardial infarction. Hence it's very important to consider possible cardiac complication during covid stay of patient and frequent ECG monitoring should be done. Echocardiography plays significant role in identifying abnormalities and cardiac dysfunction leading heart failure with or without reduced ejection fraction.

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Case Report

Esophageal Traction Diverticulum as a result of tuberculous lympadenitis

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Abstract

An esophageal traction diverticulum is a relatively rare disorder of the esophagus which is usually asymptomatic but some patients may present with symptoms of regurgitation or dysphagia. In this case report the patient presented with dysphagia and a CT scan of the thorax revealed a necrotic mass in the superior mediastinum and an esophageal outpouching communicating with the mass[15]. Upper gastrointestinal endoscopy was done which revealed a necrotic lesion 20cms from incisor teeth. Biopsy taken from the necrotic lesion was suggestive of tuberculous inflammation. Patient was managed conservatively with Anti-Tuberculosis Treatment (ATT) prescribed for a period of 6months.

Follow up endoscopy after six months revealed significant reduction in the size of diverticulum.

Keywords

Dysphagia; traction diverticulum ; Uppergastrointestinal endoscopy

Case Report

A 33yr old female, was admitted with complaints of :

Difficulty in swallowing since one month, chest pain on and off since 15 days, fever, and sore throat since 15days.

She was evaluated for pyrexia of unknown origin and received treatment for 15 days after which she was advised USG(Neck).

USG (Neck) was suggestive of mildly enlarged lymph nodes on the right side of neck, level III and level IV, largest node measured 9x11mm. Following this CT scan was done, showing findings of a well defined soft tissue density lesion in the right paratracheal region in the superior mediastinum also extending into the right subcarinal region in the posterior mediastinum .

At this level there is a focal outpouching of esophagus within this necrotic nodal mass . Subcentimeter lymph nodes were observed in pretracheal, paratracheal, precarinal, subcarinal and bilateral axillary regions.

Barium swallow did not show any esophageal diverticulum.

Upper GI scopy was suggestive of a necrotic lesion 20cms from incisors . Biopsy of the necrotic lesion was taken and sent for Histopathology which was suggestive of tuberculous inflammation. Gene expert showed tubercle bacilli.

She received Anti tubercular treatment for 6months . OGD scopy done after 6months was suggestive of significant reduction in size of diverticulum, the patient was also completely asymptomatic after Anti tubercular treatment.

Discussion

Esophageal diverticula are rare findings that have an estimated incidence of 1:500, 000 per year and a prevalence of 0. 015–2%.

Esopageal diverticulum can be categorized on the basis of origin and formation. Based on origin they can be divided into true and false diverticula. True diverticula are outpouchings that include all layers of the esophageal wall while false diverticula only include the mucosa or submucosa. [21], [22].

By formation they can be divided into three types : pulsion, traction or a mixed variety (which is a combination of both types). Pulsion diverticula are created when there is increased intraluminal pressure causing herniation of the esophageal wall in an area of weakness [21]. Most traction diverticuli arise within 4-5cm proximal to the carina and are associated with granulomatous disease of sub carinal lymph nodes. The inflamed nodes become anchored to the esophagus and the contracting scar tissue tents up the esophageal wall to form an outpouching[23].

Clinical, radiological and endoscopic features of traction diverticulum are not well defined because of its rarity and also its close resemblance with other symptomatic esophageal disorders like Zenkers diverticulum and Pulsion diverticulum. Most of the patients with traction diverticulum have non-specific findings on chest radiograph, however computed tomography of the chest shows characteristic tuberculous lymphadenitis and usually a focal out pouching of the esophagus communicating with a mediastinal mass[15], [3]. Majority of traction diverticulums are incidental findings on endoscopy[23].

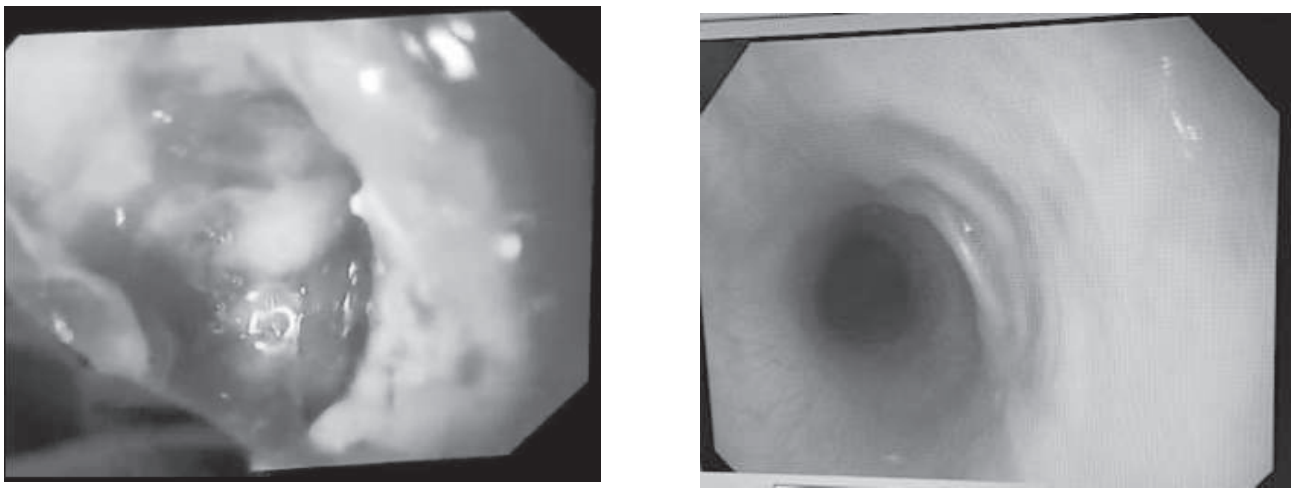
Histopathology and TB-PCR are the mainstay investigations for confirming the diagnosis [4]. Studies show PCR sensitivities ranging from 77% to more than 95% and PCR specificities of >95% for smear-positive specimens [10], [11], [12] .

Most of the patients respond well with ATT [4] and require surgery only in cases of fistulas, strictures, and perforations.

In our patient Anti tubercular treatment was initiated for 6 months with four drugs i. e. Isoniazid, Rifampicin, Pyrizinamide and Ethambutol. After ATT a significant reduction was observed in size of diverticulum on OGD scopy and on CT thorax there was no evidence of necrotic lesion in the superior mediastinum but presence of pre and para aortic sub centimetric lymph nodes. The patient was symptomatically better and was advised 3more months of Anti tubercular treatment.

it can be managed conservatively with Anti Tubercular Treatment and complications like fistula, stricture, and esophageal perforation, which might warrant surgery can be prevented.

Fig. 1



(a) (b)

Fig 1 (a) Necrotic lesion with inflamed surrounding esophageal mucosa
(b) Reduction in size of diverticulum after AKT

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Case Report

Asynchronous Mode in Management of a Patient with Permanent Pacemaker posted for Hip Arthroplasty

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Abstract:

Cardiac patients with permanent pacemaker (PPM) in situ are frequently seen posted for various non-cardiac surgeries. We report a case of 75 years old man posted for right hemiarthroplasty with permanent pacemaker in situ with Dual chamber paced, Dual chamber sensed and Dual response to sensing mode (DDD). Intra-operatively we needed to change the mode of pacemaker to avoid electromagnetic interference (EMI) induced pacemaker malfunction as monopolar cautery was used. However, because of careful management the outcome was favourable.

Key words:

Arrhythmia, Cautery, Electromagnetic interference, Permanent Pacemaker

Introduction:

Number of cardiac patients are increasingly seen in anaesthesia practice and give challenging goals to anaesthesiologists due to higher risk of perioperative morbidity and mortality. Pacemakers are one of the most reliable and definitive treatment modalities for both conduction and arrhythmia problems particularly in elderly.

In United states more than 3 million[1] patients have pacemakers while a recent survey in India showed that 37, 000 cardiac device implantation takes place annually and 80 % of these are due to bradycardia related PPMinsertions. [2] As the

number of PPMinsertions are increasing patients posted for cardiac or non-cardiac surgeries are also increasing.

Case Report:

A 75 years old male of 68 kg had history off all 3 days back while walking on road with no history of loss of consciousness, ear, nose and throat bleed or vomiting. Patient was diagnosed with right neck of femur fracture and was posted for Right Bipolar Hemiarthroplasty.

Patient is a known case of hypertension since 12 years. Initially patient was on Tablet Losartan 50 mg once in a day. He had history of syncope attacks two to three times around 10 years back. He was investigated and diagnosed to have Sick Sinus Syndrome. PPM implantation was done in 2010 under local anaesthesia and sedation without any perioperative events. He was asymptomatic after the insertion with regular follow ups. Pacemaker's battery was replaced in July, 2020. Routine working assessment and battery life check-up of pace maker done in November, 2020 showing normal working of device and battery life of 16 years.

Figure 1 : PPM device identity card with DDD Mode

Patient was currently on Tablet Cilnidipine 10 mg once in a day and Tablet Aspirin 75 mg at night. At present no history of dyspnoea on exertion, palpitations, syncope, cough, cold, fever or chest pain.

On General examination patient was afebrile with pulse 68 beats per minute, regular, bilaterally equal, no radio femoral delay. All peripheral pulses present. Oxygen saturation was 98 % on room air with blood pressure 138 / 84 mmHg and respiratory rate 14 breaths per min. Airway examination was showing adequate mouth opening with Mallampatti Classification grade I. Spine examination was within normal limits. Cardio respiratory system was normal.

All routine investigations were done, which were within normal limit with Haemoglobin 14. 3 g/dl, Platelets 1. 15 lakhs. Coagulation profile was within normal limit. Blood grouping and cross matching done.

Figure 2: Pre-op ECG

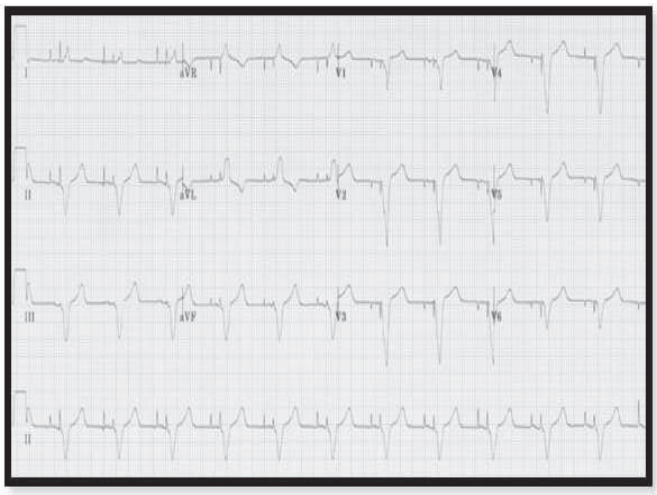

Figure 2 showing 12 lead electrocardiogram with atrial and ventricular pacing spikes.

Figure 3: Chest X-ray

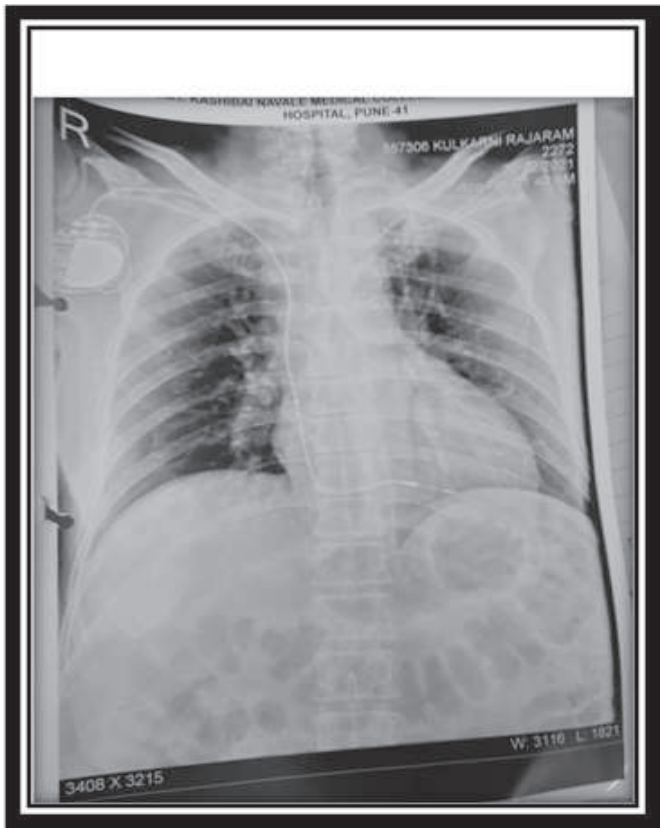

Figure 3 showing Chest X-ray Antero Posterior view of the patient with PPM device in situ situated at right axillary area with continuity of lead.

2D Echo suggestive of Left Ventricular Ejection Fraction of60 %, Grade I Diastolic Dysfunction and degenerative aortic valve changes. Cardiologist's opinion was taken, fitness given with moderate cardiac risk.

Goals

- To minimise electromagnetic interference.
- To maintain haemodynamic.
- Perioperative analgesia.
- To ensure battery of pacemaker device and availability of pacemaker technician for any technical assistance peri-operatively.

Plan of Anaesthesia

Subarachnoid Block + Epidural Anaesthesia

Anaesthesia Management

1. Pre-operative Preparation

A pre-anaesthetic assessment of permanent pacemaker type, its functioning and patient's dependency on it was done. Routine operation theatre was prepared. Emergency cardiac drugs, crash cart and defibrillator kept ready. The pacemaker magnet and trained personnel was made available in operating room beforehand. Written informed high risk consent was obtained. Nil by mouth hours, Surgical Intensive Care Unit bed, adequate blood and blood products availability were confirmed. Two large bore intravenous access were secured and surgeons advised to use bipolar cautery only.

2. Inside operation theatre

All multipara monitors including electrocardiogram, pulse oximeter and non-invasive blood pressure were attached and Ringer Lactate started. Under all aseptic precautions, Fascia Iliaca Compartment Block given with Inj. Lignocaine 2% 10 ml and Inj. Bupivacaine 0. 25 % 10 ml after negative aspiration. After the block, patient was given position for Epidural

Anaesthesia and Subarachnoid Block. Under all aseptic precautions, Epidural catheter inserted in between second and third intervertebral lumbar space and fixed at 9 cm from the skin. Under all aseptic precautions, subarachnoid block given in third and fourth intervertebral lumbar space with Inj. Bupivacaine 0. 5 % 3 cc and Inj. Fentanyl 25 mcg 0. 5 ml. T8 dermatome level of anaesthesia achieved. After 10 minutes of spinal anaesthesia, left lateral position for surgery given.

Initially surgeon used bipolar cautery but then due to surgical field requirement surgeon needed to use monopolar cautery. To avoid EMI induced PPM failure we changed the mode of pacemaker to asynchronous ventricular pacing mode (VOO) by placing magnet over the pace maker with the help of pacemaker technician. Also the electrodispersive pad placed near the site of surgery and away from pacemaker to prevent the intersection of pacemaker by the current used in monopolar cautery.

After changing the mode of pace maker to VOO ECG changes were visible showing asynchronous pacing which are shown in figure 4.

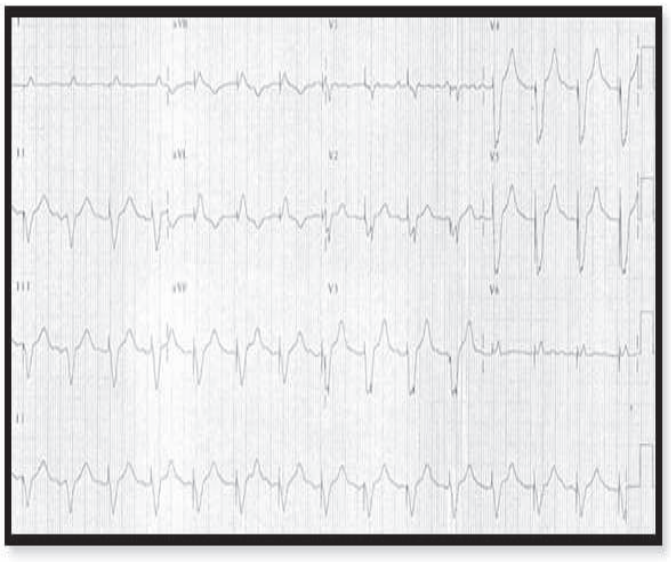

Figure 4: Intra-op ECG with VOO mode

Procedure underwent uneventfully. There was no episode of any EMI, hypotension, brady-arrthymias, tachyarrthymias, asystole or cardiac arrest. Patient was stable haemo-dynamically peri-operatively with blood loss of 400 ml which was replaced with 1000 ml Crystalloid and 500 ml colloid and urine output was 300 ml.

3. Post-op

Patient shifted to Surgical Intensive Care Unit for observation and started with epidural infusion of Inj. Ropivacaine 0. 2 % titrated according to the patient's need. After 24 hours again pacemaker's mode was changed to original DDD mode and monitored carefully for next 24 hours. Epidural catheter removed on post operative day 3, shifted to ward on post operative day 4 and discharged on post operative day7.

Discussion:

PPMs have changed significantly from the first implant, from asynchronous single chamber to rate responsive dual or multi chamber devices. Also initially they were using mercury iodide and nickel cadmium batteries which are replaced with lithium batteries increasing their life from 2. 5 years to 15 years. [1]PPMs have evolved in terms of battery endurance, software and programming, better performance, implantation technique and size making them patient friendly.

It is essential to ensure the possibility of EMI exposure during surgery. EMI source is derived either from electro cautery or diathermy. The possible of effects of electro cautery include inhibition of pacing, asynchronous pacing, device deactivation rarely myocardial burns and ventricular fibrillation. For PPM patients, it is highly recommended to use bipolar cautery as the current used in it is small and energy travels between the two poles of pen or stylus. Whereas in monopolar cautery, electrical current flow is not restricted increasing the risk of current flow to intersect pacemaker device and to cause its malfunction. [3]

However, bipolar cautery is usually used in microsurgeries and it is capable of coagulation whereas monopolar cautery may be used for dissection and coagulation, which is why it is more commonly used. If at all monopolar cautery is to be used in such cases, it should be used in short bursts of several seconds and the grounding plate should be placed as close to the operating site and as far as possible from the pacemaker. Electro cautery induced pacemaker failure has also been reported during asynchronous mode causing haemodynamic instability, which can cause severe hypotension, Brady / tachy arrhythmias or even asystole or cardiac arrest. Nercessian O A et al[4] reported a case report of intraoperative dysfunction of pacemaker caused by the use of electro cautery during total hip arthroplasty. Abdelmalak et al[5] came across with EMI in a cardiac pacemaker during cauterization with the coagulating, not cutting mode of the surgical cautery. To deal with such possible outcomes of pacemaker failure and haemodynamic instability, vasoactive agents, crash cart and pads for external defibrillation were kept ready before induction. Also the use of intra-operative diathermy should be kept as minimum as possible.

In cases of general anaesthesia, Succinyl choline, Etomidate and Ketamine should be avoided as they can cause fasciculation or myoclonus interrupting the pacemaker function. Intraoperative use of Nitrous oxide can also lead to PPM dysfunction due to its possible infiltration around PPM implantation, which can lead to accidental removal of leads from pacing generator. [6, 7]

Central neuraxial blockade is the first choice for patients with PPM. Low dose spinal anaesthesia can be given to reduce the effect of hypotension. Maintenance of normothermia is also important as muscle activity due to shivering can also interrupt pacemaker functioning.

Here, our patient was having dual chamber pacemaker in situ and current ECG was showing atrial and ventricular pacing spikes in between. So we decided to proceed with the current mode DDD along with availability of trained personnel in case of any emergency. Intra-operatively surgeon needed to use monopolar cautery so we changed the mode to VOO to avoid EMI induced pacemaker malfunction as dual-chamber pacemakers are known to be more susceptible to EMI than single-chamber pacemakers. [8]When pacemaker was taken on asynchronous mode by using a magnet[9, 10] it paced at a fixed rate without any sensing capability. It is not intrinsic with patient's intrinsic rhythm and it will pace at a fixed rhythm regardless of patient's intrinsic rhythm. There are high chances of Ventricular arrhythmias. So, cardiac drugs like Amiodarone were kept ready. But in our case after changing the mode, patient's pacemaker was functioning properly without any nuisance though there was ongoing use of monopolar cautery. Patient was haemo-dynamically stable throughout.

Once the patient with PPM comes for any surgery it is not that his arrhythmias are taken care of permanently. Thorough understanding of cardiac physiology and functioning of various modes of pacemaker with complete and utmost vigilance is necessary to manage such patient. The multidisciplinary approach, vigilant monitoring are necessary for better post-op outcomes.

Conclusion:

Patients with PPM need special attention in perioperative anaesthesia management, particularly in terms of patient's clinical condition, PPM performance with respect to EMI. It is better to avoid intra-operative use of monopolar cautery. Availability of trained technician is must inside operation theatre. Changing of mode can be decided as per the requirements intra-operatively. Re-evaluation of PPM is necessary before shifting the patient to ward.

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Case Report

A Rare Case Report of Paroxysmal Nocturnal Hemoglobinuria Presenting with Aplastic Anemia

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Abstract

Intoduction: Paroxysmal nocturnal hemoglobinuria(PNH) is an aquired hemolytic anemia characterized by a triad of intravascular hemolysis, pancytopenia and tendancy for thrombosis. Several episodes of intravascular hemolysis result in hemoglobinuria associated with thrombosis at unusual sites and these patients may have bone marrow failure. PNH presents with variable presentation, including classical PNH and PNH with aplastic anemia. Diagnosis can be confirmed by flow cytometry. In some cases, bone marrow studies show hypercellular marrow and in other we see a severely aplastic bone marrow with clinical features of PNH. Management is supportive with blood transfusion, danazol therapy and treatment of thrombosis. With evolution of treatment strategies, hemopoitic stem cell transplantation and complement inhibition with Eculizumab have been shown to be very effective.

Case report: Herein we report a young male who presented with yellowish discolouration of eyes, passage of red coloured urine, passage of blood in stools, pain in abdomen associated with generalised weakness. On examination, hepatospleenomegaly was present along with pancytopenia and evidence of intravascular hemolysis. With these clinical and laboratory findings, we suspected paroxysmal nocturnal hemglobinuria which was later confirmed by flow cytometry and bone marrow studies.

Conclusion: In this case report, a young male who presented to us with jaundice, abdominal pain, hematuria, pancytopenia and history of similar episodes in the past was found to have aquired hemolytic anemia with renal dysfunction and bone marrow failure. Our case report suggests that when a young patient presents with coomb's negative hemolytic anemia, one must suspect PNH. PNH with aplastic anemia is a uniformly fatal

disease if left untreated. Short course of androgenic synthetic steroids is helpful in the treatment when the patient is not affordable for the definitive treatment.

Key words :

Aplastic anemia, paroxysmal nocturnal hemoglobinuria, pancytopenia, danazol

Introduction

Paroxysmal nocturnal hemoglobinuria (PNH) is an acquired hemopoietic disorder which is a rarity in occurrence. Available reports suggest that the incidence of clinically significant disease is in the range of 1 to 10 cases per million population and it is chiefly a disease of adults and the peak age of onset is in third decade. Though PNH is caused by mutation of a PIG-A gene on X chromosome it affects males and females equal. This disease is classified under acquired hemolytic anemia presenting with clinical features of unexplained hemolytic anemia like fatigue, jaundice and red colored urine. Thrombosis involves venous rather than arterial system. On bone marrow studies, it is observed that there is decreased cellularity in almost all AA-PNH patients, whereas increased overall cellularity in the majority of classic PNH patients. Accurate diagnosis is important as effective therapies have become available. This has become very much possible because diagnostic testing has evolved significantly due to the better understanding of the molecular basis of the disease and eventually the pathogenesis of hemolysis in PNH. We present a 27 years old male with combination of symptoms and signs that made us to diagnose this rare disorder and also we have discussed the management of this patient.

Case Report

A 27-year-old male presented with complaints of yellowish discolouration of eyes since 5 days; passage of red coloured urine, blood in stools, abdominal pain and generalised weakness for 2 days. Patient was referred from an outside practitioner with blood investigations suggestive of thrombocytopenia with derranged liver function tests and urine analysis suggestive of hematuria. History of jaundice was present 4 months ago for which he received ayurvedic treatment and 2 pint PCV. There was no history of similar complaints in the family members. As they were unable to pin point the crux of the problem, patient was referred to our institution in view of persistent jaundice, malena and hematuria. On examination he was afebrile, pulse rate 84/ min, blood pressure 118/ 76 mmHg, marked pallor and icterus [Figure 1] was present. Cardiovascular, respiratory and CNS examination were normal. On per abdomen examination, diffuse tenderness was present with Grade 1 hepatomegaly and grade 2 spleenomegaly. Initial laboratory tests (Table 1) revealed pancytopenia, raised LDH, elevated bilirubin along with raised SGOT, negative direct and indirect coombs test and raised serum creatinine. Peripheral blood smear was suggestive of anisopoikilocytosis with raised MCV. As PBS was inconclusive of the possible type of anemia, serum iron, TIBC and serum vitamin B12 levels were done, which were within normal limits. Urine analysis was suggestive of 8-10 RBCs, amorphous material, hemoglobinuria and hemosiderinuria. At this point of time, we came to a conclusion that our patient had intravascular hemolysis, with raised LDH and pancytopenia. These features made us to suspect PNH. 24 hours urine sample collection showed reddish brown colour throughout[Figure-2]. Ultrasonography (USG) of abdomen and pelvis was normal. Hence, two criterias were fulfilled out of the triad of PNH. Prussian blue test on urine for Hemosiderin was positive. We did Ham's acid serum test as a

screening test for PNH which came to be positive. In order to confirm the same, flow cytometry was performed using gating antibodies CD45, CD33, CD235a and GPI linked antibodies CD59, CD157 as well as fluorescent aerolysin (FLAER) which was suggestive of PNH clones identified of WBCs (Monocytes-80. 5% and Granulocytes-90. 3% i. e, CD157 deficiency) and RBCs (Type 3-18. 1% i. e, complete CD59 deficiency and Type 2-2. 4% i. e, Partial CD59 deficiency). With the clinical features and a positive flow cytometry, final diagnosis of paroxysmal nocturnal hemoglobinuria was made. Bone marrow aspiration and biopsy was done to rule out bone marrow failure. Dry tap was obtained with biopsy suggestive of possibility of aplastic anemia. Hematologist opinion was sought and patient was started on Cap. Danazole 200 mg twice a day, Tab. Prednisolone 20 mg once a day for 4 weeks along with vit. B12 and Folic acid supplement. He was also given three units of packed cell transfusions. As a definitive therapy, patient was advised bone marrow transplantation and furthur workup regarding the same. As he was not affording the same, we could not proceed further. Patient's complete blood count improved by then and passage of normal colored urine was observed 7 days after starting the treatment [Figure-3]. He was discharged with the treatment to be continued as advised by the hematologist. On subsequent follow-up patient was asymtomatic and hemogram showed well preserved hemoglobin, leukocyte and platelet counts. When patient has been followed up for almost 8months, we found that he had persistent pancytopenia, without hematuria, malena, renal dysfunction or features suggestive of thrombosis.

Table 1 : Outside Reports

Hemoglobin	5.5 g/dl
Total leucocyte count	3600
Platelets	1.2L/mm^3
Total protein	7.0
Albumin	3.9
Globulin	3.1
Total bilirubin	6.7
Direct	1.4
SGOT	120
SGPT	320
ALP	110
Urine analysis	
Proteins	+
RBCs	25-30
Bile salts, pigments	absent
Casts	absent

Table 2 : Laboratory investigations on admission

Hemoglobin	4.3g/dl
Total leucocyte count	3090
Platelets	90000
MCV	104.8fl
MCHC	31.2g/dl
PBS	Anisocytosis++, predominently, Macrocytes+ microcytic with hypochromic+few tear drop cells, few pencil cells, schistocytes, spherocytes Lecopenia,no hypersegmented neutrophils
Coomb's test	Negative
Serum creatinine	2.2
Total bilirubin	6.5mg%
Direct bilirubin	0.7mg%
SGOT	568 IU/L
SGPT	47 IU/L
Alkaline phosphatase	28 IU/L
Retic count	3.12
Serum LDH	5092 U
PT/INR	14.4/1.2
Urine analysis	Protein 2+, RBCs-8-10, casts ++, hemoglobinuria+ hemosiderinuria+
Pruccian blue test on urine	positive
Bone marrow studies	hypocellular marrow S/O Aplastic anemia

Figure 1-demonstration of icterus

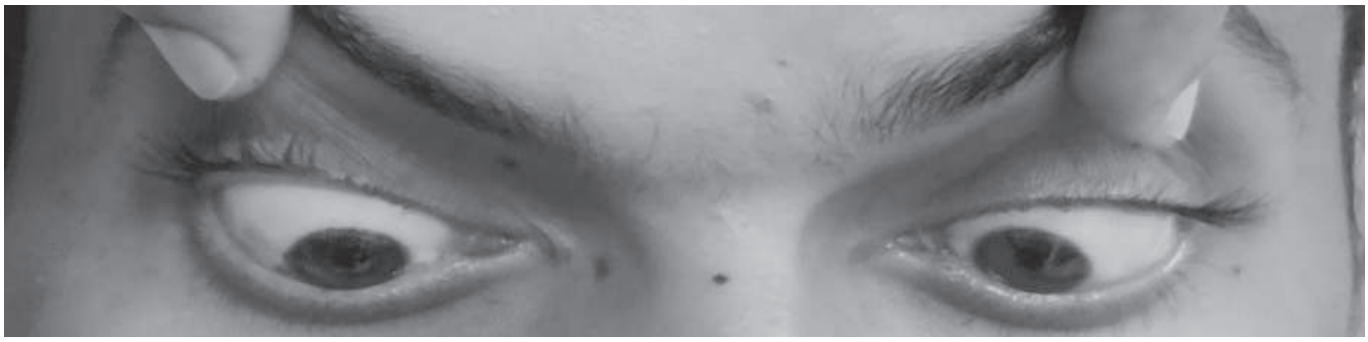

Figure 2 - 24 hours Urine sample collection

Figure 3 - No Evidence of hematuria 7 days after starting the treatment

Discussion

We report a young male who presented with hematuria, jaundice, abdominal pain and malena with history of similar episodes in the past was found to have pancytopenia and evidence of intravascular hemolysis. Diagnosis as PNH was suspected by clinical features, laboratory investigations and confirmed by flow cytometry. In PNH there is complement induced lysis of RBCs due to the abnormal sensitivity of RBC cell membrane. This is due to an acquired defect in the gene for phosphatidylinositol class A (PIG A) thereby causing deficiency of glycosylphosphatidylinositol (GPI) which is sheet anchor for cell membrane proteins [1]. CD55 and CD59, complement regulatory proteins which block intravascular and extravascular hemolysis respectively in normal human, are deficient in PNH [2]. Hemolysis occurs in PNH because these patient's RBCs lack GPI anchor which is required to attach CD55(decay accelerating factor[DAF]) and CD59(membrane inhibitor of reactive lysis[MIRL]) to the surface of RBC [2]. This permits unregulated formation of certain complement attack complex which damages RBC membrane resulting in intravascular hemolysis. This causes reduction in hemoglobin and hemoglobinuria with resultant increase in LDH [1]. The clinical features of PNH result from high levels of complement-mediated lysis of PNH clones as well as the intravascular release of hemoglobin[1]. The latter

is associated with kidney dysfunction and depletion of nitric oxide, which plays a role in smooth muscle function. PNH is broadly characterized by hemolytic anemia, thrombosis, and bone marrow hypocellularity. Patient symptoms may include fatigue, shortness of breath, bruising or bleeding, headaches, chest or abdominal pain, pulmonary hypertension, erectile dysfunction, and bouts of dark urine. Thrombosis is the leading cause of death in patients with PNH [2]. The pathogenesis is hypothesized to be due to free hemoglobin resulting from hemolysis attracts nitric oxide which induces vasoconstriction and damages the vascular endothelium forming a nidus for thrombus formation. Also platelets release procoagulant particles during complement induced hemolysis, which facilitate thrombosis. Thromboses involve the venous rather than the arterial system [2]. Minority of patients develop pancytopenia due to bone marrow disorders like aplastic anemia or primary myelofibrosis. PNH is classified into classic PNH (presence of hemolysis with no marrow abnormality), PNH with marrow disorders(aplastic anemia/myelodysplastic syndrome (MDS)/primary myelofibrosis (PMF) and subclinical PNH–without clinical evidence [3]. Aplastic anemia arises from bone marrow failure that encompasses all 3 blood cell lineages, leading to peripheral pancytopenia and marrow hypoplasia. The disease presents most commonly in people between the ages of 15 and 25 years, with a second, smaller peak of incidence after 60 years of age. [4] In older patients, aplastic anemia tends to be associated with more severe symptoms. The relationship between PNH and aplastic anemia has been proposed to arise from partially overlapping etiologies. [5] Aplastic anemia arises from a T-cell–mediated autoimmune attack against hematopoietic stem cells. The attack may be directed specifically at the GPI anchor, as well as other molecules. PNH arises from the same autoimmunity in combination with the PIG-A mutation, whereas the PIG-A mutation alone leads to subclinical effects. Because of the underlying autoimmunity, immunosuppressive therapy is effective for treatment of both conditions. It is important to test for PNH in patients with aplastic anemia, not only to establish the presence of PNH clones, but also because the presence of PNH cells is associated with a superior response to immunotherapy. For patients with PNH clones and aplastic anemia, it is important to monitor levels of PNH cells every 6 months to provide early evidence of clonal expansion. Expansion of the PNH clone may be accompanied by intravascular hemolysis. Persistent intravascular hemolysis causes anemia, hemoglobinuria, and other complications. Breakdown of the red blood cells commonly occurs during the night, with ongoing concentration of the urine leading to dark, cola-colored urine in the morning. The diagnosis of PNH can be suspected when we come across cases of coombs negative hemolytic anemia or confusing cases of pancytopenia. The established therapies for patients with classical PNH are allogeneic hematopoietic cell transplantation (HCT) and complement inhibition with eculizumab [3]. Patients with hemolysis are better managed with danazol and eculizumab [6]. Patients with thrombosis are managed with therapeutic anticoagulation and eculizumab. Most of the patients will not be able to access this therapy due to its high cost. Allogeneic HCT is advised for patients with severe cytopenias, patients with poor response to eculizumab or when not accessible to eculizumab [3]. Supportive therapy includes red blood cell (RBC) transfusions, supplemental iron and folic acid (1 to 2 mg daily). Our patient had features of PNH with bone marrow failure i. e. pancytopenia, hemolysis and aplastic anemia. Renal dysfunction was evident from passage of cola coloured urine not only in the morning but throughout the day for several days with raised serum creatinine level. We learn that it is difficult

to diagnose this disease unless we have a high index of suspicion. We present this case due to its rarity and the management when both bone marrow transplant and eculizumab were not feasible.

CONCLUSION

In this case report, a young male who presented to us with jaundice, abdominal pain, hematuria, pancytopenia and history of similar episodes in the past was found to have aquired hemolytic anemia with renal dysfunction and bone marrow failure. Our case report suggests that when a young patient presents with coomb's negative hemolytic anemia, one must suspect PNH. PNH with aplastic anemia is a uniformly fatal disease if left untreated. Short course of androgenic synthetic steroids is helpful in the treatment when the patient is not affordable for the definitive treatment.

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Case Report

Solid Pseudopapillary Tumor of the Pancreas 'Frantz tumor'

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Abstract

Solid pseudopapillary neoplasms(SPN) of the pancreas are rare neoplasms accounting for 1-2% of all pancreatic tumors and have a female predominance. We report a case of SPN involving the head and neck of the pancreas. A 19-year-old female patient presented with complaints of pain in abdomen and menstrual irregularities, 6 months ago. She was evaluated in peripheral hospital for same complaints. USG suggestive of Pancreatic mass. To confirm contrast enhanced Computed Tomography (CT) scan of the abdomen done showed a mass measuring 4. 7cm × 4. 5cm ×3. 7cm, arising from the pancreas with an enhancing cystic component suggestive of SPN. SPN are rare entity of a controversial origin but is considered as a low-grade malignancy. Surgical resection to achieve complete excision constitutes the mainstay of treatment, which mostly results in an excellent prognosis. Even with metastasis and vascular invasion, surgical excision is the treatment of choice. So the decision taken for exploratorylaparotomy, whichrevealedamassoccupying head andneck of pancreas. Thus, weproceededwith a whippleprocedure. The SPNdiagnosis was confirmed by histopathology. The pathophysiology behind thedevelopment of SPN and its cellular origin is still a matter of debate with multiple proposed hypotheses. Rare extrapancreatice SPN cases are reported in subhepatic region, ovary and testis.

Keywords

Pseudopapillary; neoplasms; Frantz; pancreas; case report; pancreatectomy.

Introduction

Solid pseudopapillary neoplasms(SPN) of the pancreas, also known as 'Frantz tumor' attributed to Virginia K. Frantz, who was the first to describe it in the 1950s. It's official nomenclature done by the World Health Organization (WHO) in 1996 (1, 2). It was recognized by the WHO as a low-grade epithelial malignant neoplasm in 2010 (1, 2). It was reported to have an incidence of 1–2% of all pancreatic tumors (Benign and malignant) with a favorable prognosis after surgical excision (3). SPNs are usually presented in young adult females, with a female to male ratio of 11 to 1; nevertheless, a small percentage occurs in the pediatric age group (4-6). The tumor location tends to be in the neck or tail of the pancreas in 60% of the cases, while the remaining are located in the head of the pancreas (1, 6, 7). Even though SPNs are labeled as low malignant tumors, there have been multiple reports of metastasis (6, 8, 9), with an estimated incidence reaching up to 10% of the cases (1, 2).

Case presentation

A 19-year-old female patient having pain in abdomen. She was referred to our institute after she presented to outside hospital complaining of menstrual irregularities, which was started 6 months ago. She denied any history of vomiting, change in bowel habits, weight loss, night sweats, pruritis and scleral or urinary discoloration. Surgical and family history of pancreatic diseases were negative. An ultrasound was performed in the referring facility and showed a heterogeneously hypoechoic irregular mass that is originating from the proximal pancreas. A contrast-enhanced CT scan of the abdomen (Figure 1) showed a mass measuring 4. 7 cm × 4. 5 cm × 3. 7 cm, arising from the pancreas with an enhancing cystic component. These findings confirmed on MRCP before proceeding to surgery and showed the same findings.

In our hospital, her abdominal examination showed: a soft, non-tender abdomen with a palpable mass occupying umbilical region. All of her hematological and biochemistry investigations done, were within normal limits. Tumor markers such as CEA and CA 19. 9 were normal.

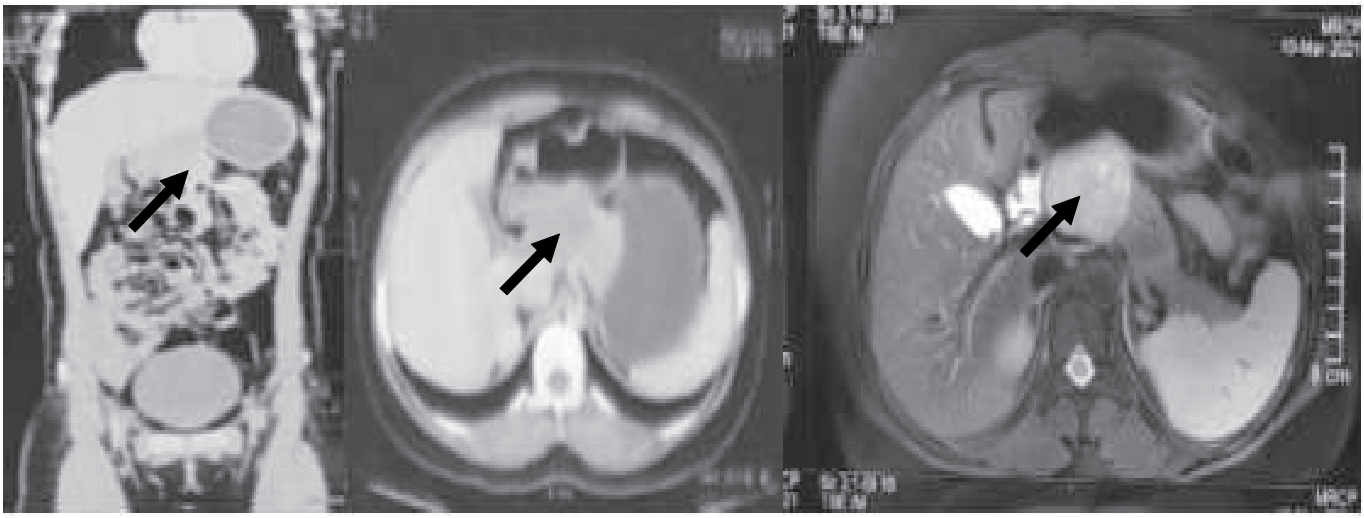

Figure 1 :

A CECT scans of the abdomen showing a large, well-defined and heterogeneous tumor measuring 4. 7 cm × 4. 5 cm × 3. 7 cm, arising from the pancreas with an enhancing cystic component.

With all the radiological findings and to achieve complete resection, the decision to perform whipple procedure was made. Cardiopulmonary status and pulmonary function test was done prior surgery and within normal limits. The patient underwent exploratory laparotomy, which revealed a mass occupying head and neck of the pancreas. Subsequently, we proceeded with a whipple procedure. The gross examination of the mass revealed an encapsulated, heterogeneous mass with both cystic and solid components involving the pancreatic head and neck with no local invasion to the adjacent organs. (Figure 2).

Histopathological examination of the surgical specimen (H&E staining) demonstrated a pseudopapillary architecture (Figure 3). The diagnosis of a solid pseudopapillary tumor was confirmed with negative resection margins.

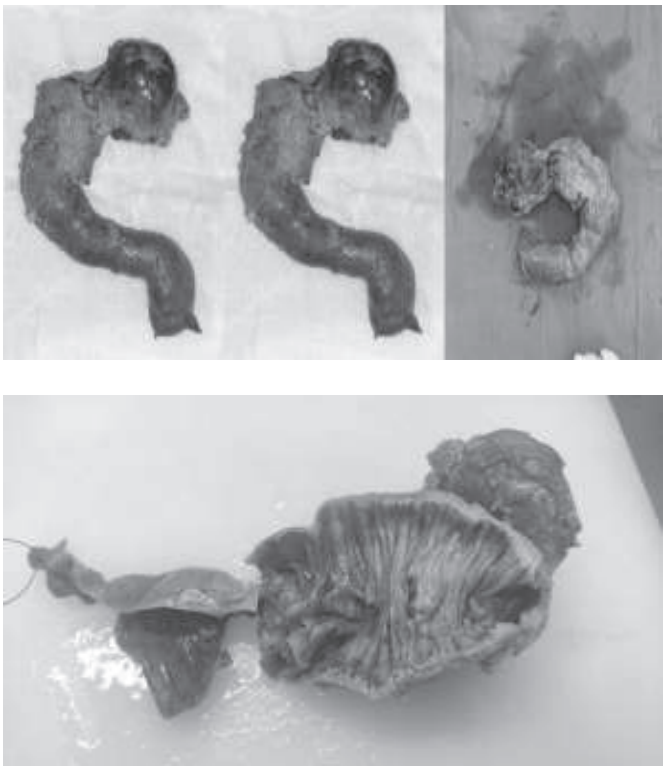

Figure 2.

Gross examination of the resected mass showing an encapsulated, heterogeneous mass with both cystic and solid components.

Discussion

SPNs account for a small percentage of all pancreatic tumors (Benign and Malignant) ranging from 0. 17% to 2. 7% (7). The pathophysiology behind the development of SPN and its cellular origin is still a matter of debate with multiple proposed hypotheses in the literature (5, 10, 11).

A hypothesis attributes the development of SPNs to different genetic mutations, and the most studied is the nuclear expression of b-catenin and vimentin secondary to genetic mutation and the interference with the Wnt signaling pathway, which has been reported to be present in up to 90% of these tumors (5, 6). The role of other genetic mutations like the p53 gene and k-ras has been studied, but no evidence of their involvement was found (5, 6).

Although, 70% of all cases are symptomatic, SPNs are discovered incidentally in 30% of the cases (17). Once the tumor grows and becomes large enough to cause pressure symptoms to the adjacent organs. Most patients complain of abdominal pain, followed by an increase in abdominal girth (1, 17). That was evident in our case as the patient had an on-and-off abdominal pain for 6 months.

Even though SPNs are slow-growing tumors with a low Ki-67 index, several case reports have shown different growth rates in terms of doubling time starting from 240 to 765 days (11-13). This wide range suggests that although these are collectively slow-growing neoplasms; however, the growth rate varies significantly (12).

One of the rare presentations of SPNs is tumor rupture that is commonly seen after blunt abdominal trauma, which has been reported to represent 8% of the cases (14). Interestingly, Xu et al. reported a spontaneous rupture of SPN in a 22 years old female who presented to the Emergency Department (ED) complaining of abdominal pain associated with leukocytosis and hemoglobin drop secondary to spontaneous SPN rupture and bleeding (14).

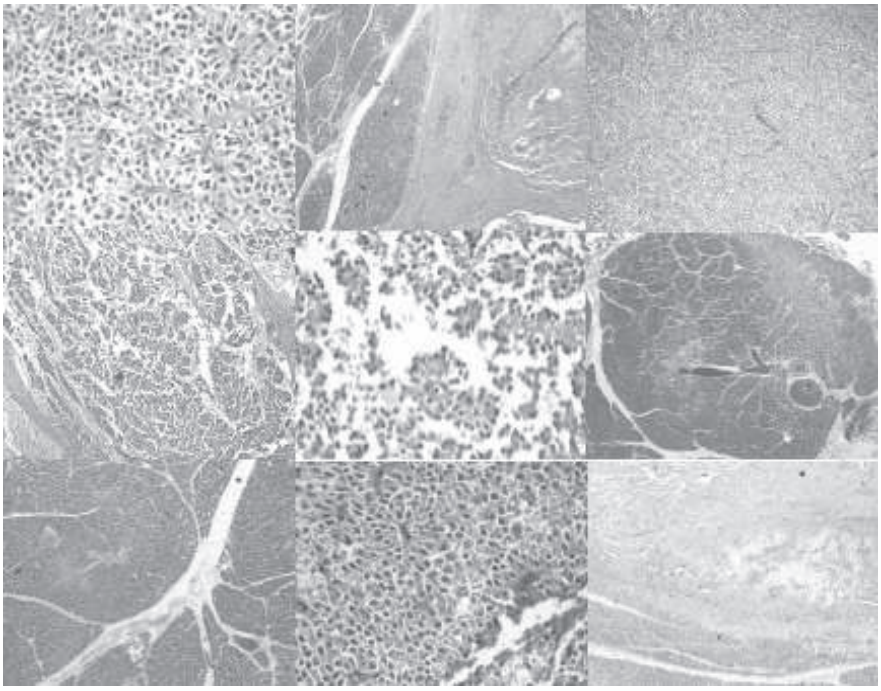

Figure 3.
Histopathological examination of the surgical specimen (×20). Demonstrating a pseudopapillary architecture.

The suggested theory of spontaneous rupture is that the cystic part of the SPN undergoes internal degeneration with a subsequent hemorrhage; consequently, if the bleeding was significant enough, it can lead to increased intramural pressure causing the spontaneous rupture (14). The pre-operative diagnosis of SPNs remains a clinical challenge despite all the current advances in diagnostic modalities (9). This is due to the overlap with a wide range of differential diagnoses such as benign cystic lesions, including pseudocysts, hydatid cysts, cystadenoma, lymphangioma, and hemangioma; as well as, different malignant lesions such as; cystadenocarcinoma or intraductal papillary mucinous neoplasms (5, 7). When it comes to the pediatric age group, pancreatic tumors of secondary origin like neuroblastoma, leukemia, lymphoma, and lymphoproliferative disorders are more common (5).

Tumor markers like alfa fetoprotein, carcinoembryonic antigen, CA19. 9, CA125, and CA242 might be elevated, but they are not specific for SPNs (6). Nevertheless, these tumor markers and pancreatic tumor markers should be considered during the work-up as other malignant tumors are still part of the differential diagnosis of SPNs (9).

Imaging wise, abdominal CT scan with intravenous contrast has been reported to be the best imaging modality because it provides not only the origin, size and layout of the tumor but also the presence of local invasion and metastasis (5). As SPNs have a mix of both solid and cystic components, areas of enhancing and non-enhancing lesions are seen and are surrounded by a capsule along with intratumoral calcifications (5). Furthermore, hemorrhage may result due to the growth of the tumor and subsequent internal degeneration (14). The presence of an encapsulated mass consisting of both cystic and solid components and intratumoral hemorrhage are useful factors to distinguish SPNs from its other malignant differentials (5, 10, 14). With the presence of these pathognomonic features of SPNs, a CT scan is considered adequate to establish the pre- operative diagnosis (15, 16).

On the other hand, Magnetic Resonance Imaging (MRI), is considered as a second-line imaging modality as it can demonstrate further information with regards to hemorrhage and necrosis of the tumor's tissue (15, 16). Typically,

SPNs would show a vascular, encapsulated mass composed of both mixed cystic and solid components with a high-signal intensity on T1 and low signal intensity on T2 series representing hemorrhagic areas on MRI (14). Dan et al. have highlighted that MRI was not necessary in their reported cases of SPNs located in the tail of the pancreas, where a CT scan was able to demonstrate the pathognomonic features of SPN (15, 16).

A pre-operative histopathologic diagnosis could be achieved by endoscopic ultrasound (EUS) biopsy (17). Still, its use has the downside of seeding of tumor cells into the peritoneum or the gastric wall, which has been reported in multiple cases of pancreatic adenocarcinoma (7, 17). Yamaguchi et al. have reported the seeding of SPN cells into the gastric wall with a subsequent tumor formation secondary to EUS biopsy 67 months after the procedure (18).

Hanada et al. conducted a nationwide, multicentric, retrospective, and questionnaire-based survey study across Japan to assess the clinic-pathological features of SPNs (18). The study included 288 patients who were diagnosed with SPN between January 1990 and March 2015 (18). They have evaluated the capability of using a single imaging modality to establish a pre-operative diagnosis, which ranged between 50% to 70%. Additionally, the detection of the cystic component was higher on both MRI and EUS compared to CT scan, while the detection of calcifications on CT scan and EUS was of similar rate (18). Hence, the recommendation was to use a combination of imaging modalities in order to establish a pre-operative diagnosis (18).

Surgical management with free surgical resection margins is the mainstay of treatment even with metastasis and vascular invasion, surgical excision should be performed whenever feasible (9). Radical lymphadenectomy is not indicated in these cases (5). The recurrence rate after surgical resection has been reported to be 3–9% (10). Regardless, patients should be promptly followed up due to the risk of potential recurrence or emergence of metastatic lesions (13). Even in case of recurrence or metastasis, surgery remains the treatment of choice. However, in unresectable lesions, surgical debulking might be justified (7, 9).

There are two types of resection, depending on the location of the tumor. When it is located in the neck or tail of the pancreas, distal pancreatectomy with or without splenic preservation should be performed (5). On the other hand, whipple procedure is performed if the tumor is located in the head of the pancreas (5). The surgical resection must be performed with caution to avoid rupture or spillage of the tumor content, which can result in the seeding of the tumor cells into the peritoneum (8, 18). Due to the encapsulation and low malignant potential of SPNs, it has been advocated to perform the surgical management as conservatively as possible (5).

Even though SPN has a low malignant potential, local invasion and metastasis have been reported (10). Moreover, major sites affected were the liver and peritoneal cavity (10, 14). Nevertheless, the outcome is encouraging, as long-term survival in patients with liver metastasis showed better chances when an excisional resection was performed (5). In addition to the radiosensitivity characteristic of SPN, chemotherapy with metastatic liver lesions seems to have a valuable role (5). However, both modalities are still under scrutiny and only considered as an alternative in the case of surgical contraindications (5, 13). Besides, extrapancreatic SPNs coexisted in 0. 62% of reported cases, and are frequently seen with either testicular or ovarian origin (6).

Although SPN grows largely with features of invasion, nearly all patients who received complete surgical excision have demonstrated an excellent

chance for long-term survival (5). The prognosis of SPN limited to the pancreas is generally excellent, with over 95% cure rate following complete surgical resection (5). Furthermore, local invasion and metastasis are not considered contraindications for surgical resection, and even patients with unresectable tumors can survive for more than ten years post-surgical debulking (5, 10).

Conclusions

SPN is a rare entity of a controversial origin but is considered to be of a low-grade malignancy and a favourable prognosis. It shows strong female predominance with unspecified presentation. Imaging modalities aid to differentiate this entity from other malignancies; however, postoperative histopathological examination and immuno-histochemistry remain the primary diagnostic tools. Surgical resection to achieve complete excision constitutes the mainstay of treatment and mostly results in an excellent prognosis. The survival benefit of repeated surgical resection for recurrence is encouraging.

Acknowledgments

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Ethical Statement :

The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee(s) and with the Helsinki Declaration (as revised in 2013). Written informed consent was obtained for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of the journal on request.

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Case Report

Anesthesia management in a case of dilated cardiomyopathy with chronic obstructive restrictive lung disease posted for total abdominal hysterectomy

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Abstract

The anaesthetic management of a patient with dilated cardiomyopathy (DCM) associated with lung disease undergoing elective non-cardiac surgery poses a challenge for anaesthesiologist due to ventricular enlargement, poor systolic and diastolic dysfunction hypokinesia, risk of Chronic Cardiac Failure, malignant arrhythmias and sudden cardiac death. Here we are presenting a case of 43 year old female having multiple uterine fibroids in a dilated cardiomyopathy with ejection fraction of 25-30%, moderate pulmonary hypertension and mixed obstructive restrictive lung disease posted for total abdominal hysterectomy. We managed the case successfully under segmentalEpidural anaesthesia.

Keywords

Dilated cardiomyopathy; Epidural anaesthesia; Obstructive restrictive lung disease; total abdominal hysterectomy

Background

Dilated cardiomyopathy (DCM) is a primary myocardial disease which reduces global myocardial contractility, leading to left ventricular (LV) or biventricular dysfunction. DCM presents with decrease in LV ejection fraction (LVEF), congestive heart failure (CHF) and ventricular

arrhythmias. [1]A maximum number of cases are idiopathic and known causes may be ischemia, valve dysfunction and viral infection. [2]

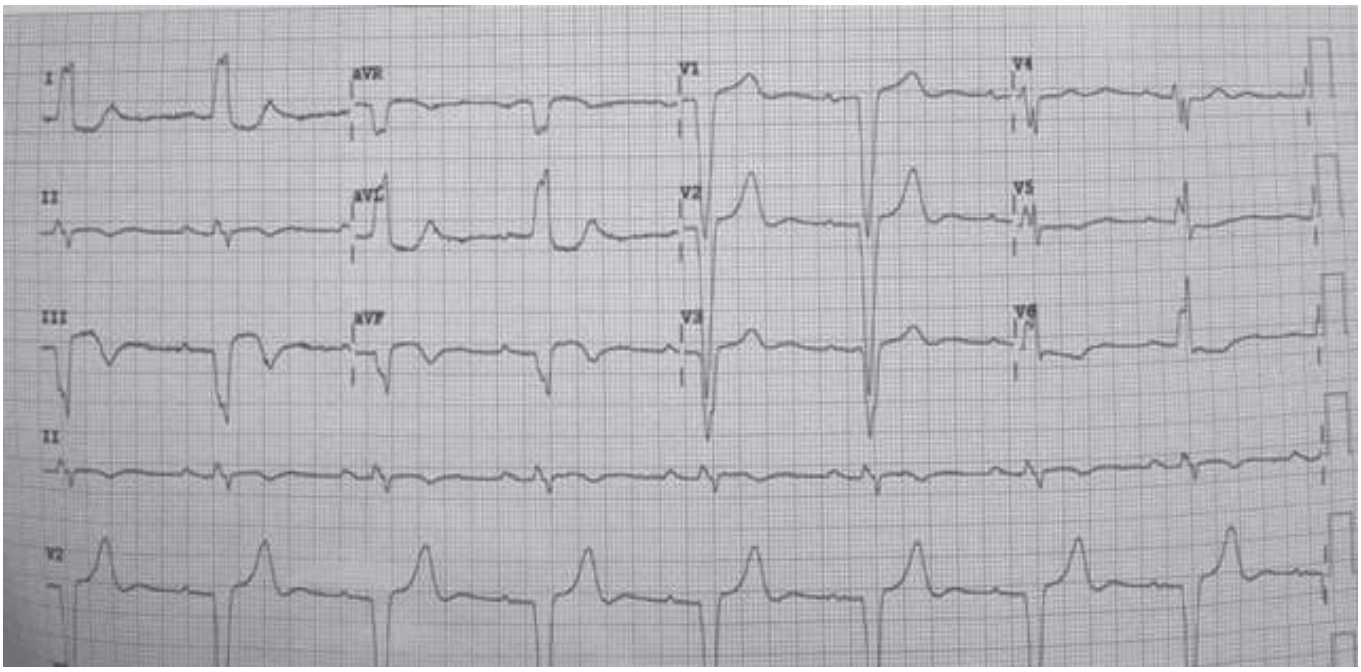
Therefore, preoperative assessment medications and appropriate anaesthetic management is very important in patients with DCM. The anaesthesiologist should have a thorough knowledge on its pathophysiology, clinical features, diagnostic evaluations and the treatment modalities. This has to be followed by a careful planning, for the provision of safe anaesthesia.

Case Description

43 year para 3 live 3 (P3L3) tubectomised female presented with pain in abdomen and abnormal uterine bleeding (AUB) since 2 months and was diagnosed as bulky uterus with multiple uterine fibroids. She was recently diagnosed as a case of mixed restrictive obstructive lung disease with Dilated Cardiomyopathy (DCM) in a known case of hypertension, after evaluation for the complaints of dyspnea on exertion of new york heart association (NYHA) class III. She was started on Dry Powder Inhaler (DPI) formoterol fumarate and budesonide 200mg BD and T. Furesemide 20mg BD, T Ramipril 2. 5mg and T. Aspirin 75mg + T. Atorvastatin 10mg HS since 15 days.

Her Pulmonary function test was done to assesse the dyspnea, which suggested mixed obstructive plus restrictive lung disease with good reversibility to bronchodilator. Her ECG (electrocardiography) showed Left Bundle Branch Block[Figure 1] Chest Xray showed cardiomegaly [Figure 2] Echocardiogram (Echo) showed severely compromised ejection fraction of 25-30%, left ventricle dilated and severe global left ventricle hypokinesia, mild mitral regurgitation, grade II diastolic dysfunction, mild tricuspid regurgitation and moderate pulmonary artery hypertension with pressure of 50mmHg. Coronary angiography (CAG) done preoperatively was found to be normal. On examination her pulse was 100/min, regular; blood pressure of 104/76 mmHg, respiratory rate (RR)- 20/min, oxygen saturation (Spo2)- 96% on Room Air; on systemic examination: early systolic murmur in mitral area and air entry was reduced at bases.

Figure 1: ECG Suggestive of LBBB



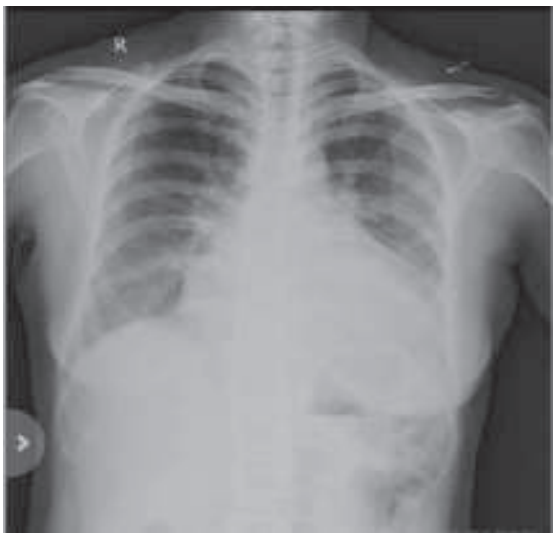


Figure 2 : Chest X-ray Suggestive of Cardiomegaly

Written informed high risk consent for was taken from the patient under American Society of Anaesthesiologists (ASA) Grade II/III. The anaesthetic technique and the need for postoperative ICU monitoring was explained to the patient. Adequate blood and blood products were reserved. The patient was taken in the operation theatre and all multipara monitors (pulse oximetry, non-invasive blood pressure and electro-cardiograph) were attached. Intravenous assess was secured with wide bore interacath of (18G). Continuous oxygen was supplied through oxygen mask at 4L/min. The patients parameter were Pulse of 76-82/min, Mean Arterial Pressure (MAP) 68-72mmHg, and Spo2-98-100%.

After all aseptic precaution, epidural catheter was inserted using 18G Touhey's needle using loss of resistance to air technique in L2-L3 interspace. Space was found at 3. 5 cm from skin and catheter fixed at 9cm from skin. The procedure was uneventful, and we changed the patient position into a supine position. Epidural test dose was given with 2% lignoadrenaline 3ml and epidural was activated. Anaesthesia was instituted with titrated doses of local anaesthetics according to the level assessed. We gave Bupivacaine 0. 5% 8ml plus Fentanyl 10mcg and waited for 10 mins, the level assessed was found to be inadequate we repeated the dose with Bupivacaine 0. 5% 5ml, level was assessed after 10 mins. Patient was able to move her legs and sensory level of T6 was achieved. Epidural infusion was started of ropivacaine 0. 75% at 10ml/hr for providing continuous anaesthesia. Inj fentanyl 50 mcg intravenous (IV) was given for sedation.

Surgeon performed the total abdominal hysterectomy, one mass was also found to be attached to the mesentery which was removed uneventfully[Figure 3]. The patient was hemodynamically stable intraoperatively with Pulse of 74-80/min, Mean Arterial Pressure (MAP) 66-70mmHg, and Spo2-98-100%. The surgeons were satisfied with the relaxation of abdomen. The surgery was completed within 60mins, with replacement of fluids with 750ml of crystalloid and blood loss of 200ml. The patient was catharized postoperatively with urine output of 200ml. The patient was shifted to recovery room.

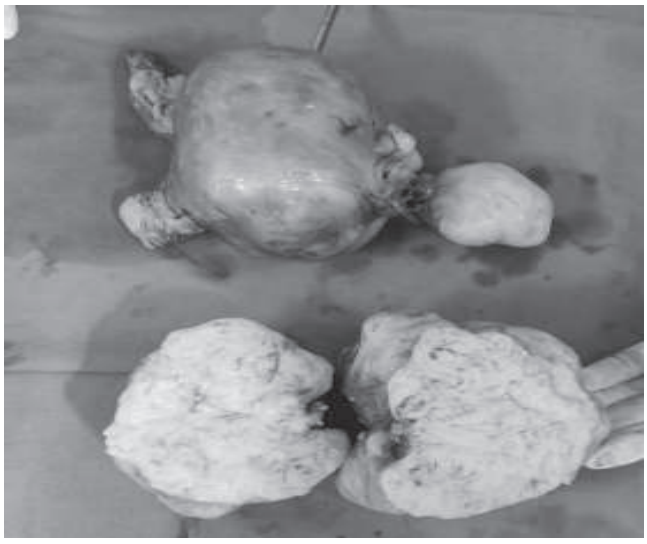


Figure 3 : Hysterectomy specimen and mass excised

In recovery room patient had hypotension with fall in MAP of less than 60mmHg. The patient was started on Noradrenaline infusion (80mcg/ml) at 2ml/hr IV to maintain the desired MAP of 68-70mmHg. Epidural infusion of ropivacaine 0.

2% was continued at 6ml/hr. The patient was shifted to Intensive Care Unit (ICU) for observation.

Discussion

The key hemodynamic features of patients with dilated cardiomyopathy (DCM) are elevated filling pressures, myocardial contractile dysfunction, and a marked negative relation between stroke volume and afterload. [3]The compensatory mechanism explained by Frank-Starling law which states that, myocardial force at end diastole compared with end systole increases as muscle length increases are blunted in dilated cardiomyopathies. The entire pressure-volume (P-V) loop shifts to the right with an increased in end-diastolic pressure and end diastolic volume. [Fig.4]

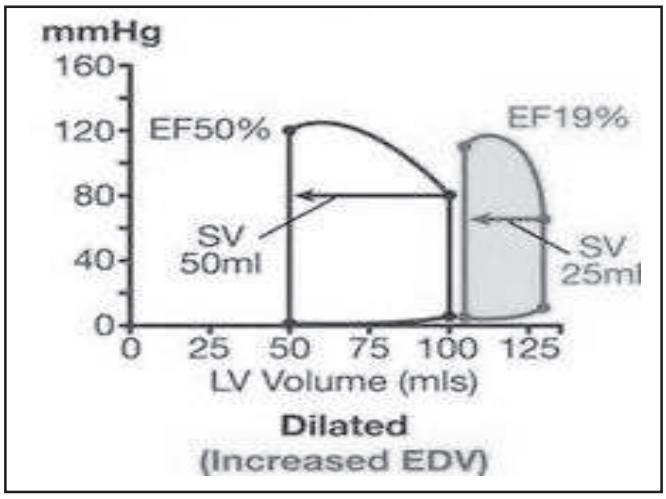


Figure 4 : Pressure-Volume loop in dilated cardiomyopathy

In accordance with the physiological changes, the goals of anaesthetic management are as follow: (i) avoiding myocardial depression by carefully titrating the anaesthetic drugs; (ii) maintaining normovolaemia; (iii) avoiding overdose of drugs during induction as the circulation time is slow; (iv) avoiding increase in ventricular afterload and (v) avoiding sudden hypotension where regional anaesthesia is the choice (vi) avoid tachycardia (vii) judicious fluid therapy (viii) avoid increase in peripheral vascular resistance by avoiding hypoxia, hypercarbia, hypothermia, acidosis and nitrous oxide. [4, 5]Apart from these primary goals, maintenance of acid-base and electrolyte balance and normothermia, adequate pain relief, avoidance of hypoxia, and hypercapnia are of paramount importance. [4]The intraoperative fluid management in DCM patients should be managed cautiously because of poor cardiac ejection, ventricular enlargement, hypokinesia and elevated filling pressures, the fluid overload in the perioperative period could lead to heart failure and pulmonary oedema. [6]

As the patient was a case of mixed obstructive restrictive lung diseased with DCM it was better to avoid General anaesthesia which requires airway handling, myocardial depression due to various anaesthetic agent, stress of laryngoscopy and intubation response which are also not desirable in these patients. Spinal anaesthesia causes sympathetic blockade, decrease in preload and afterload and precipitates hypotension which are dangerous in the patients with DCM. [7] We chose epidural anaesthesia considering its advantages of hemodynamic stability and titration of level over subarachnoid block, reduces afterload and help to maintain forward flow from the left ventricle and also effective for postoperative analgesia. [8]Regional anaesthesia was chosen considering patients lower airway problems similarly it attenuates neurohumoral stress response to surgery, produces vasodilatation thereby decreasing afterload, decreases incidence of DVT, pulmonary embolism, and respiratory depression, avoids polypharmacy, and is associated with early recovery. [9]

Agrawal et al has found that titrated epidural anaesthesia with judicious fluid and ionotropic support is a prudent choice in peripartum cardiomyopathy for cesarean section. [10] We have given 750ml of crystalloid and inotropes were used when there was fall in blood pressure. Yadav et al.

has studied that graded epidural anesthesia with slow blockade of dermatomes can be effectively used in patients with DCM with low LVEF. [11]Bin Suhaym et al has found that Bupivacaine and fentanyl provides adequate epidural anaesthesia with less variation in hemodynamic status. [12]

Ropivacaine is a pure S-enantiomer and it provides more differential sensory-motor block and has less central nervous system and cardiovascular toxicity. Ropivacaine is less lipid soluble than bupivacaine which offers anadvantage in providing analgesia with minimal motor block. [13]Mehta et al has found in his study that epidural ropivacaine 0. 2% produces effective analgesia similar to bupivacaine 0. 2% with a distinct sensory-motor dissociation without motor blockade. [14]Pradeep et al has studied graded epidural in DCM patient posted for femur fracture and found Epidural anaesthesia produces minimal effects on the heart rate, and contractility. [15]

Conclusion

Epidural segmental anesthesia with judicious fluid and ionotropic support is a prudent choice of anesthesia in patients with dilated cardiomyopathy and chronic obstructive restrictive lung disease for abdominal surgeries.

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Case Report

Klippel–Trenaunay–Weber Syndrome : A Case Report

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Abstract

A 35 year old male was admitted in surgery ward for right lower limb varicose vein with infected wound on lateral malleolus and referred to ophthalmology for h/o loss of Vision in right eye since childhood and was found to have elevated intraocular pressure (IOP) and glaucomatous optic atrophy of disc in right eye while left eye ocular and fundus findings within normal limit.

He had capillary malformations on the right side of face (port wine stain), right upper limb, chest and back. Right eye managed with IOP lowering topical medications and Left eye is under observation. Patient managed conservatively for varicose ulcer by General Surgeon.

This case exhibits a very rare occurrence of overlapping syndromes of Sturge–Weber syndrome (SWS) and Klippel Trenaunay syndrome (KTS) reported only a handful of times in literature. Most cases with Sturge–Weber syndrome have ipsilateral glaucoma affecting the eye on the same side as the port wine stain.

Sturge–Weber syndrome is a congenital, sporadic, encephalotrigeminal angiomatosis affecting about 1 in 50, 000 and is characterized by facial capillary malformation called port wine stain involving the eyelids, glaucoma, and vascular lesions seen in the ipsilateral brain and meninges. [1] Klippel–Trenaunay–Weber syndrome is a rare congenital mesodermal phakomatosis, affecting 1 in 100, 000, predominantly involving limbs and is characterized by cutaneous hemangiomas, venous varicosities, and asymmetric hypertrophy of soft tissues and bones. [1, 2]

The management of glaucoma in Sturge–Weber syndrome patients is particularly challenging because of early onset, frequently associated severe visual field impairment at the time of diagnosis, and unresponsiveness to standard treatment. Several surgical approaches have been proposed, but long-term prognosis for both intraocular pressure control and visual function remains unsatisfactory in these patients.

Keywords :

Unilateral Glaucoma, Klippel Trenaunay syndrome, Sturge–Weber syndrome, Port wine stain, Trabeculectomy

Case Report

35 year old male was admitted in surgery ward for right congenital varicose veins with infected wound on lateral malleolus and referred to ophthalmology for h/o loss of Vision in right eye since childhood. His best corrected visual acuity (BCVA) in right eye was HMCF (perception of light + and projection of rays accurate). Anterior segment evaluation of right eye showed megalocornea (13. 2mm) with scleral thinning, diffuse corneal oedema, relative afferent pupillary defect (RAPD) and nystagmus while left eye BCVA was 6/6 and anterior segment was within normal limit except nystagmus.

Fundus examination revealed glaucomatous optic atrophy in the right eye with tortuous veins and cup disc ratio 0. 3:1 with healthy neuro-retinal rim in the left eye. On applanation tonometry, intraocular pressure (IOP) was found to be 52 and 14 mmHg in the right and left eye, respectively. A four mirror gonioscopy revealed multiple small PAS 360 in right eye while open angles in left eye. Central corneal thickness was 616μ and 540μ in right and left eye respectively. The retinal examination was normal and did not reveal any choroidal hemangiomas.

Physical examination revealed lesions over the right side of face (port wine stain) [Fig-1] and extensive bluish discoloration of the skin was seen over the upper back and chest on right side [Fig-2]. His right upper and lower limbs showed mild hypertrophy compare to left side. Varicosity of veins seen on both lower limb (more on right side compared to left side) [Fig-3].

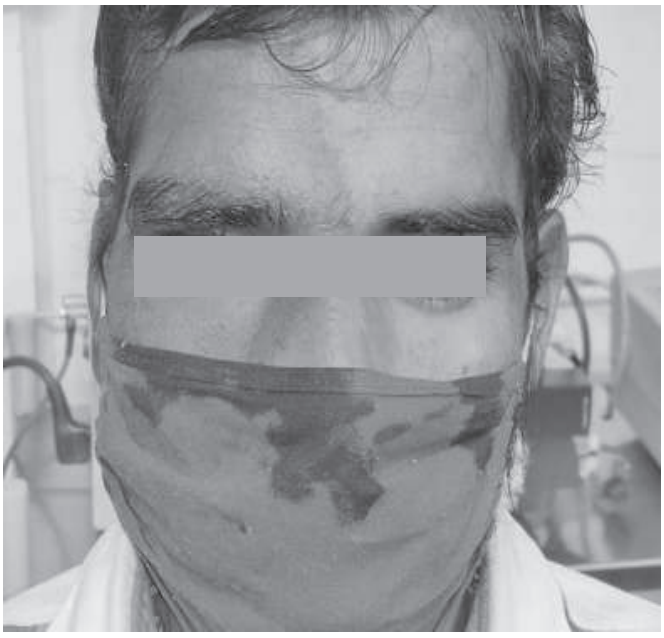

Fig-1: Port Wine Stain

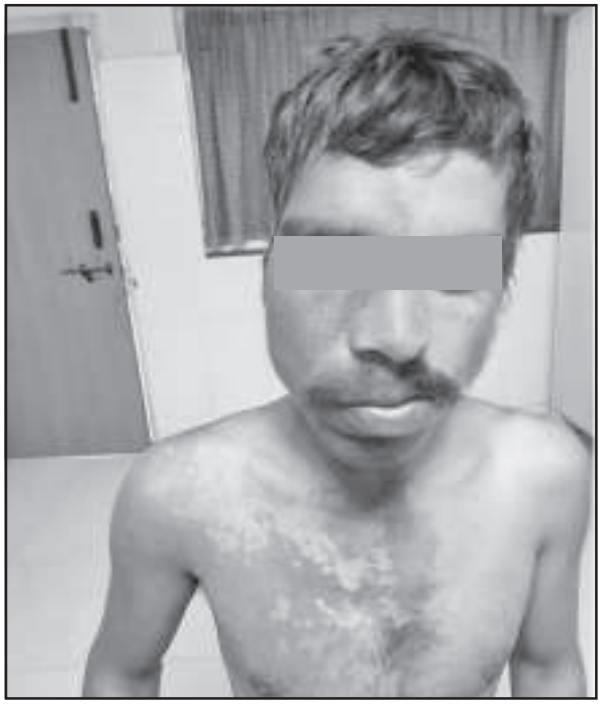

Fig-2: Bluish discoloration

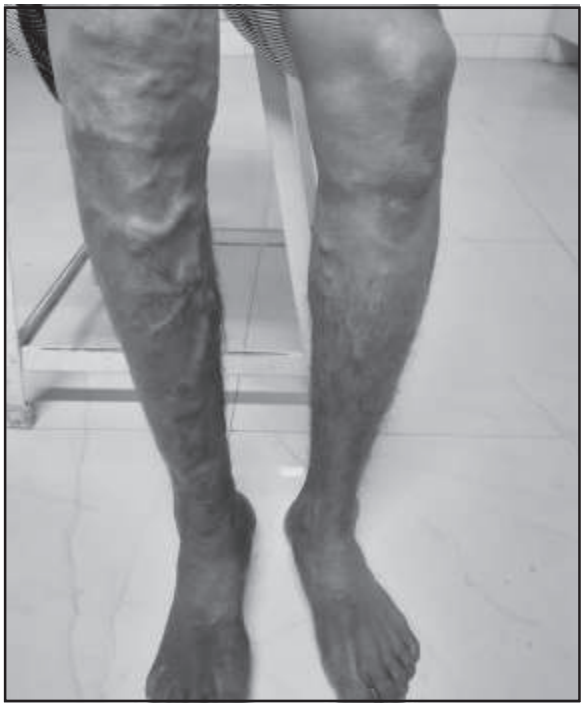

Fig-3: Varicosity of veins

- Patient was investigated for varicose veins and following investigations were done.
- Hemogram, Blood sugar levels, Renal function test, Liver function test were normal
- 2D echo study was normal.
- USG (abdomen+ pelvis) showed no significant abnormality
- Venous & Arterial Doppler of right lower limb-
- Incompetence in right sapheno-femoral junction with multiple varicosities & tortuous dilated veins along great saphenous vein and its tributaries

Discussion

Sturge–Weber syndrome (SWS), also known as encephalotrigeminal angiomatosis, is a condition that includes leptomeningeal hemangioma, facial angiomatosis or nevus flammeus (also called port-wine stain [PWS]), and ocular pathological changes. [3–6]

No significant difference between males and females. [7] No hereditary pattern or predisposition has been shown, and no malignant transformation has been demonstrated. [8, 9] Several genes in the 17p1-p13 region are known to be involved in SWS. The embryologic basis of SWS has been reported to be related to an impaired development of the cell precursors in the neural crest during the first embryological trimester, leading to the characteristic malformations observed in the central nervous system, skin, and eyes. [10]

Shirley et al recently published a ground-breaking study where a mutation in the GNAQ gene was identified [11]

Diagnosis is easily performed when the classical clinical signs of SWS are present, consisting of unilateral facial PWS along the first branch of the trigeminal nerve, hemiatrophy, progressive seizures, contralateral hemiparesis, mental deficiencies, hemianopia, and ipsilateral glaucoma. [12]

Neuroimaging techniques help to perform the diagnosis, showing gyriform calcifications that engage the parietal and occipital lobes. [13]

The diagnosis of SWS is based on the presence of at least two of the three manifestations of the classic triad (leptomeningeal angioma, PWS, and ocular abnormalities)

Table 1 Classification of Sturge–Weber syndrome

Type	Facial angioma	Leptomeningeal angioma	Glaucoma	Systemic manifestation
Type I	+	+	±	±
Type II	+	-	±	-
Type III	-	+	±	-
Type IV	+	+	±	±

Notes : + Present; - absent; ± feature can be observed but is not ubiquitous.

Glaucoma in these syndromes is attributable to malformations of the anterior chamber angle or high episcleral venous pressure.

Glaucoma Pathogenesis

1. Congenital malformation of the anterior chamber angle. [14]
2. Increase in episcleral venous pressure (EVP) due to arteriovenous shunts into the episcleral hemangioma. [15]
3. Fluid hypersecretion by either the ciliary body or the choroidal hemangioma. [16]
4. Abnormal hemodynamics of the episclera and the anterior chamber angle due to premature aging of the trabecular meshwork–Schlemm's canal complex, as observed in SWS later-onset glaucoma. [17]

Elevated EVP is only a risk factor for glaucoma onset. [18] Retrobulbar blood flow was also impaired in SWS patients, suggesting an increased risk to develop glaucoma with aging.

Ciliary body effusion induced angle closure by moving the iridolenticular diaphragm forward, which led to acute glaucoma attack. This mechanism of glaucoma induction has also been described following the use of the drug topiramate, which is used for seizures that can occur in SWS patients with leptomeningeal involvement. [19] Angle-closure glaucoma in SWS has also been described as related to pupil block with or without ectopia lentis and pigment dispersion. [20, 21]

The management of glaucoma in Sturge–Weber syndrome patients is particularly challenging because of early onset, frequently associated severe visual field impairment at the time of diagnosis, and unresponsiveness to standard treatment. Several surgical approaches have been proposed, but long-term prognosis for both intraocular pressure control and visual function remains unsatisfactory in these patients.

Topical antiglaucoma drugs seem to be less efficacious in SWS patients with congenital glaucoma, while they represent first-line therapy for patients with late-onset glaucoma.

Ong et al showed that latanoprost eye drops, as adjunctive therapy, were effective in controlling glaucoma in 50% of 14 patients with SWS at 1 year of follow-up. [22]

A hypothesis to justify the low efficacy of antiglaucoma drugs in controlling SWS-related glaucoma is that most of these drugs do not affect EVP, highlighting the need for novel antiglaucoma medications specifically targeting EPV.

Surgical management include filtering procedures such as trabeculectomy with or without trabeculotomy is first line of management in congenital glaucoma and in late-onset glaucoma patients, if medical management is not sufficient to control IOP, surgical management is done. In cases of trabeculectomy failure, valve implant surgery is considered.

Conclusion

We present a very rare case of overlapping Sturge–Weber syndrome and Klippel–Trenaunay syndrome with unilateral blind eye due to glaucoma that was managed conservatively. Glaucoma secondary to SWS is a challenging disease due to its early development and poor response to standard medical treatment.

Surgery is frequently required to obtain long-term control of IOP in order to avoid visual function loss. However, several severe complications related to surgical procedures have been described in these patients, including choroidal effusion, expulsive haemorrhage, and exudative retinal detachment. Moreover, in SWS, the surgical success rate is the lowest among secondary glaucomas, since surgical failure, uncontrolled IOP, and low vision outcomes have been frequently reported. [16, 23, 24]

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Simplified Post Covid –19 Checklist : SARS -COV Complications.

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To,

The Editor

Respected Sir/Madam,

The purpose of this simplified mnemonic for post covid care is to assess the clinical symptoms and to tackle the residual impact of covid 19 in terms of it's complications and follow up care after discharge of patient. Though the recovery rate of COVID has improved, late complications after recovery are increasing too. There is need for meticulous follow-up after covid infection and this mnemonic is going to help us for the routine check-up and assess the progress of the patients.

Introduction:

The Novel Corona virus disease 2019 (COVID-19) is an illness caused due toSARS-CoV-2, with more than 121 million documented infections and 7 million deaths worldwide across 221 countries, the coronavirus disease 2019 (COVID-19) pandemic continues unabated. The clinical spectrum of severe acute respiratory syndrome corona virus (SARS-CoV) 2 infection ranges from asymptomatic infection to life-threatening and fatal disease. Current estimates are that approximately 150 million people globally have "recovered"; however, clinicians are observing and reading reports of patients with persistent severe symptoms and even substantial end-organ dysfunction after SARS-CoV-2 infection. Because COVID-19 is a new disease, much about the clinical course remains uncertain—in particular, the possible long-term health consequences. The Second wave of COVID-19 pandemic is sweeping across the world, and much of the initial research was

focused solely on understanding its health-related impacts.

A post-acute syndrome is well recognized in patients who are recovering from a serious illness, in particular an illness that required hospitalization and admission to the intensive care unit. Follow up visits should be done regularly. There has to be systemic assessment in such recovered patients, they should first be tested for thrombotic complications across all organs. This urges us to suggest that it is highly important to provide counselling, moral support as well as a few recommended guidelines to the recovered patients and society to restore to normalcy.

As the post covid care is equally important, especially for patient those who requires intensive care and of moderate to severe disease. This post covid check list is very important to manage the patient on routine follow up so, we can check every aspect of patient by remembering a simple mnemonic that is "SARS - COV Complications".

Post Covid -19 Checklist

Mnemonic – "**SARS –COV Complications(GUD DOCTORNegates Complications)"**

1) S - Symptoms or complaints of patient afterdischarge

2) A - Advice on discharge :– (see if patient following and counsel regarding the same)
- Diet and fluid intake
- CARP Protocol
- Chest physiotherapy or Breathing exercises orPranayam or Yoga
- Incentive spirometry

3) R - Report on follow up :-
- HRCT – To rule out CT severity score. (If indicated)
- 2DECHO –To see cardiac status
- Inflammatory marker- CRP/ESR/Serum Ferritin/LDH/CPK-Total
- BSL/Serum Creatinine /PT/INR
- Repeat Covid reports – Positive and Negative (If indicated)

4) S - Special treatment and watch for any complications of
Steroids, Fibrinolytic drugs, Anticoagulants / Antiplatelets, Statins,Antibiotics

5) C- Comorbidities :- (If any)
Check for current treatment of Diabetes Mellitus /Hypertension/Bronchial Asthma/ COPD /Cerebro-vascular Accident /CKDand Other comorbidities.
And Need for Modification in Drugs

6) O – Oxygenation :–
Check for need of Home Oxygenation or BiPAP.
Teach & counsel patient and their relatives accordingly
Also counsel for self SPO2 monitoring

7) V – Vitals :-
Check Pulse Rate/Blood Pressure/Respiratory Rate/SPO2/6MWT on each visit.

8) C- Complications : – (Mnemonic :- **GUDDOCTORN**egates **C**omplications)

To Check for post covid complications

1)	**G**	**G**astrointestinal System	Nausea/Vomiting andAcute mesenteric Ischemia leading to Intestinal Gangrene(rare)	History, Clinical Examination, X-ray Abdomen, USG(A+P)
2)	**U**	**U**rological (Renal) System	Acute Kidney Injury/ Acute Tubular Necrosis/ Renal Vein Thrombosis/ Electrolyte Disturbances	RFT with Electrolytes, USG(A+P) to look for kidney size and texture, Urine (R/M , C/S)Renal Artery Doppler
3)	**D**	**D**iabetes & Endocrinal system	Hyperglycaemia/ Thyroiditis/ Hyperlipidemia	freeT3,freeT4,TSH, TPO Antibodies, Lipid Profile , BSL(F/PP)
4)	**D**	**D**ermatological	Hair Loss/ Acne/ Rashes	Dermatologist Consultation
5)	**O**	**O**pportunistic Fungal Infection	Mucormycosis/ Aspergillosis/Candidiasis	HRCT(Thorax), CT-PNS, KOH Mount, Sr.Galactomanin, Sputum forFungal Elements, CXR(PA View), Biopsy/ Histopathology,ENT / Ophthalmology / OMFS opinion
6)	**C**	**C**ardiovascular System	Chest Pain/Myocardial infarction/Myocarditis/ Arrhythmias/Stress Myopathy /Heart Failure	2D-ECHO, ECG, Cardiac Enzymes(CPK MB, CPK Total, Sr.LDH) , Sr.PRO-BNP, Procalcitonin,Stress Test(TMT)
7)	**T**	**T**hrombo-embolic Events	Deep Vein Thrombosis / Pulmonary Thrombo-embolism/ Renal vein Thrombosis/Disseminated Intravascular Coagulation	B/L Lower Limb Colour Doppler.Carotid Doppler, CTPA, MR Angiography, Coagulation Profile (BT/CT/PT/ INR/D-Dimer, aPTT)
8)	**O**	**O**ther Manifestations	Fatigue/Weakness/ Rhabdomyolysis/Wt Gain or Loss/Anosmia/ Loss of Taste	History, Clinical Examination
9)	R	Respiratory System	Pulmonary Thrombo-embolism, Pulmonary Hypertension, Fibrotic ARDS, Bacterial Infections.	HRCT(Thorax) , PFT, Breath Holding(Single Breath Count) ,6-min Walk Test, SPO2 Monitoring
10)	**N**egates	**N**europsychiatric	Anxiety/PTSD/Panic Attacks/Depression/ Psychosis	Psychiatrist Consultation, Detailed History& Evaluation
11)	**C**ompli-cations	**C**entral Nervous System	Encephalitis/ Encephalopathy/CVA/ GBS/ Polyneuropathy	Stroke Protocol, MRI (Brain+ Angio) , Lumbar Puncture, CSF Study(Gm/ZN stain,ADA, R/M, C/S , Glucose/Proteins), EEG, EMG, NCV

Post Acute COVID 19 Syndrome:-

It is defined as persistence of signs & symptoms and/or delayed or long term complications beyond **4 Weeks** from onset of symptoms of Covid 19 Pneumonia, even after receiving appropriate treatment and care during acute infection.

SARS–COV Complications is a simple mnemonic to screen the post covid patient from their symptoms to the complications which might develops after the covid -19 infection.

S - Symptoms of the patient- Most common symptom after the covid is Fatigue and Generalized weakness, Muscle weakness, depression, palpitations,anxiety, new onset dyspnoea etc.

A - Advice on Discharge – check whether patient is following special advice given by physician and ask for any progress in his /her symptoms.

R – Reports – check for post-covid lab reports like Inflammatory markers and other essential labs and patients covid reports i.e., RT-PCR/RAT positive or negative and radio imaging (if advised) and it will help for prognosis of the patient

S - Special advice – check whether patient is taking the important medications which was given at the time discharge like anticoagulants/ antiplatelets , fibrinolytics , steroids, statins , antibiotics or antiviral medications .

C - Co-morbidities- Diabetes / Hypertension / IHD /CVA/ COPD/ thyroid disorder etc. Specially screen for their routine medication , required labs and required essential treatment for that.

O - Oxygenation – check and counsel regarding the need of home oxygenation (O2 concentrator or home BiPAP) in elderly,obese patient admitted in ICU and patients whose CT score is too high.

V - Vitals- Most important parameter to be screen on post covid follow up , the vitals of the patient , pulse / blood pressure / respiratory rate / spo2 and spo2 after 6 min walk test.

C- Complications–

1) **Dermatological: -**Hair loss is predominant symptom and has been reported in approximately 20% of Covid 19 survivors. Othersymptoms like Acne, Rashes have been reported in patients

2) **Opportunistic Infections :-** COVID-19 patients are more susceptible to Opportunistic Infections like Mucormycosis, Aspergillosis, Candidiasis due to prolonged steroid use, immunomodulator use, high ferritin levels, acidosis in DKA and CKD, prolonged antibiotic use. This disease carries high morbidity and mortality. Hence, all efforts must be done to prevent it, diagnose it at early stage, and manage effectively.

3) **Cardiovascular System:-** Includes palpitations, dyspnoea and chest pain, myocardial fibrosis or scarring, myocardial inflammation, myocarditis, arrhythmias, myocardial infarction, tachycardia and autonomic dysfunction.

4) **Thrombo-embolic Events :-**Direct oral anticoagulants and LMWH may be considered for extended thromboprophylaxis in patient with predisposing risk factor for Immobility, persistently elevated D dimer levels (greater than twice the upper limit of normal).

5) **OtherManifestations:**-SARS COVID 19 have wide spectrum of manifested complications which are still currently under study most common among them are Fatigue/Weakness/ Nausea &Vomiting /Rhabdomyolysis/Wt Gain or Loss/Anosmia/Loss of Taste.

6) **Renal System :–**Most common renal complications due to dehydration which may leads to Acute Kidney Injury / Acute Tubular Necrosis /renal vein thrombosis.
The development of AKI in COVID-19 patients increases the risk of mortality.

7) **EndocrineSystem:–**Common complications are Thyroiditis /hyperlipidemia/hyperglycaemia. Diabetes is the third most common co-morbidity in COVID-19 patients, and is associated with more severe disease, increased ICU admission, and a higher risk of death.

8) **Neuropsychiatric complications-**Anxiety, Depression, Sleep disturbances, and PTSD have been reported in 30-40% of COVID 19 Survivors. The pathophysiology of neuropsychiatric complications is mechanistically diverse and entails immune dysregulation, inflammation, micro vascular thrombosis, iatrogenic effects of medications and psychosocial impact of infection. individuals recovering from COVID-19 may be at even greater risk of depression, anxiety, posttraumatic stress disorder, and substance use disorder

9) **Pulmonary System :-**Dyspnoea, Decreased exercisecapacity, Hypoxia are the most common and persistent symptoms. Reduced diffusion capacity, Restrictive pulmonary physiology, ground glass opacities and fibrotic changes on imaging have been noted at the followup of Covid 19 Survivors. Assessment of progression of recovery of pulmonary disease and function may include Home Pulse Oximetry, 6 MWTs, PFTs, HRCT Thorax, Pulmonary Angiography as Clinically Appropriate

10) **CNS System :-I**nclude headache, dizziness, loss of consciousness, and cerebrovascular disease, encephalitis and meningitis. Possible PNS manifestations seen so far include the loss of sense of taste, smell, and vision and rare manifestation seen in Guillain–Barré syndrome. Increased D-dimer levels may be indicative of blood clots, which have been seen as a very concerning symptom of COVID-19.

Conclusions

Outpatient post–COVID-19 clinics are opening in many localities where large outbreaks have occurred, and the term "LONG-HAULERS" has been suggested to refer to these patients. It is imperative that the care of this vulnerable patient population take a multidisciplinary approach, with a thoughtfully integrated research agenda, to avoid health system fragmentation and to allow the comprehensive study of long-term health consequences of COVID-19 on multiple organ systems and overall health and well-being. This simplified pneumonic is helpful to approach the physical and mental health of people who recover from COVID-19.

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Determinants of waiting time of a patient in casualty department of tertiary care hospital in Pune : The role and importance of time : a short observational cross sectional work study

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ABSTRACT :

Background : The emergency department, being at the heart of any hospital organisation, should be capable of providing efficient services in a time of national emergency. The crucial time a patient loses can be saved and reutilised productively with the least amount of financial investment.

Methods : The study was undertaken to understand the determinants of waiting time in the casualty department of a tertiary care hospital. It is a cross sectional study conducted over 2 weeks comprising of 113 patients selected via non probability convenient sampling.

Results : The data revealed that the average patient journey length from entry till disposal was 89. 48 minutes with a Standard Deviation of 41. 23 minutes.

Conclusion : Various factors responsible for this delay include shifting patient to and from diagnostic procedure, shifting patient for admission or transfer, or waiting for resident doctor to arrive.

i) Introduction :

The function of an emergency department is to be at the heart of a medical organisation, serving as a point of entry for critical patients from where they flow into the rest of the hospital. (1, 2)Patients and their relatives who avail the services of an emergency department of a tertiary care hospital have the primary expectation of being provided fast and smooth services in a time of dire need.

Considering that the emergency departments of all hospitals have been under immense strain during the COVID-19 pandemic, it is as important as ever to determine the factors affecting the waiting time in the emergency department of a tertiary care hospital in Pune. In the context of the ongoing pandemic, it was especially important to achieve efficiency in order to reduce overcrowding and enhance the ability of the Casualty department to receive a high volume of patients, since hospitals can also be a source of infection for vulnerable individuals. (3)

Patients often experience extended waiting times in the Casualty of a hospital due to high patient load leading to an accumulation and overcrowding of critical patients. They are also affected by disorganised work flow, shortage of supporting staff such as ward boys and maushis, and backlog of patients due to lack of working machines and technicians. Delayed treatment of any patient can lead to disastrous and inevitable consequences, which are certainly avoidable. (4)

The parameters to be observed were determined by analysing patient flow from arrival until disposal or admission. An acute need to increase efficiency arose during the first wave of the COVID-19 pandemic which called for understanding where time can be saved when receiving, triaging and treating or transferring deteriorating patients. (5)This also allowed for me, the observer, to look at patient flow from the point of view of clientele satisfaction. (6)The long term benefits of clientele satisfaction can definitely be appreciated by both the institute as a whole as well as treating doctors. The study was conducted in the Casualty of a tertiary care hospital in Pune. Data was collected purely through observation, and data was analysed to draw conclusions regarding factors affecting the waiting time of patients.

The present study was undertaken to understand the determinants of waiting time of a patient in the casualty department in a tertiary care hospital and to further understand ways in which the waiting time can be shortened by making small changes with the least amount of financial strain. (7)The need for the study arose from personal observations made during my casualty posting as well as hearing negative feedback and suggestions from patients and relatives during the same time period. It became clear that a potentially haphazard and chaotic work flow can be streamlined by making small yet significant changes with minimal investment.

ii) Material and Methods :

A cross sectional observational study was conducted. Non probability convenient sampling was employed, meaning that final number of subjects included in the study was purely determined by patient flow. The total number of patients involved in the study was 113.

The parameters to be observed as well as the self employed "time study sheet" were pre approved by the institutional ethics committee comprising of a panel of experts.

The observer was not participating in the patient care activities and only present for the purpose of data collection. The data was collected during the evening shift, as that was the time period during which patient load was highest. To minimise bias, treating doctors were not informed of ongoing observations. (8)

The following parameters were observed :

1. Time taken for patient to be shifted from vehicle/ambulance to stretcher, and then transferred to bed in casualty.
2. Time for first staff member to approach newly arrived patient.
3. Time for Casualty Medical Officer to be informed and approach the patient.
4. Time taken for staff member to successfully contact resident doctor.
5. Time taken for Resident doctor to arrive.
6. Time taken for Resident doctor to explain

admission/referral procedure.

7. Time taken for ward boy/maushi to shift patient for diagnostic procedure and return
8. Time taken for patient to be shifted to ward (if being admitted) OR Time taken for relative to shift patient out of bed.

iii) Results

The data was collected over a 14 day period. The Casualty department of the institute has 1 main entrance with a ramp, 1 side entrance via a staircase and one inlet to the radiology department. There is a cabin for enquiry where all on call nurses and doctors have a seating area. The registration counter is manned by rotating technicians or on call staff depending on availability.

The time taken for patient to be shifted from vehicle/ambulance to stretcher, and then transferred to bed in casualty was 5. 15 minutes, with a Standard Deviation of 9. 34 minutes. Various factors responsible for this include absence of clearly assigned ambulance bay, which leads to time wastage from the side of the ambulance driver who is unable to dock the ambulance in a fixed spot. Another piece of feedback is that patients who enter by themselves are unable to understand the layout at first glance. Often times, the stretcher is not available or difficult to locate.

The time for first staff member to approach newly arrived patient was 4. 20 minutes, with a Standard Deviation of 3. 26 minutes. Additionally, The time for the Casualty Medical Officer to be informed and subsequently approach the patient was 7. 03 minutes, with a Standard Deviation of 6. 46 minutes. A factor affecting this has been the recurring issue faced by relatives arriving with the patient experience which is the lack of staff to intercept the newly arrived ambulance and transfer the gurney. There is also a confusion among staff members as to who is meant to approach the patient first, from the nurse, intern, resident, or on call resident.

The time taken for staff member to successfully contact resident doctor was 4. 38 minutes, with a Standard Deviation of 4. 29 minutes. Compounded with this, the time taken for Resident doctor to arrive was 23. 57 minutes, with a Standard Deviation of 18. 80 minutes. This is the area where a lot of time is spent waiting by the patient as the on call resident is difficult to get in touch with.

The time taken for Resident doctor to explain admission/referral procedure was 12. 38 minutes, with a Standard Deviation of 9. 43 minutes. Feedback received from relatives frequently indicates that they would benefit from instructional banners placed around the campus which list the important documents needed for administrative and billing procedures as at times they have to travel a long distance acquire these documents from their family home at the last minute. This would save the relatives time as well as hasten admission of critical patients, as well as make processing these admissions faster and more efficient.

The time taken for ward boy/maushi to shift patient for diagnostic procedure and return was 26. 98 minutes, with a Standard Deviation of 16. 52 minutes. An issue often experienced with respect to this is the absence of technicians or lack of working machines on that day which leads to a backlog and overcrowding of patients. It also means that essential diagnostic investigations are potentially delayed.

The time taken for patient to be shifted to ward (if being admitted) OR Time taken for relative to

shift patient out of bed was 26. 28 minutes, with a Standard Deviation of 20. 86 minutes. This makes the average patient journey length from entry till disposal was 89. 48 minutes with a Standard Deviation of 41. 23 minutes. It is unclear to the relatives whether they are responsible for shifting their patient out, and time is often wasted waiting for a member of staff to help them and for ambulance/private vehicle to arrive to transfer them, as they cannot afford ambulance services.

(9) The bed which is assigned to them remains occupied and cannot be reassigned to incoming patients, which disrupts flow.

The conclusion is that the most amount of time is spent in shifting patient to and from diagnostic procedure, followed by time taken for patient to be shifted out of casualty either to ward or for transfer. Finally, the 3rd most amount of time is spent waiting for resident doctor to arrive. A study conducted in North India by Toward et al. showed that patient care impacted by overcrowding resulting from poor patient flow and excess waits can result in delayed treatment, long patient waiting time and stay, overburdened working staff, patient elopement, high medical error rate, low throughput and poor patient outcomes. (9)

iv) Discussion :

The data was analysed using descriptive statistics.

The primary drivers of the study were:

- Slashing the waiting time of patients who are in poor health.
- Reducing confusion among relatives who have arrived with the patients as to the procedure of admission / referral / billing, etc.
- Improving/Upgrading methods of communication amongst health care providers (Residents, Interns, Allied Supportive Staff) to ensure productive and efficient messages are sent across with respect to patient status and treatment.

v) Conclusion :

The project was carried out to understand determinants of waiting time of patients in an emergency department of a tertiary care hospital and to identify factors which contribute to the delay if any.

Data can be collected at regular intervals and subsequent quality improvement projects can be done to ensure constant cyclical elevation of standards keeping clientele satisfaction in mind. Successive audit cycles can be used to document progress and changes can be tailor made to fit the needs of an evolving emergency department. The data can be compared to other studies conducted in India to establish a comparable standard to use as a yard stick when measuring improvement and reduction of waiting time.

Recommendations :

It is my proposal that the following changes be made to further reduce patient waiting time :

1. Clearly labelled entry and exit points.
2. Clearly labelled Ambulance parking outside Casualty.
3. Designated Area for Stretcher.
4. Designated Waiting area for relatives.
5. Instructions to relatives in order to reduce over crowding : - Only one relative allowed inside per patient, and one relative required for billing, purchase of medicines, always wear a mask, etc.
6. Division of beds inside the Casualty, so that beds are not assigned randomly and JRs are able to easily locate patients according to designation.
7. Labelling inside the casualty and instructions to relative related to documents required for MPJAY, paper registration, admission etc.
8. Label put on bed when patient has gone for any investigation, so that patient whereabouts are made known to other staff.
9. Arrows on the floor, which guide the patient from entry to the "first point of contact" at the counter where sister/intern sits.

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