STETH TALKS

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FOREWORD

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I reiterate that our undergrads should develop the skill of scientific writing, much like the thrust on clinical skills & knowledge. Our students have the responsibility as an MMCian to learn to write flawlessly in scientific language and proudly publish those writings in peer reviewed medical journals of repute. Based on this long term vision for the campus, we have enunciated a scientific journal independently managed by our undergrads called STETH TALKS.

Steth Talks shall grow as an undergraduate medical journal of Madras Medical College populated by peer reviewed scientific writing of our students, based on the vast variety of clinical cases that one bound in the various hospitals attached to Madras Medical College. I wish the editors a scientific journey of learning how to write & how to manage a medical journal.

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A CASE OF PROGRESSIVE SUPRANUCLEAR PALSY

Yashwin Tejas, 2021 Batch

Abstract

Progressive Supranuclear Palsy (PSP) is a rare neurodegenerative disease with prevalence of four to five persons per 100,000 people. It is classified under the group of neurological conditions known as Parkinson-Plus syndromes (Atypical parkinsonism). The condition is characterised by the accumulation of 4R-tau protein aggregates in various regions of the brain. These pathological changes mainly affect the brainstem and the basal ganglia, resulting in distinctive MRI features. It presents with a wide array of motor, cognitive, neuropsychiatric, and behavioural manifestations. PSP shows clinical heterogeneity and presents as different phenotypes, the most classical being Richardson's syndrome (PSP-RS). These features often overlap with those of Parkinson's Disease and other Parkinsonism syndromes, making the diagnosis challenging. Current treatment options available are limited and inadequate. Several clinical trials are underway to test novel therapies that target tau-protein in various ways, such as modulating its post-translational modifications, stabilizing its interaction with microtubules, or enhancing its clearance by immunotherapy. These approaches may offer new hope for slowing down the progression of PSP.

Keywords: Progressive Supranuclear Palsy, Parkinson-Plus Syndromes, tauopathy, vertical gaze palsy, vertical nystagmus, saccadic intrusions,

INTRODUCTION:

Progressive supranuclear palsy is a rare, progressive, and ultimately fatal neurodegenerative brain disease. Individuals with PSP are often diagnosed in the sixth decade of life with male predilection. The clinical presentation is heterogenous, with the most common early symptoms being postural instability, falls, vertical gaze palsy, bradykinesia, and frontal lobe cognitive impairment. Though thorough history taking can help in differentiating such conditions belonging to Parkinson-plus syndromes from Parkinson's Disease, these clinical features frequently overlap with each other, leading to misdiagnosis and inadequate treatment. This confusion is compounded by the fact that several cases of PSP show moderate initial therapeutic response to levodopa. PSP itself is classified into two major clinical phenotypes – Richardson's Syndrome (RS) and PSP-parkinsonism (PSP-P). Treatment options are limited to symptomatic and supportive therapies, and there remains no approved disease-modifying treatment for PSP. Progression of the disease is rapid, with life expectancy after disease onset being approximately 8–10 years. Main causes of death include

bulbar palsy, aspiration pneumonia, sepsis, and complications of severe falls and injuries.

CASE REPORT:

A 60-year-old man from Thiruvallur, who was a farmer by occupation, presented to the neurology OP at RGGH on 2nd December 2025, with complaints of persistent imbalance and falling backwards while walking for the past three years, which was insidious in onset, gradually progressive, and associated with difficulty in turning corners. The patient had difficulty in climbing stairs, in the form of slippage when coming downstairs.

He also commented on generalised stiffness of voluntary movements and mild involuntary oscillatory movements distally in his left arm for the past two years, both at rest and when reaching for objects, resulting in spillage of food and water and difficulty in buttoning shirts.

The attenders noted generalised slowing of movements, slowness of speech and staring look, along with stooped posture and short shuffling steps while walking – all of which were present for the 1-2 years, insidious in onset with gradual progression. They also commented on the lack of attention (eye contact) and emotions while conversing with the patient, inappropriate behaviour in the form of starting random conversations with grandchildren, along with confusion in performing routine daily activities (e.g. confusion in order of making a cup of tea).

The patient was conscious, oriented, moderately built and nourished, right-handed. Patient did not maintain eye contact and there was frequent loss of attention, along with decreased blink rate and hypomimia. Tremors were noticed in distal extremities of both upper limbs (left > right) – both at resting and intentional tremors. Pill rolling movements noted in left hand. There was no visible wasting or muscle twitching.

Vitals were stable on the day of admission. Hypophonia was noted. Micrographia was present. Frontal Lobe Dysfunction present – Frontal Assessment Battery (FAB): Verbal fluency test (lexical fluency), Luria's motor sequencing tests, Trail making test, Go-No Go test were impaired (score – 13/18). Applause sign was positive. Ideational apraxia (executive dysfunction) present. MMSE Score was 26/30.
Extraocular Movements were restricted in all directions (both eyes). Broken pursuit with square wave jerks (Saccadic intrusions) present, along with vertical nystagmus.
Cogwheel rigidity was seen in the elbow and wrist of both upper limbs, and both knees.

Plantar Reflex – Striatal Toe (Pseudo-Babinski) in both left and right feet. Finger-nose, finger-finger-nose incoordination present, dysdiadochokinesia present on both sides. Rebound phenomenon noted bilaterally.

Myerson sign was positive. Palmomental reflex was present on both sides. Pull test impaired. No cardiovascular, respiratory or abdominal symptoms or signs were noted.
MRI Brain revealed atrophy of pons and upper cerebellar peduncles, with midbrain-to-pons area ratio of 0.11. This pattern of imaging was consistent with Progressive Supranuclear Palsy. Final diagnosis was made using both clinical examination and radiological findings, according to MDS clinical criteria.

DISCUSSION:

Progressive Supranuclear Palsy is a form of Atypical Parkinsonism, with accumulation of 4R-tau proteins. Pathological findings in the brain include neuronal loss, gliosis, and tau-positive inclusions, such as neurofibrillary tangles, tufted astrocytes, and coiled bodies. In addition to the tauopathy, PSP involves the degeneration of dopaminergic neurons and cholinergic neurons, leading to loss of basal ganglia, cerebral cortex, and brainstem structures – particularly dorsal midbrain (midbrain tegmentum and pedunculopontine nucleus), which leads to postural stability, and the rostral interstitial medial longitudinal fasciculus, leading to decrease in vertical excitatory burst neurons – thus impaired vertical gaze, broken vertical pursuits and slow vertical saccades are seen. The motor nuclei of the cranial nerves are involved in advanced stages of the disease.

a. PSP-postural instability (PSP-PI)
b. PSP-cerebellar ataxia (PSP-C)
PSP can be divided into a variety of subtypes many of which overlap with other Neurodegenerative Diseases (tauopathies):

1. Classic:
a. PSP-Richardson syndrome (PSP-RS)

2. Brainstem variants:
a. PSP-predominant parkinsonism (PSP-P)
b. PSP-progressive gait freezing (PSP-PGF)
c. PSP-ocular motor (PSP-OM)

3. Cortical variants:
a. PSP-corticobasal syndrome (PSP-CBS)
b. PSP-frontal variant (PSP-F)
c. PSP-speech/language disorder (PSP-SL)
d. PSP-progressive non-fluent aphasia (PSP-PNFA)

4. Other variants:

Patients with PSP, unlike Parkinson's Disease, tend to present with early onset of postural instability and falls, supranuclear vertical gaze palsy and frontal lobe cognitive dysfunction (impaired planning, execution, inhibition and behaviour). There tends to be poor response to levodopa and usually develop progressive decline in mobility (often needing a wheelchair), dysphagia, dysarthria (pseudobulbar palsy), constipation and urinary incontinence. Tremors and rigidity tend to be asymmetric (axial >limbs) and not necessarily purely resting tremors. Eye involvement initially

presents with supranuclear vertical gaze palsy in the form of inability to look down and falling when going downstairs, followed by broken pursuits, vertical saccades, squarewave jerks, and eventually ophthalmoplegia. Cerebellar involvement can also be present, due to the involvement of superior cerebellar peduncles.

There is significant overlap in clinical presentation with Parkinson's Disease and other disorders classified under Atypical Parkinsonism – Corticobasal degeneration, Lewy Body Dementia, Multiple System Atrophy. These should all be considered under the differential diagnoses.

MRI imaging can help in favouring PSP over alternative clinical diagnoses, but is usually accurate only in classical cases. MRI features include:

1. Midbrain Atrophy:
a. Raised MR Parkinsonism Index (MRPI)
b. Reduced midbrain-to-pons area ratio to approximately 0.12 (normal ~ 0.24) – most accurate imaging feature which also helps to distinguish it from MSA-P.
c. Reduced midbrain-to-pons width ratio to <0.52.
d.Midbrain Width: reduced in the midline sagittal plane to <9.35 mm.
e.Hummingbird Sign (Penguin Sign): Flattening or concave outline to the superior aspect of the midbrain which should be upwardly convex.
f. Mickey Mouse Sign: Reduction of anteroposterior midline midbrain diameter, at the level of the superior colliculi on axial imaging, to <12 mm
g. Morning Glory Sign: loss of the lateral convex margin of the tegmentum of midbrain.

2. Atrophy of other structures:
a. Pontine tegmentum
b. Superior cerebellar peduncles

3. T2: diffuse high-signal lesions in:
a. Pontine tegmentum
b. Tectum of the midbrain
c. Inferior Olivary Nucleus

Treatment is aimed at symptomatic improvement, and usually includes levodopa combination therapy, although response may be limited in cases of Atypical Parkinsonism like PSP. Novel therapies that target tau-protein in various ways are currently under research. These approaches may offer new hope for slowing down the progression of PSP.

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TABLE 1:

Level of certainty	Ocular motor dysfunction	Postural instability	Akinesia	Cognitive dysfunction
Level 1	O1: Vertical supranuclear gaze palsy	P1: Repeated unprovoked falls within 3 years	A1: Progressive gait freezing within 3 years	C1: Speech/language disorder, i.e., nonfluent/agrammatic variant of primary progressive aphasia or progressive apraxia of speech
Level 2	O2: Slow velocity of vertical saccades	P2: Tendency to fall on the pull-test within 3 years	A2: Parkinsonism, akinetic-rigid, predominantly axial, and levodopa resistant	C2: Frontal cognitive/behavioral presentation
Level 3	O3: Frequent macro square wave jerks or "eyelid opening apraxia"	P3: More than two steps backward on the pull-test within 3 years	A3: Parkinsonism, with tremor and/or asymmetric and/or levodopa responsive	C3: Corticobasal syndrome

HYPERTENSION IN AN ADOLESCENT AS A MANIFESTATION OF IgG4-RELATED DISEASE

Yashwin Tejas, 2021 Batch

Abstract

IgG4-related disease (IgG4-RD) is an idiopathic, chronic, fibroinflammatory autoimmune condition, which was first identified in 2001, characterised by the tendency to form tumefactive lesions, and with male-to-female ratio of 3:1. Commonly affected organs include pancreas, biliary tract, major salivary glands, periorbital tissues, kidneys, lungs, lymph nodes and retroperitoneum. IgG4 is the least abundant subclass of IgG, playing a role in the activation of antibody-dependent immune effector responses. Raised serum IgG4 levels occur in healthy individuals and in response to various stimuli, including allergens, parasites, autoimmune reactions, and malignancy. Due to its multiorgan involvement, it mimics several other pathologies (e.g. sarcoidosis). In 2019, the American College of Rheumatology/European League Against Rheumatism (ACR/EULAR) published a diagnostic criteria checklist for IgG4-related disease. It is important to correlate the clinical, serologic, radiologic and pathologic findings to rule out more common differential diagnoses. Glucocorticoids are the first line of therapy, although immunotherapy may be required for those with relapsing or glucocorticoid-resistant disease.

Keywords: IgG4-related disease, autoimmune pancreatitis, retroperitoneal fibrosis, Mikulicz's disease, pseudotumour, aortitis.

INTRODUCTION:

In human serum, immunoglobulin G4 (IgG4) is the least abundant subclass of IgG. The main roles of IgG4 include activation of the antibody-dependent immune effector response and a blocking effect on the immune response or the IgG4 target protein. The normal serum levels of IgG4 range from <10 mg/dL to 140 mg/dL, but levels <200 mg/dL have been identified in healthy individuals without active inflammatory disease. IgG4 levels can also be elevated in response allergens and parasites, autoimmune responses, and malignancy. In 2001, Hamano and colleagues described 20 patients in Japan with autoimmune sclerosing pancreatitis (currently termed as Type 1 Autoimmune Pancreatitis) and high serum levels of IgG4, which they identified as IgG4-related disease. Subsequently, cases with elevated IgG4 levels were found to be associated with diverse organ involvement, including submandibular sialadenitis, Riedel's thyroiditis, idiopathic retroperitoneal fibrosis and Mikulicz syndrome – all with similar histopathology, including the presence of IgG4-positive plasma cells.Patients usually present with the disease in the fifth to sixth decade of life,

, with male preponderance. However, the following patient was diagnosed with the disease as an adolescent, and with an unusual clinical presentation.

CASE REPORT:

A 17-year-old male school student, who was a known hypertensive, presented with complaints of: blood-tinged urine for past 2 days – not associated with fever, dysuria, decreased urine output, or pain (suprapubic, loin or backpain).

The patient was diagnosed with hypertension 2 years ago, when he had presented to the OP at a local government hospital with complaints of headache, nausea, vomiting, along with angina-type chest pain and acute dyspnoea (NYHA grade IV) – and was subsequently diagnosed with hypertensive cardiac failure with acute pulmonary edema, for which treatment was initiated.

Examination was unremarkable. Ultrasound and Doppler of the renal arteries showed stenosis of the right renal artery (hence angiotensin receptor blockers were not recommended for hypertension control). ESR and CRP levels were elevated. Urine analysis, electrolyte concentration, thyroid profile, endocrine workup (cortisol, metanephrines, aldosterone-renin ratio, VMA, 5-HIAA) were found to be normal.

USG Abdomen and Renal Artery Doppler showed mild enlargement of both kidneys with stenosis of right renal artery. CT Abdomen showed retroperitoneal thickening with encasement of renal arteries.

Immunological profile showed elevated levels of IgG4 antibodies. ANA profile, Rheumatoid Factor, anti -CCP, ANCA, lupus anticoagulant, cardiolipin and beta-2-glycoprotein profile were negative.
Based on radiologic and serologic evidence, the patient was diagnosed with IgG4-related disease. Subsequently he was started on prednisolone tablets (30mg/day) along with anti-hypertensive medication.

DISCUSSION:

IgG4-related disease is an idiopathic, chronic, fibroinflammatory condition, with multiorgan involvement – the most common being pancreas, hepatobiliary tree, major salivary glands, lungs, kidneys, lymph nodes and retroperitoneum, with characteristic tendency to form tumefactive lesions ('pseudotumours'). The symptoms are organ- specific, along with significant association with allergic features (atopy, eczema, asthma, nasal polys, sinusitis) and moderate peripheral eosinophilia. Chronic organ involvement can lead to organ failure, while destructive bone lesions in the head, paranasal sinuses and middle ear cleft can mimic granulomatosis with polyangiitis (Wegner's Granulomatosis). Due to the wide spectrum

of clinical presentation, it mimics various other systemic granulomatous disorders (e.g. sarcoidosis, disseminated tuberculosis), infections (e.g. abscesses), autoimmune disease (e.g. Sjogren syndrome), vasculitides (Wegner's Granulomatosis, Churg-Strauss Disease), and organ-specific tumours. Some patients undergo major surgeries (e.g. Whipple's Procedure, thyroidectomy) for purpose of tumour resection, before the correct diagnosis is identified.

However, the pathologic findings are consistent across all affected organs. These findings include lymphoplasmatic infiltrate with a high percentage of IgG4-positive plasma cells, characteristic 'storiform' pattern of fibrosis, obliterative phlebitis, and a mild to moderate eosinophilia. The inflammatory lesions tend to aggregate around ducts of glands, and often aggregate into tumefactive masses that cause destruction solid organs. The inflammatory infiltrate is composed of an admixture of B and T lymphocytes. B-cells are typically organised in germinal centers, while plasma cells (CD19, CD138, IgG4+) radiate outwards. T-cells (CD4+) are distributed more diffusely. Fibroblasts, histiocytes, and eosinophils are also found in moderate numbers. The number of IgG4-positive plasma cells can be quantified by either counting the number of cells per high-power field (HPF), or by calculating the ratio of IgG4 to IgG-bearing plasma cells. Tissue fibrosis of 'storiform' pattern predominates in the latter phases of organ involvement. Serological examination reveals elevated levels of IgG4 and IgE antibodies, decreased levels of complement factors (C3 and C4), along with raised plasma cell count and peripheral eosinophilia. However, assays can show false low-levels due to prozone effect, which can be corrected by dilution of the plasma sample.

Next-generation sequencing studies of CD4+ effector cells have demonstrated unique CD4+ cytotoxic T-cells, which are found at disease sites. These cells release interferon-gamma, T-cell growth factor-beta, and interleukin-1, all of which may contribute to storiform fibrosis. They also elaborate perforin, granzyme A and B, and granulysin, which cause cytotoxicity. Oligoclonal expansion of plasmablasts are also seen. IgG4-related disease is reported to present in patients in their fifth to seventh decades of life, with male predominance, including pancreaticobiliary disease and retroperitoneal disease, whereas IgG4-related disease limited to the head and neck most commonly affects women.

The clinical features are organ-specific and are as follows:

1. Pancreas: Type 1 Autoimmune Pancreatitis, obstructive jaundice & 'sausage-shaped' pancreas on imaging
2. Liver and Biliary Tree: Sclerosing Cholangitis, obstructive jaundice & steatorrhoea
3. Kidneys: Tubulointerstitial Nephritis & Membranous Glomerulonephritis (rare)

4. Lungs: inflammatory pseudotumour, paravertebral mass, central airway disease, pleural lesions and effusion
5. Retroperitoneum: Lower backpain, hydronephrosis & lower limb edema
6. Aorta: Lymphoplasmatic Periaortitis, abdominal aneurysm & aortic dissection
7. Thyroid Gland: Reidel's Thyroiditis & fibrosing variant of Hashimoto's Thyroiditis
8. Lymph Nodes: Generalised non-tender lymphadenopathy
9. Orbit and Periorbital tissues: Painless periocular swelling, orbital pseudotumour, dacryoadenitis, dacryocystitis & orbital myositis
10. Salivary Glands: Submandibular and/or Parotid gland enlargement
11. Ear, Nose and Paranasal Sinuses: Allergic phenomena, rhinorrhoea, sinusitis & bone destructive lesions (rare)
12. Meninges: Mass lesions, headache, radiculopathy & cranial nerve palsies
13. Hypothalamus and Pituitary Glands: anterior pituitary hormone deficiency, central diabetes insipidus & lymphocytic hypophysitis

The revised Japanese Comprehensive Clinical Diagnostic (CCD) criteria for IgG4-related disease comprises of three domains: clinical and radiological features, serological diagnosis, and histopathology, which now include three further criteria, including the histological identification of storiform fibrosis and obliterative phlebitis

However, none of the criteria described are diagnostic for any specific chronic inflammatory disease, which is a significant challenge for the identification of IgG4-related disease.

The ACR and EULAR criteria comprises a three-step classification process for IgG4-related disease – the involvement of at least one of eleven possible organs with a characteristic presentation, application of exclusion criteria (32 clinical, laboratory, imaging, and histopathologic findings), and eight weighted inclusion criteria are required, including clinical findings, laboratory results, imaging assessments, and histopathology results. Periaortic chronic inflammation and fibrosis, with or without aortic dilatation ('inflammatory aneurysm') and ureteric involvement, is included in the current classification of IgG4-related disease involving the retroperitoneum. chronic periaortitis is described, based on histopathological and imaging findings, as the triad of aortic atherosclerosis, medial thinning, and adventitial chronic inflammation consisting of lymphoplasmacytic infiltrates, lymphoid follicles, and varying degrees of fibrosis. Vital organ involvement (e.g. liver, kidney, pancreas, thyroid) must be treated aggressively due to risk of organ failure. Glucocorticoids are the first-line therapy, beginning with 40 mg/day of prednisolone, followed by tapering or maintenance dose of 5mg/day.

Conventional disease-modifying

antirheumatic drugs (DMARDs) can be combined with glucocorticoids for induction therapy. Relapse is common and there is significant risk of steroids-induced morbidity.

In such cases, Rituximab (anti-CD20 monoclonal antibody) helps in rapid decrease of IgG4 antibody concentration. Methotrexate and Azathioprine can also be used in severe cases. Novel strategies include inhibition of Bruton's Tyrosine Kinase (BTK), depletion of CD19+ B-cells, and targeting of SLAM-F7 molecule on surface of both B-cells and CD4+ cytotoxic T-cells.

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THE FINAL COUNTDOWN – AN UNSUSPECTING PRESENTATION OF STAGE 4 HIV/AIDS

Aarav Joshua Paul, 2024 Batch

Abstract

Stage 4 of HIV/AIDS, considered the last phase of infection after which death remains likely in untreated cases, is a grave condition which is difficult to manage due to high viral load and opportunistic infections involved. Caused by the Human Immunodeficiency Virus, the name implies that the virus thrives by diminishing the host's immune capabilities to subvert both the infection of the virus itself as well as external ones. These external infections manifest with a variety of symptoms. Often times, patients may not present with these typical symptoms and may be incidentally found to be HIV positive during screening. Here we present a case of Stage 4 HIV/AIDS, who presented with pericardial effusion and interstitial pancreatitis.

Keywords: Stage 4 HIV/AIDS, pericardial effusion, opportunistic infections, antiretroviral therapy, toxoplasmosis, primary CNS lymphoma

INTRODUCTION:

HIV/AIDS is one of the most serious and difficult to manage clinical conditions globally. With improved antiretroviral therapy and public health interventions, there has been a reduction in new infections and mortality, currently estimated at approximately 1.3 million new infections and 630,000 deaths annually worldwide [1]. Stage 4 HIV corresponds to the advanced clinical stage of infection, characterized by profound CD4 depletion and high viral burden, spiralling into a compromised immune state leaving death the eventual outcome [2].

Two major classifications exist for the grading of HIV, one being the WHO clinical classification and the other being the CDC criteria. The WHO criteria, split into 4 stages, is based on clinical symptomatic staging purposefully designed for low-income countries where CD4 counts are difficult to reproduce routinely for testing every suspected case [2].

The final stage is comprised of symptoms such as Slim disease (HIV wasting syndrome), presence of HIV associated cancers such as Kaposi sarcoma, hairy cell leucoplakia and opportunistic infections [2]. The CDC criteria is divided into 3 stages based on the CD4 count of the host, with AIDS being the last stage characterised by a count of < 200/mm3 [3].

The advent of better antiretroviral therapy is helping us combat with the ongoing pandemic against AIDS complementary to more strategic screening efforts. This leaves us with an increased number in persons

living with HIV (PLHIV) due to the increased longevity of patients [1].As a result of this, there is an increase in disease burden in the global population. With deeper study into the various manifestations of the infection at different stages of disease, we begin to understand that the observed symptoms can be either caused by associated conditions discussed above or by virtue of the virus itself (HIV induced encephalitis) [1,4].

This stage is associated with many incidental infections as mentioned above, the intuitively named "opportunistic infections", which include but are not limited to Pneumocystis jirovecii pneumonia, tuberculosis, cryptococcosis, toxoplasmosis, and cytomegalovirus infection [5,6]. However, patients may also present with atypical manifestations involving cardiovascular or other organ systems [7]. Early diagnosis and timely initiation of antiretroviral therapy are essential to reduce progression and improve survival [1]. Discussed below is the case of a 38-year-old adult male, who came to us with only the chief complaints of abdominal pain, found to have moderate pericardial effusion and interstitial pancreatitis and was incidentally diagnosed HIV/AIDS positive

CASE REPORT:

A 38-year-old male patient presented to our outpatient department with the complaints of diffuse abdominal pain for nearly 2 months accompanied by easy fatiguability. He had no other complaints and other history was found to be insignificant even after probing. While examining the patient for vitals, it was found that they were all within the normal ranges. The patient was conscious and oriented and was afebrile at the time of examination. He was of a very thin build, notably pale and had insignificant systemic findings apart from the fact that his abdomen was distended.

As part of the routine investigations done on admission, a complete blood count (CBC) was ordered which revealed pancytopenia (refer Table 1 for values), accompanied by decreased Hemoglobin (80 gm/L). The peripheral smear showed dimorphic anemia, leukocytosis and thrombocytopenia, thus confirming the clinical findings and establishing pancytopenia as part of the provisional diagnosis. An ultrasound B mode scan indicated ascites with mild splenomegaly. The first of two significant findings came via imaging; a moderate pericardial effusion and interstitial pancreatitis as confirmed by echocardiography and contrast emission computed tomography (CECT) respectively.

Given the exceedingly low platelet count on the CBC (50 x 109/L) and thus pancytopenia, platelet and packed cell transfusion was

indicated. As part of routine blood screening tests for HIV, Hepatitis B Surface Antigen (HBsAg), Hepatitis C (HCV), syphilis and malaria was done, and he was found to be HIV positive. The ensuing CD4 cell count revealed the count to be only 34 cells per mm3, which indicated that the patient was at the end stage of HIV infection of clinical stage 4 HIV/AIDS. Regardless, the packed cells and platelets were transfused and the patient's blood counts were normalized. In spite of advice given to him, he refused any antiretroviral treatment, and he was subsequently discharged.

20 days after discharge, the same patient was brought unconscious and admitted to our neurosurgery department; based on history provided by the attender he had suddenly fallen unconscious and was subsequently rushed to the hospital. While admitted, a head CT scan revealed multiple space occupying lesions in the brain. Unfortunately, before any further treatment could be initiated, the patient succumbed to the severity of the disease the following day. Despite prompt and appropriate resuscitation efforts including advanced life support measures, the patient could not be revived.

Discussion:

HIV/AIDS is more often than not associated with poor outcomes, as almost all infected patients succumb due to the disease or complications caused by it. However, death is frequently caused by the latter, and is usually clinically apparent both via the symptoms of the patient as well as through investigation findings [5,6].

The above case represents an atypical presentation of Stage 4 HIV/AIDS, in which multiple seemingly unrelated clinical manifestations were observed. A comparable instance of respiratory distress secondary to HIV-associated cardiomyopathy has been reported [7]; however, in our patient, the predominant cardiac finding was pericardial effusion, which may have been contributed to by pancytopenia noted during evaluation. Pericardial effusion is a recognized manifestation in HIV infection, particularly in severely immunosuppressed patients with low CD4 counts with causes that include Kaposi sarcoma, immune dysregulation, and inflammatory effusions [8]. Although our patient remained asymptomatic from a cardiovascular standpoint, such cases may progress to cardiac tamponade [9]. Antiretroviral therapy has significantly reduced the incidence of these complications but has not completely eliminated them [1].

We also identified reports of HIV-associated chronic pancreatitis with pseudocyst formation and splenic rupture [10]; in comparison, our patient demonstrated splenomegaly along with interstitial

pancreatitis, with abdominal pain as the only presenting symptom. Pancreatitis in HIV-infected individuals has been reported as an adverse effect of certain antiretroviral therapies [11], particularly in cases presenting with nonspecific abdominal pain unrelated to alcohol or gallstone disease.This is supported by a documented case of didanosine-tenofovir induced pancreatitis, which resolved after drug withdrawal [11]. In our scenario, the patient refused to take antiretroviral medication, which implies that the pancreatitis present may have been due to some other etiology, possibly by hypothesised mechanisms described in other papers described as the "pancreas – spleen" axis, which may be the driving force behind this combination of pathologies [10].

While existing literature documents pericardial effusion and pancreatitis separately in HIV infection, no reported cases describe the coexistence of both pericardial effusion and interstitial pancreatitis in the same patient either simultaneously or at different stages of disease. This highlights the importance of maintaining a high index of suspicion in patients with multisystem involvement.

The incidental detection of HIV infection during transfusion screening emphasizes the importance of diagnostic testing [12]. Early identification improves prognosis, as timely initiation of antiretroviral therapy significantly improves survival and quality of life [1]. Modern antiretroviral regimens have reduced mortality and increased life expectancy among PLHIV [1]. This is well demonstrated by the success of WHO's first line treatment regimen for newly diagnosed patients via the Tenofovir, Lamivudine and Dolutegravir (TLD) therapy [13]. Additional drugs such as Emtricitabine have also shown success and are indicated in HIV-Hepatitis B co-infection as well as post exposure prophylaxis of HIV, albeit with multiple side effects [13]. Other newer regimens also have lower rates of adverse reactions including that to pancreatitis compared to earlier therapies [14], though continued pharmacovigilance is necessary. Patients must be convinced at maximum to accept treatment, but at the same time the autonomy of the patient must always be upheld except in very rare scenarios or special circumstances.

Globally, tuberculosis remains the leading cause of mortality in advanced HIV/AIDS [15]. In this case, the space occupying brain lesions were most likely suggestive of toxoplasmosis-related infection contributing to the fatal outcome [16]. However, similar radiological findings may also be seen in primary CNS lymphoma, which can mimic toxoplasmosis and vice versa, complicating diagnosis [17]. Delay in diagnosis can be fatal. Management focuses on reducing raised intracranial pressure to prevent herniation and its complications, along with targeted antimicrobial or oncological therapy depending on the cause [16,17].

Future implications include a deeper understanding into stage 4 HIV/AIDS, its complications and improved strategies to detect the condition earlier. Medical practitioners can also benefit from better imaging techniques that can help guide them to a faster diagnosis, thus improving the standard of healthcare in helping patients cope with this calamitous infection.

CONCLUSION:

This case highlights the atypical and multisystemic presentation of advanced HIV/AIDS, where seemingly unrelated clinical features may coexist. Pericardial effusion is a common presentation in such patients, as seen in the above case and multiple others. Pancreatitis of atypical etiology in an HIV-positive patient may indicate profound immunosuppression and advanced disease, including severely low CD4 counts. This finding may also be correlated with incidence of spleen related pathologies, warranting investigations to confirm the same.

Patients with Stage 4 HIV/AIDS may develop symptoms caused by sudden central nervous system involvement due to opportunistic infections or malignancies. Therefore, rapid differentiation of the underlying cause is essential for timely treatment and improved outcomes. Refusal of treatment, if the patient demands so must be respected, but at the maximum they must be convinced by explaining the advantages and disadvantages of therapy. Improvements in screening techniques and policies can help reduce disease burden in society. Further improvements in medication and investigations are imperative for controlling the rapid rate of progression seen if the condition is left unchecked.

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Table 1 – Laboratory Investigation Findings

Variable	Value	Reference range
White Blood Cell count (10^9/L)	3.4	4.0—10.0
Haemoglobin (g/L)	80	131—172
Platelet count (10^9/L)	50	100—300
Urea (mg/dL)	26	15–40
Creatinine (mg/dL)	1.2	0.7–1.3
Uric acid (mg/dL)	7.6	3.4–7.0
Sodium (mEq/L)	141	135–145
Potassium (mEq/L)	3.7	3.5–5.0
Lactate dehydrogenase (U/L)	318	140–280
Serum ferritin (ng/mL)	254	30–400
RPI	0.86	1.0–2.0

RPI – Reticulocyte Proliferation Index

THREE FACES OF SELF-DESTRUCTION: A CASE SERIES OF WARM, COLD, AND MIXED AUTOIMMUNE HEMOLYTIC ANEMIA

Mohammed Thaha, 2024 batch

Abstract

Autoimmune hemolytic anemia (AIHA) is an immune-mediated condition in which red blood cells are destroyed by autoantibodies. It is classified as warm, cold, or mixed based on the antibody involved. The clinical presentation ranges from mild anemia to severe hemolysis, and it may occur as a primary disease or secondary to infections, autoimmune disorders, or hematological malignancies. Diagnosis depends on clinical findings along with immunohematological tests, specifically the direct antiglobulin test (DAT). We report three patients with different types of AIHA. The first patient was a 58-year-old woman who presented with severe anemia, low blood counts, and hepato-spleenomegaly. Her blood tests showed cold agglutinins and a positive direct antiglobulin test, and further evaluation revealed B-cell acute lymphoblastic leukemia, confirming secondary cold AIHA. The second patient was a 55-year-old woman who presented with anemia, jaundice, and evidence of hemolysis, and she was diagnosed with warm AIHA. The third patient was an 18-year-old woman who presented with severe anemia and splenomegaly. Her blood tests showed both warm and cold antibody activity, and she was diagnosed with mixed AIHA. All three patients were treated with appropriate therapy and supportive care, with clinical and hematological improvement. This case series shows the different ways AIHA can present and highlights the need for detailed immunohematological testing to identify the exact type. It also shows the importance of looking for an underlying cause, since this helps guide treatment and improves outcome.

Keywords: autoimmune hemolytic anemia, AIHA, direct antiglobulin test, hemolysis, cold agglutinins, immunohematology.

INTRODUCTION:

Autoimmune hemolytic anemia (AIHA) is an immune-mediated condition in which red blood cells are destroyed by autoantibodies. It is classified into warm, cold, and mixed types based on the type of antibody involved and the temperature at which it reacts [1]. Warm AIHA is the most common form and is mediated by IgG antibodies [2], whereas cold AIHA is mediated by IgM antibodies that activate complement-mediated immunity [3]. Mixed AIHA has features of both warm and cold antibody activity, making it a distinct but less common subtype [4].

The clinical presentation of AIHA is often similar across all types, with patients presenting with anemia, jaundice, and laboratory evidence of hemolysis . However, identifying the exact subtype is challenging, as routine investigations do not clearly differentiate between them [5]. The direct antiglobulin test is the key diagnostic test,

but further evaluation with monospecific testing and cold agglutinin studies is often required for accurate classification [6].

AIHA may occur as a primary condition or secondary to an underlying disorder, and identifying the clinical etiology is important in patient evaluation. Secondary causes commonly include autoimmune diseases, lymphoproliferative disorders, infections, and drug exposure [7]. Warm AIHA is more frequently associated with autoimmune conditions such as systemic lupus erythematosus and with hematological malignancies, particularly lymphoproliferative disorders [2]. Cold AIHA is often linked to infections such as Mycoplasma pneumoniae and Epstein-Barr virus, as well as clonal B-cell disorders [8]. Drug-induced immune hemolytic anemia is also an etiology in which medications can induce antibody formation against red blood cells through immune-mediated mechanisms, with commonly implicated medications including beta-lactam antibiotics and chemotherapeutic drugs [9]. Mixed AIHA may be associated with autoimmune diseases, infections, or malignancies, but is often under-recognized due to overlapping clinical and serological features, which can delay diagnosis and management [10]. Distinguishing between warm, cold, and mixed AIHA is important because the underlying cause and management differ between subtypes.

This series highlights the importance of careful immunohematological evaluation and the need to identify the subtype and any underlying cause for appropriate management. In this case series, we report three patients representing three different types of AIHA. The first patient had cold AIHA secondary to B-cell acute lymphoblastic leukemia. The second patient had warm AIHA. The third patient had mixed AIHA.

CASE REPORT:

Case 1: Cold Autoimmune Hemolytic Anemia

A 58-year-old female presented with complaints of easy fatigability and breathlessness on exertion for seven days. There was no other significant history. On clinical examination, the patient had pallor and icterus along with hepatosplenomegaly. There was no generalized lymphadenopathy.

Laboratory investigations revealed severe anemia with a hemoglobin level of 3.7 g/dL, leukopenia with a total leukocyte count of 1.6 × 10^3/µL, and thrombocytopenia with a platelet count of 37 × 10^3/µL, suggesting pancytopenia. Red cell indices at presentation showed an MCV of 86.3 fL, MCH of 26.7 pg, and MCHC of 31.0 g/dL. These findings were consistent with a dimorphic anemia. Liver function tests showed hyperbilirubinemia, with a total bilirubin of 4.1 mg/dL, direct bilirubin of 1.6 mg/dL, and indirect bilirubin of 2.5 mg/dL, suggestive of hemolysis. The erythrocyte sedimentation rate was elevated (Table 1).

Further work up showed a positive direct antiglobulin test (DAT) with cold agglutinins. DAT specificity showed C3d positivity, consistent with cold agglutinin disease. Screening for HIV and VDRL was negative. Renal function tests and serum electrolytes were within normal limits.

Peripheral smear showed microcytic hypochromic anemia with anisopoikilocytosis, along with normocytic normochromic red blood cells, suggesting dimorphic anemia. Viral markers and ANA were negative. Thyroid profile was within normal limits, and serum folate level was 7.25 ng/mL. Imaging showed hepatomegaly on ultrasonography, and CT of the chest revealed left lower lobe consolidation, suggesting active pulmonary infection.

In view of the pancytopenia and hepatosplenomegaly, bone marrow evaluation was performed. Bone marrow biopsy showed increased blasts with grade 3 marrow fibrosis. Based on these findings, a diagnosis of B-cell acute lymphoblastic leukemia (B-ALL) was made. Serum protein electrophoresis was normal, with no monoclonal band, excluding monoclonal gammopathy-associated cold agglutinin disease. These findings supported a diagnosis of secondary cold agglutinin disease associated with B-ALL.

The patient was treated with oral prednisolone at a dose of 1 mg/kg/day, along with a single dose of intravenous rituximab. In view of severe anemia, she received transfusion of 3 units of packed red blood cells. Supportive treatment included injectable vitamin B12 (1000 mcg), oral folic acid, B-complex tablets, albendazole, and paracetamol.

On follow-up, hematological improvement was noted. The reticulocyte count increased from 0.65% at presentation to 4.59%, indicating marrow recovery. Red cell indices also stabilized, with MCV increasing from 86.3 fL to 91.9 fL, MCH from 26.7 pg to 28.1 pg, and MCHC maintained around 30-31 g/dL, reflecting improvement in erythropoiesis.

Case 2: Warm Autoimmune Hemolytic Anemia

A 55-year-old female presented with complaints of easy fatigability for 20 days, bilateral lower limb swelling for 20 days, and progressively worsening breathlessness for one week, corresponding to New York Heart Association class III. She also reported yellowish discoloration for one week and hematuria. There was no history of fever, giddiness, or palpitations. She was not a known case of hypertension, diabetes mellitus, chronic obstructive pulmonary disease, bronchial asthma, or epilepsy.

On examination, the patient was conscious and oriented. Pallor and icterus were present, along with bilateral pedal edema. Oxygen saturation was 93% on room air, and

she was afebrile. Systemic examination was normal. Ultrasonography of the abdomen showed no significant abnormalities.

Laboratory investigations revealed severe anemia with a hemoglobin level of 5.6 g/dL, a total leukocyte count of 5.2×10^3/µL, and a platelet count of 2.6×10^5/µL. Red cell indices showed macrocytosis, with an MCV of 112 fL and MCH of 35.7 pg, along with an elevated red cell distribution width of 21%. Peripheral smear showed anisocytosis, macrocytes, schistocytes, elliptocytes, and pencil cells . Iron studies showed reduced serum iron (36 µg/dL), elevated total iron-binding capacity (352 µg/dL), and transferrin saturation of 23%. Vitamin B12 level was 214 pg/mL. The macrocytosis despite iron deficiency is explained by reticulocytosis, as reticulocytes are larger cells (Table 2).

Further evaluation revealed a reticulocyte count of 26.36% and elevated lactate dehydrogenase (LDH) of 381 U/L, indicating ongoing hemolysis. Serum bilirubin was elevated, with a total bilirubin of 3.06 mg/dL and direct bilirubin of 0.82 mg/dL. Liver enzymes (AST/ALT) were within normal limits. Renal function tests showed urea levels ranging from 26-33 mg/dL and creatinine levels between 0.6-0.8 mg/dL. Coagulation parameters, including PT (13.7 seconds) and INR (1.17), were within normal limits. Direct antiglobulin test (DAT) was positive for IgG. Urine examination showed no significant abnormalities.

Based on the positive DAT, elevated reticulocyte count, raised LDH, and hyperbilirubinemia, the patient was diagnosed with warm autoimmune hemolytic anemia. She was treated with oral prednisolone at a dose of 1 mg/kg/day, packed red blood cells and folic acid supplementation.

Case 3: Mixed Autoimmune Hemolytic Anemia

An 18-year-old female presented with complaints of breathlessness on exertion for 10 days and fever for two days. She also had a history of cough with yellow-colored sputum for 10 days, which was non-foul-smelling. Her menstrual cycles were regular, with menorrhagia in each cycle. On general examination, the patient was conscious and oriented, with severe pallor. Her pulse rate was 112/min, suggesting tachycardia. Other vital signs were within normal limits. Abdominal examination was soft, with splenomegaly. Systemic examination was otherwise normal. Ultrasonography of the abdomen showed mild splenomegaly.

Laboratory investigations revealed severe hypochromic microcytic anemia with a hemoglobin level of 4.2 g/dL. Liver function tests showed a total bilirubin of 1.2 mg/dL, direct bilirubin of 0.4 mg/dL, and indirect bilirubin of 0.9 mg/dL. Red cell indices showed an MCV of 84 fL, MCH of 17 pg, and MCHC of 20 g/dL. Peripheral smear showed

microcytic hypochromic red cells with anisopoikilocytosis, elliptocytes, tear drop cells, and polychromatophils. Reticulocyte count was 3.5%. Platelet count was 2.92 × 10^5/µL. LDH was 146 IU/L. Renal function tests, electrolytes, thyroid profile, and urine analysis were within normal limits. An iron deficiency component was considered in view of the microcytic hypochromic anemia and history of menorrhagia.(Table 3)

Immunohematological evaluation confirmed the diagnosis. Blood grouping showed O Rh D positive status. DAT was positive, with monospecific testing showing both IgG and C3d positivity. Indirect antiglobulin test was positive, and antibody screening with eluate showed panagglutination. Autocontrol was positive at 4°C, 22°C, and 37°C, with a cold antibody titer of 1:128. Further evaluation showed a positive antinuclear antibody (ANA) with a cytoplasmic pattern and strong 3+ intensity, suggesting an underlying autoimmune predisposition. Based on these findings, the patient was diagnosed with mixed autoimmune hemolytic anemia.

The clinical presentation was likely precipitated by a recent respiratory tract infection, for which she received azithromycin. She was treated with oral prednisolone at an initial dose of 100 mg/day, given as 50 mg in the morning, 25 mg in the afternoon, and 25 mg in the evening, for the first five days. This was subsequently tapered to 40 mg/day in divided doses of 20 mg in the morning and 20 mg in the afternoon. She also received azithromycin 500 mg once daily, ranitidine 150 mg, and intravenous iron sucrose 200 mg diluted in normal saline. Trimethoprim-sulfamethoxazole (480 mg) was administered twice weekly as prophylaxis. During hospitalization, she showed hematological improvement, with hemoglobin rising to 6.3 g/dL, MCV to 82.4 fL, MCH to 21 pg, MCHC to 25.6 g/dL, and platelet count to 3.65 × 10^5/µL after four days of therapy

The patient improved clinically and hematologically during the hospital stay. At discharge, she was conscious, afebrile, hemodynamically stable, non-dyspneic, and adequately hydrated. She was advised to continue oral prednisolone 50 mg/day. Trimethoprim-sulfamethoxazole 480 mg was prescribed twice weekly. She was also prescribed oral iron supplementation, along with ranitidine and calcium. She was advised to follow an iron-rich diet and regular follow-up for monitoring of hemoglobin levels and disease activity.

DISCUSSION:

Autoimmune hemolytic anemia (AIHA) is an immune mediated disorder characterized by premature destruction of red blood cells [5]. It is classified into warm, cold, and mixed subtypes based on the type of autoantibody and thermal reactivity, which has implications for diagnosis and

management, as each subtype differs in its pathophysiology, site of hemolysis, associated conditions, and response to therapy [6].

Warm AIHA is mediated by IgG antibodies and results in extravascular hemolysis, predominantly in the spleen. Whereas cold AIHA is mediated by IgM antibodies with complement activation, leading to hemolysis that may be intravascular or extravascular. Mixed AIHA involves coexistence of warm autoantibodies and complement mediated hemolysis, resulting in complex serological findings [6]. Complement mediated red cell destruction plays a significant role, particularly in cold and mixed AIHA [7].

Diagnosis requires integration of clinical and laboratory findings. The direct antiglobulin test is the primary diagnostic tool for AIHA. Additional laboratory findings include anemia, reticulocytosis, elevated lactate dehydrogenase, indirect hyperbilirubinemia, and reduced haptoglobin [5]. Cold agglutinin titers and thermal amplitude testing are useful in suspected cold and mixed AIHA, while monospecific DAT helps differentiate IgG and complement mediated hemolysis [6].

Cold AIHA is associated with lymphoproliferative disorders and requires evaluation for underlying disease [8]. Drug induced immune hemolysis is another secondary cause that should be considered [9]. Mixed AIHA is less common and may be under recognised due to overlapping serological features. It is characterized by the presence of both IgG antibodies and complement mediated hemolysis [10]. A systematic review has shown that mixed AIHA accounts for a small proportion of cases and is associated with autoimmune conditions and hematological malignancies [11].

Previous studies have reported mixed AIHA presenting with severe hemolysis and diagnostic difficulty. Patients demonstrate both IgG positivity and clinically significant cold agglutinins, contributing to increased hemolysis [12]. Serological studies have shown panagglutination and broad thermal amplitude, which can complicate interpretation of immunohematological testing [13].

In the present series, similar patterns were observed across the three cases. The cold AIHA case demonstrated C3d positivity with cold agglutinins and was secondary to an underlying hematological malignancy (B-cell acute lymphoblastic leukemia), consistent with the known association of cold AIHA with lymphoproliferative disorders [8]. The warm AIHA case showed IgG positivity on DAT with features of extravascular hemolysis and responded to corticosteroid therapy, in line with previous articles [6].

The mixed AIHA case in this series showed both IgG and C3d positivity on monospecific DAT, along with panagglutination and a significant cold agglutinin titer, reflecting the dual pathophysiology described in previous studies [12-13]. The presence of a broad thermal amplitude and positive autocontrol at multiple temperatures further supports the overlap of warm and cold antibody activity. In addition, the association with a positive antinuclear antibody indicates an autoimmune background, as reported in mixed AIHA [11]. Compared to previously reported cases, the mixed AIHA patient in this series also presented with features suggestive of an infectious trigger, which may have contributed to disease onset. The coexistence of iron deficiency features added further complexity to the clinical picture, highlighting the diagnostic difficulty in such cases.

Management of AIHA depends on subtype and severity. In warm AIHA, corticosteroids are the first line treatment and are initiated as prednisolone at a dose of 1 mg/kg/day [6]. Rituximab at a dose of 375 mg/m² weekly for four weeks is used in steroid refractory cases [14]. In cold AIHA, corticosteroids have limited efficacy, and management includes avoidance of cold exposure and treatment of the underlying disorder, with rituximab based therapy used in symptomatic patients [8]. Mixed AIHA requires an individualized approach due to its dual pathophysiology [10], where corticosteroids are initiated but additional therapy such as rituximab may be required for sustained remission [11].

In the present series, the warm AIHA patient showed improvement with corticosteroid therapy alone. The cold AIHA patient required combined management including transfusion and rituximab, along with treatment of the underlying malignancy. The mixed AIHA patient demonstrated hematological improvement with corticosteroids alone.

Taken together, this case series highlights the varied presentations of AIHA and emphasizes the importance of careful immunohematological evaluation. Early identification of the subtype and associated conditions is crucial for guiding treatment and improving outcomes. This series adds to the existing literature by demonstrating the coexistence of all three major AIHA subtypes within a single clinical setting.

CONCLUSION:

Autoimmune hemolytic anemia (AIHA) is an immune-mediated condition in which red blood cells are destroyed by autoantibodies and is classified as warm, cold, or mixed type. It can present with varying severity and may occur as a primary condition or secondary to infections, autoimmune disorders, or hematological malignancies, with diagnosis based on clinical findings

and immunohematological tests, especially the direct antiglobulin test (DAT).

In this case series we report three patients with different types of AIHA. A 58-year-old woman with cold AIHA secondary to B-cell acute lymphoblastic leukemia, a 55-year-old woman with warm AIHA, and an 18-year-old woman with mixed AIHA showing both warm and cold antibody activity. All patients showed clinical and hematological improvement with appropriate therapy. This case series highlights that AIHA can present in different forms and emphasizes the importance of accurate immunohematological evaluation and identification of underlying causes for proper management.

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TABLE 1:

Parameter	Findings	Reference value
Age / Sex	58/F	—
Presentation	Easy fatigability, breathlessness on exertion (7 days)	—
Clinical examination	Pallor, icterus, hepatosplenomegaly; no lymphadenopathy	—
Hemoglobin	3.7 g/dL	12-16 g/dL
Total leukocyte count	1,600 cells/mm³	4,000-11,000 cells/mm³
Platelet count	37,000/mm³	1.5-4.5 × 10^5/mm³
Peripheral smear	Dimorphic picture: microcytic hypochromic + normocytic normochromic RBCs with anisopoikilocytosis	Normal: normocytic normochromic RBCs
Reticulocyte count	0.65% (initial)	0.5-2.5%
Total bilirubin	4.1 mg/dL	0.3-1.2 mg/dL
Direct bilirubin	1.6 mg/dL	0-0.3 mg/dL
Indirect bilirubin	2.5 mg/dL	0.2-0.8 mg/dL
Lactate dehydrogenase	150 U/L	140-280 U/L
DAT (Direct antiglobulin test)	Positive (C3d; IgM-mediated)	Negative
Other immunohematology	Cold agglutinins present	Absent
ANA	Negative	Negative
Imaging / special tests	USG: hepatomegaly; CT chest: left lower lobe consolidation; bone marrow: B-ALL with fibrosis	—
Underlying cause	Secondary to B-cell acute lymphoblastic leukemia	—
Treatment	Prednisolone 1 mg/kg/day + single-dose rituximab + 3 units PRBC transfusion + vitamin B12 (1000 mcg) + folic acid + B-complex + albendazole + supportive care	—

Table 1: Clinical presentation, hematological parameters, biochemical findings, immunohematological profile, underlying cause, and treatment details of the patient with cold autoimmune hemolytic anemia.

TABLE 3:

Parameter	Findings	Reference value
Age / Sex	18/F	—
Presentation	Breathlessness (10 days), fever (2 days), cough with yellow sputum, menorrhagia	—
Clinical examination	Severe pallor, tachycardia, splenomegaly	—
Hemoglobin	4.2 g/dL	12-16 g/dL
Total leukocyte count	Within normal limits	4,000-11,000 cells/mm³
Platelet count	2.92 × 10^5/mm³	1.5-4.5 × 10^5/mm³
Peripheral smear	Microcytic hypochromic RBCs with anisopoikilocytosis, elliptocytes, tear drop cells, polychromatophils	Normal: normocytic normochromic RBCs
Reticulocyte count	3.5%	0.5-2.5%
Total bilirubin	1.2 mg/dL	0.3-1.2 mg/dL
Direct bilirubin	0.4 mg/dL	0-0.3 mg/dL
Indirect bilirubin	0.8 mg/dL	0.2-0.8 mg/dL
Lactate dehydrogenase	146 U/L	140-280 U/L
DAT (Direct antiglobulin test)	Positive (IgG + C3d)	Negative
Other immunohematology	Panagglutination, positive IAT, cold antibody titre 1:128, autocontrol positive at 4°C, 22°C, 37°C	Absent
ANA	Positive (3+)	Negative
Imaging / special tests	Ultrasonography: mild splenomegaly	—
Underlying cause	Primary autoimmune cause	—
Treatment	Prednisolone 100 mg/day (5 days) → tapered to 40 mg/day + azithromycin 500 mg/day + IV iron sucrose 200 mg + TMP-SMX 480 mg (twice weekly) + ranitidine + calcium + oral iron	—

Table 3: Clinical presentation, hematological parameters, biochemical findings, immunohematological profile, underlying cause, and treatment details of the patient with mixed autoimmune hemolytic anemia.

TABLE 2:

Parameter	Findings	Reference value
Age / Sex	55/F	—
Presentation	Easy fatigability (20 days), bilateral pedal edema, breathlessness, jaundice, hematuria	—
Clinical examination	Pallor, icterus, bilateral pedal edema	—
Hemoglobin	5.6 g/dL	12-16 g/dL
Total leukocyte count	5,200 cells/mm³	4,000-11,000 cells/mm³
Platelet count	2.6 lakh/mm³	1.5-4.5 × 10^5/mm³
Peripheral smear	Macrocytes, anisocytosis, schistocytes, elliptocytes, pencil cells (dimorphic picture)	Normal: normocytic normochromic RBCs
Reticulocyte count	26.36%	0.5-2.5%
Total bilirubin	3.06 mg/dL	0.3-1.2 mg/dL
Direct bilirubin	0.82 mg/dL	0-0.3 mg/dL
Indirect bilirubin	2.24 mg/dL	0.2-0.8 mg/dL
Lactate dehydrogenase	381 U/L	140-280 U/L
DAT (Direct antiglobulin test)	Positive (IgG)	Negative
Other immunohematology	No cold agglutinins detected	Absent
ANA	Not done	Negative
Imaging / special tests	Ultrasonography abdomen: normal	—
Underlying cause	Primary autoimmune cause	—
Treatment	Prednisolone 1 mg/kg/day + folic acid + supportive care	—

Table 2: Clinical presentation, hematological parameters, biochemical findings, immunohematological profile, underlying cause, and treatment details of the patient with warm autoimmune hemolytic anemia.

TABLE 4:

Parameter	Case 1: Cold AIHA	Case 2: Warm AIHA	Case 3: Mixed AIHA
Age / Sex	58/F	55/F	18/F
Presentation	Easy fatigability, breathlessness on exertion (7 days)	Easy fatigability (20 days), bilateral pedal edema, breathlessness, jaundice, hematuria	Breathlessness (10 days), fever (2 days), cough with yellow sputum, menorrhagia
Clinical examination	Pallor, icterus, hepatosplenomegaly; no lymphadenopathy	Pallor, icterus, bilateral pedal edema	Severe pallor, tachycardia, splenomegaly
Hemoglobin (12–16 g/dL)	3.7 g/dL	5.6 g/dL	4.2 g/dL
Total leukocyte count (4,000–11,000 cells/mm³)	1,600 cells/mm³	5,200 cells/mm³	Within normal limits
Platelet count (1.5–4.5 × 10^5/mm³)	37,000/mm³	2.6 lakh/mm³	2.92 × 10^5/mm³
Peripheral smear	Dimorphic picture: microcytic hypochromic + normocytic normochromic RBCs with anisopoikilocytosis	Macrocytes, anisocytosis, schistocytes, elliptocytes, pencil cells (dimorphic picture)	Microcytic hypochromic RBCs with anisopoikilocytosis, elliptocytes, tear drop cells, polychromatophils
Reticulocyte count (0.5–2.5%)	0.65% (initial)	26.36%	3.5%
Total bilirubin (0.3–1.2 mg/dL)	4.1 mg/dL	3.06 mg/dL	1.2 mg/dL
Direct bilirubin (0–0.3 mg/dL)	1.6 mg/dL	0.82 mg/dL	0.4 mg/dL
Indirect bilirubin (0.2–0.8 mg/dL)	2.5 mg/dL	2.24 mg/dL	0.8 mg/dL
Lactate dehydrogenase (140–280 U/L)	150 U/L	381 U/L	146 U/L
DAT (Direct antiglobulin test)	Positive (C3d; IgM-mediated)	Positive (IgG)	Positive (IgG + C3d)
Other immunohematology	Cold agglutinins present	No cold agglutinins detected	Panagglutination, positive IAT, cold antibody titre 1:128, autocontrol positive at 4°C, 22°C, 37°C
ANA	Negative	Not done	Positive (3+)
Imaging / special tests	USG: hepatomegaly; CT chest: left lower lobe consolidation; bone marrow: B-ALL with fibrosis	Ultrasonography abdomen: normal	Ultrasonography: mild splenomegaly
Underlying cause	Secondary to B-cell acute lymphoblastic leukemia	Primary autoimmune cause	Primary autoimmune cause
Treatment (Present cases)	Prednisolone 1 mg/kg/day + single-dose rituximab + 3 units PRBC transfusion + vitamin B12 (1000 mcg) + folic acid + B-complex + albendazole + supportive care	Prednisolone 1 mg/kg/day + folic acid + supportive care	Prednisolone 100 mg/day (5 days) → tapered to 40 mg/day + azithromycin 500 mg/day + IV iron sucrose 200 mg + TMP-SMX 480 mg (twice weekly) + ranitidine + calcium + oral iron

MORVAN'S SYNDROME – A GREAT MIMICKER

Yashwin Tejas, 2021 batch

Abstract

Morvan's Syndrome is an autoimmune disease with classical triad of hyperexcitability of peripheral nerves, and dysfunction of the central and autonomic nervous systems. Augustin-Marie Morvan, a French physician, had described it for the first time in 1890, using the term 'la chorie fibrillare'. Morvan's Syndrome is a mimicker of many neuropsychiatric disorders, autoimmune encephalopathies and peripheral neuropathies.

KEYWORDS:

Autoimmune, voltage-gated potassium channel, peripheral hyperexcitability, encephalopathy, neuromyotonia, SIADH- related hyponatremia.

INTRODUCTION:

Morvan's syndrome is an extremely rare and complex neurological condition, with only around 60 case reports published in English and French language medical literature. It is usually misdiagnosed due to the varied presentation and polysomatic nature of the disease, which overlap with other neuropsychiatric disorders, limbic encephalitis, autoimmune neuropathies, myopathies and neuromyotonia. It is associated with autoantibodies against voltage-gated potassium channel complex (VGKC) – specifically CASPR2 and LGI1. It is frequently paraneoplastic – most commonly associated with malignant thymoma.

CASE REPORT:

A 26-year-old male paramedic student presented with complaints of painful cramps and twitching of calf muscles of both lower limbs and both forearms. It was non-radiating, aggravated on exertion and partially relieved on rest. The patient also noted excess post- exertional fatigue out of proportion to the degree of physical exertion. The patient also had episodes of frontal headache for past 6 months, dull-aching with no specific aggravating or relieving factors. Gradually, he developed decreased sleep for past 4 months. The patient noted that he had been having frequent urges to urinate throughout the day for the past 2 months. The patient also reports erectile dysfunction.

Subsequently, he was diagnosed with Morvan's Syndrome after extensive investigation and was prescribed medications for 2 months. Due to the excess distance and time required for travelling, subsequent follow up was lost.
Muscle fasciculations noted in the forearm of both upper limbs. No visible wasting.

Tilting Table Test showed abnormalities suggestive of orthostatic hypotension - Heart Rate increased by 48bpm from baseline, maximum heart rate of 142 bpm, systolic blood pressure decreased by 30 mm Hg and Valsalva Ratio was 1.215. When performing isometric handgrip – increase in diastolic blood pressure by 20 mm Hg was noted.

CSF Analysis was strongly positive for CASPR2 antibodies. Nerve Conduction Studies and Electromyography showed predominantly neurogenic pattern, with neuromyotonia and myokymia.

The patient was started on Intravenous Methylprednisolone 500mg twice a day for 5 days, followed by oral regimen of prednisolone tablets daily, along with amitriptyline, pregabalin and B-complex tablets. Subsequently the patient started showing improvement with symptomatic relief within 2 months.

DISCUSSION:

Morvan's Syndrome is an extremely rare autoimmune condition with incidence less than 1 in 1 million, causing peripheral hyperexcitability, and dysfunction of the central and autonomic nervous systems. Central nervous system is involved in the form of insomnia – with reduced sleep spindles and K complexes (stage 2 NREM), behaviour changes, disorientation, psychosis, encephalopathy, amnesia, faciobrachial dystonic seizures, REM sleep behaviour disorders. Insomnia occurs due to involvement of thalamus, hypothalamus, locus coeruleus and raphe nuclei. Dysautonomia is characterized by hyperhidrosis, pruritic, palpitations, arrhythmias, constipation, diarrhoea, lacrimation, orthostatic hypotension, polydipsia, urinary incontinence and erectile dysfunction. Monoaminergic diencephalic and brainstem are involved in arousal and autonomic homeostasis. Hyponatremia secondary to SIADH occurs due to Anti-VGKC antibodies acting against hypothalamic paraventricular neurons.

Peripheral Hyperexcitability presents in the form of neuromyotonia, myokymia, cramps, areflexia and stocking-type sensory loss. The most commonly involved autoantibodies are CASPR2 and LGI1 – belonging to the VGKC (neurexin) channel and AMPA-R receptor respectively.CASPR2 is involved in peripheral nervous system hyperexcitability, whereas LGI1 is involved in limbic encephalitis, central nervous

system dysfunction, REM sleep behaviour disorder and faciobrachial dystonic seizures. Morvan Syndrome is frequently paraneoplastic – secondary to malignant thymoma, and hence can be associated with myasthenia gravis.

FDG-PET scan may reveal autoimmune encephalitis. Differential Diagnoses include Limbic Encephalitis (autoimmune CNS dysfunction), Acquired Neuromyotonia (Isaac Syndrome), myotonic disorders, Stiff Person Syndrome, Guillain Barre Syndrome (usually occurs following a prodrome of viral infection or diarrhoea), and rarely, Fatal Familial Insomnia (a prion disease). Comorbid conditions – such as Myasthenia Gravis, Hashimoto Thyroiditis, Systemic Lupus Erythematous, Sarcoidosis, autoimmune cytopenias, solid organ and hematologic malignancies – should be ruled out.

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A WOLF IN BUDD-CHIARI'S CLOTHING: PSEUDO-BUDD-CHIARI SYNDROME IN TUBERCULOSIS PERITONITIS

Roshini S, 2024 batch

Abstract

Budd-Chiari syndrome and decompensated chronic liver disease are two different disorders of the liver. However, they share clinical presentations that can mimic one another, some of which are hepatomegaly, portal hypertension, and ascites. We report a rare case of pseudo-Budd Chiari syndrome in a 55-year-old female caused by a tuberculosis (TB) infection (TB peritonitis). She presented with complaints of abdominal pain, distension, and breathlessness. Both a CECT of the abdomen and a slice MD CT demonstrate hepatomegaly, free fluid in the abdomen and pelvis, and narrowing of the inferior vena cava, without any event of thrombosis, ruling out Budd-Chiari syndrome. Blood investigations show decreased total protein levels, deranged bilirubin levels, and an elevated prothrombin time. An omentum biopsy and ascitic fluid tapping were also done. An IVC angioplasty was performed on the patient, after which she was managed on anti-tuberculosis therapy, then discharged.

KEYWORDS:

Pseudo Budd Chiari syndrome, PBCS, Pseudo-Budd Chiari Syndrome, Budd Chiari Syndrome, Tuberculosis peritonitis

INTRODUCTION:

Budd-Chiari syndrome is a rare condition characterized by hepatic venous outflow obstruction at any level from the small hepatic veins to the junction of the inferior vena cava with the right atrium, which is not caused by cardiac or pericardial disease. This obstruction leads to hepatic congestion and hypertension, leading to hepatic injury. This condition is classified into primary Budd-Chiari syndrome, which results from thrombosis or inflammation of the hepatic vein walls, and secondary Budd-Chiari syndrome, caused by external compression or invasion, often due to malignancies. The disease presents in acute, subacute, or chronic forms, with symptoms including abdominal pain, ascites, and hepatomegaly.

Pseudo-Budd-Chiari Syndrome, however, is a clinical and radiological mimic of true Budd-Chiari syndrome, where a patient shows classic symptoms like an enlarged liver and fluid buildup, but the major hepatic veins remain physically open (patent) rather than blocked by a clot or tumor. The apparent impairment to the outflow can be caused by a diffuse compression by an enlarged liver, but it is never caused by a primary venous lesion.

Tuberculosis (TB) peritonitis is a form of extrapulmonary tuberculosis affecting the peritoneum. Risk factors for peritoneal involvement include a concomitant HIV infection, peritoneal dialysis, or cirrhosis. Reactivation of tuberculous collections lying dormant in the peritoneum accounts for most cases. Direct spread may occur from the gastrointestinal tract, and dissemination through lymphatic or hematogenous means has also been described. The abdomen is the most common site of extrapulmonary tuberculosis, with peritoneal disease being the most common form within the abdomen.

The etiology for pseudo-Budd-Chiari syndrome is generally attributed to those that damage the liver, such as decompensated liver diseases, alcoholic steatohepatitis, liver-associated tumors, and others that occur due to extrahepatic causes, such as pericardial conditions and right-sided heart failure, and systemic conditions like systemic lupus erythematosus, antiphospholipid antibodies, myeloproliferative neoplasms.

It is because of the significant overlap in the clinical presentations that accurate differentiation between true and pseudo-Budd-Chiari syndrome relies heavily on investigations such as various forms of imaging (CT/CECT scans, Ultrasound, angiography/venography) as well as liver biopsies, to better determine the differential diagnosis.

CASE REPORT:

A 55-year-old female presented with features of abdominal pain and distension for a week, along with breathlessness for a period of 5 days. On examination of the abdomen, it was found to be soft, and free fluid could be felt. Vitals were normal, with a pulse rate of 86/min and BP of 130/70 mm Hg. She has had a history of Diabetes mellitus for the past 15 years, and is in the early stages of diabetic neuropathy with complete rectal prolapse.

Blood investigations showed a slight decrease in hematocrit, total protein, and albumin levels. There was a substantial decrease in the percentage of lymphocytes. However, there were significantly elevated levels of fasting blood glucose, prothrombin time, and bilirubin. Urine showed the presence of sugar, protein, and albumin. In contrast, liver enzyme test results were mostly within the normal ranges.

Moreover, tests for anticardiolipin, Beta -2 glycoprotein I (to rule out Antiphospholipid antibody syndrome) , HbSAg (Hepatitis B surface Antigen), HCV (Hepatitis C virus), and HIV (Human immunodeficiency virus), anti-nuclear antibodies (to determine SLE-Systemic Lupus erythematosus), and JAK2V617F mutation (seen in myeloproliferative neoplasms) all came out to be negative.

An Ultrasound of the abdomen showed liver with coarse echoes, splenomegaly (spleen

size of 13.8), free fluid in the abdomen and pelvis indicating moderate ascites, and renal collaterals in the pelvis indicating portosystemic collaterals due to portal hypertension.

A slice MD CT of the abdomen revealed nodular surface of the liver (IMAGE 1,2,3), as well as the splenomegaly and free fluid in the abdomen and pelvis. The CT angiogram of the abdomen (IMAGE 4) showed multiple perisplenic and splenorenal varices, recanalized paraumbilical vein with perigastric and coronary collaterals, tortuous left gonadal vein, a few tiny calcified granulomas in the right lobe of the liver, and intrahepatic narrowing of the inferior vena cava noted secondary to external compression by hypertrophied segments of liver (IMAGE 4) . A CECT of the abdomen also shows the same features.

The Esophagogastroduodenoscopy revealed pan-gastritis. Omentum Biopsy with haematoxylin and eosin staining was also performed, revealing caseating granulomatous lesions, which suggests a tuberculosis infection. Additionally, a fine needle aspiration cytology was done from the pericardiac lymph node, from which reactive lymphadenitis was interpreted. Finally, an ascitic fluid tapping was done, which showed a lymphocytic effusion, indicating the decreased number of lymphocytes in the blood investigations.

A diagnosis of Tuberculosis peritonitis causing pseudo- budd chiari syndrome was made. However, the Serum Ascites Albumin Gradient (SAAG), calculated from the ascitic fluid, was found to be greater than 1.1 g/dL, which is unusual, as the SAAG in tuberculosis is generally less than 1.1 g/dL 8. Following this, the patient underwent an inferior vena cava angioplasty due to severe stenosis of the inferior vena cava. There were no significant events postoperatively, and the patient was managed on anti-tuberculosis therapy, after which she was discharged.

DISCUSSION:

Pseudo-Budd Chiari syndrome (PBCS) is a condition that is not well-known. The less than 20 reports found in the literature for PCBS (compared to thousands for true BCS) had patients with a mechanical compression of the hepatic outflow due to an enlarged liver and liver cirrhosis.

Dhawan et al in 1978, described a patient with clinical and radiological findings of BCS and liver cirrhosis. A complete constriction of the right HV and a narrowed left HV were shown to be present due to the hypertrophy of the left lobe of the liver and a regenerative nodule. However, there were no thrombotic occlusions seen at the autopsy. This was the first paper to introduce the term pseudo-BCS.

Another report was made by Janssen et al. It described three patients with alcoholic liver disease and BCS, without any thrombotic

occlusion. These cases were denominated pseudo-BCS.

Rector et al also reported a patient with liver cirrhosis, probably due to non-alcoholic steatohepatitis and BCS. There was a distortion of the IVC caused by cirrhosis and increased abdominal pressure, which suggested BCS due to membranous obstruction, but no thrombus or membranous occlusion was found.

Some of the described patients had a good evolution after alcohol withdrawal.
In this case however, PBCS is caused by a tuberculosis infection, i.e., TB peritonitis. While there are cases of TB peritonitis causing BCS, this is the first documented case of a TB peritonitis causing PBCS.

The diagnosis of PBCS is difficult because clinical and radiological findings are extremely similar to BCS, making invasive methods necessary.

Mechanical compression of the hepatic outflow due to an edematous liver and liver cirrhosis can mimic the imaging of BCS. Those with an uncertain or false positive diagnosis require venography or arteriography, and/ or a liver biopsy to make the correct diagnosis.

In essence, all the investigations were necessary to help narrow down the diagnosis; the ultrasound, which showed splenomegaly and coarse echoes of the liver, the CT and CECT of the abdomen revealing multiple varices and collaterals formed due to the portosystemic hypertension, and most importantly, the intrahepatic narrowing of the inferior vena cava. The omentum biopsy revealed the true cause of the disorder, i.e., a possible tuberculosis infection. The ascites tapping due to the presence of a moderate amount of free fluid in the abdomen and pelvis explained the decrease in the percentage of lymphocytes in the blood. Although the lymph nodes from the CECT scans were subcentimetric, the fluid needle aspiration cytology showed reactive lymphadenitis.
The possibility of Antiphospholipid antibody syndrome, systemic lupus erythematosus, HIV infections, Hepatitis B and C infections were ruled out, as they were some of the important etiologies of many liver diseases, including Budd-Chiari syndrome.

According to the 2016 European Association for the Study of the Liver (EASL) recommendations on Budd-Chiari syndrome, the first-line diagnostic study is Doppler ultrasonography; MRI and CT scanning are for diagnostic confirmation.

Catheterization and venography can clearly delineate the nature and severity of an obstruction. Occasionally, therapeutic interventions can be undertaken at the same time, including balloon angioplasty, localized thrombolysis, and the placement of a stent or transjugular intrahepatic portacaval shunt 12,16-19. Liver biopsy can be of prognostic assistance, particularly if liver transplantation is being considered, to

establish the degree of hepatocellular damage, and also to provide information for differential diagnoses. However, in current practice, venography is rarely considered necessary for establishing a diagnosis. For patients who consume alcohol, cessation of its consumption may cause reversibility of this disorder.

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A limitation of this report is that, while omentum biopsy reports, ascitic fluid tapping, and abdominal ultrasound were conducted, the corresponding images were unavailable.

In the future, one could incorporate existing imaging techniques with advanced modalities like Multiphase contrast-enhanced 3D MR angiography (3D CE-MRA) , which is a non-invasive imaging modality used to differentiate pseudo-Budd-Chiari syndrome (pseudo-BCS) from true Budd-Chiari syndrome (BCS).3D CE-MRA can distinguish between intrinsic obstruction (thrombosis, webs, or tumor invasion) seen in true BCS and extrinsic compression of hepatic veins/IVC caused by hepatomegaly or inflammatory masses, which is characteristic of pseudo-BCS.

The diagnosis of pseudo-Budd Chiari Syndrome is difficult because clinical and radiological findings are extremely similar to BCS, making invasive methods necessary. Ultrasound, CECT, and CT scans, along with angiography/ venography, are crucial both for arriving at the correct diagnosis and for finding possible collateral channels. Tissue examination through omentum and liver biopsy, and ascitic fluid typing are equally essential in determining the cause and nature of the disorder at the cellular level. Early recognition and treatment are crucial for both conditions - decompensated liver disease and pseudo-budd chiari syndrome - as they can significantly improve the patients' survival rate. Moreover, a possible reversibility with alcohol abstinence makes this clinical disorder a must for physicians to know.

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TABLE 1: Blood investigation results

Lab Parameters	Values	Reference ranges
Total leucocyte count	7500 cells/mm^3	4000-11000 cells/mm^3
Differential count (PMNL %/lymphocytes %)	80/7	40-70/20-40
MCV	86.6 fL	80-100 fL
MCH	27 pg/cell	27-33 pg/cell
MCHC	31.1	32-36 g/dl
Hematocrit	33.2%	36-48% for women
Platelet count	162 × 10^9 cells/L	150-450 × 10^9 cells/L
Prothrombin Time	21.22 seconds	10-13.5 seconds
APTT	34.52 seconds	25-35 seconds
urea	25 mg/dl	6 – 24 mg/dl
creatinine	0.53 mg/dl	0.7 – 1.3 mg/dl
Random blood sugar	99 mg/dl	<140 mg/dl
Fasting blood sugar	110 mg/dl	70-99 mg/dl
INR	1.77	0.8-1.2

(PMNL- Polymorphonuclear leucocytes, MCV- mean corpuscular volume, MCH- mean corpuscular haemoglobin, MCHC – mean corpuscular haemoglobin concentration, APTT- activated partial thromboplastin time, INR – International Normalized Ratio)

TABLE 2:Liver enzyme values on days 1, 2, 5, 6

Day	1	2	5	6	Reference range
TB/DB (mg/dl)	2.24/1.18	1.98/0.88	1.3/0.6	2/0.4	0.1-0.2/0.0-0.3
SGOT/SGPT (U/L)	29/14	39/10	75/23	56/19	5-40/7-56
ALP (IU/L)	102	132	116	113	44-147
Total protein (g/dl)	7.4	6.4	8.1	6.3	6.0-8.3
Albumin (g/dl)	2.5	3.4	2.8	2.5	3.5-5

(TB- total bilirubin , DB – direct bilirubin, SGOT - serum glutamic-oxaloacetic transaminase, SGPT - Serum Glutamic Pyruvic Transaminase, ALP- alkaline phosphatase)

TABLE 3: Urinalysis Analysis

Urine sugar	1+
albumin	2+
blood	1+

IMAGE 1

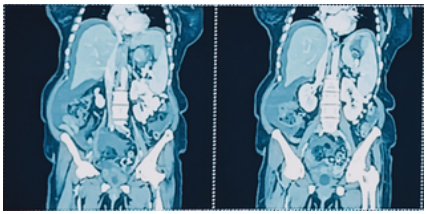

IMAGE 2

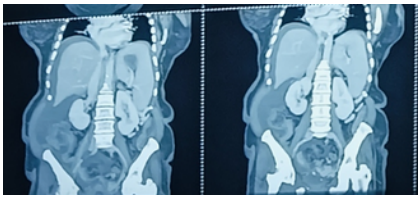

IMAGE 3

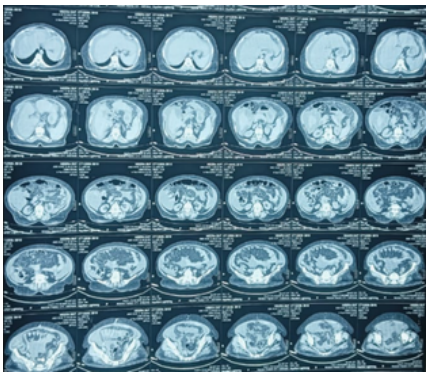

IMAGE 1,2,3: CT abdomen showing nodular surface of liver along with splenomegaly and moderate free fluid in the abdomen and pelvis.

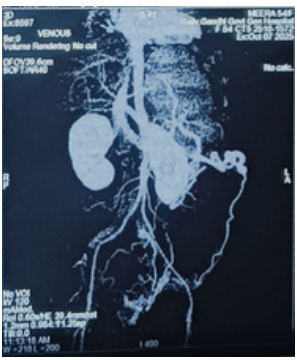

IMAGE 4: CT angiogram of the abdomen revealing collaterals and intrahepatic narrowing of the inferior vena cava.

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