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A RARE CASE OF CASTLEMAN DISEASE VARIANT OF POEMS SYNDROME WITH PULMONARY TUBERCULOSIS

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ABSTRACT

A 52 year old male patient, known case of Castleman's disease with chronic inflammatory demyelinating polyneuropathy, was admitted with complaints of dyspnoea, cough with expectoration, loss of weight and loss of appetite. Patient was on immunosuppressants and steroids since 2 years. Chest skiagram and CECT thorax revealed thick walled cavitating lung lesions. His sputum examination was negative for mycobacteria but lung biopsy revealed tuberculous pneumonia. On detailed workup he was diagnosed with a variant of POEMS syndrome. Patient improved on starting anti-tuberculous treatment. We report here a rare case of Castleman disease variant of POEMS syndrome with pulmonary tuberculosis in a patient on immunosuppressant therapy.

I. INTRODUCTION

POEMS syndrome is a rare multisystem disorder characterised by polyneuropathy, organomegaly, endocrine abnormality, monoclonal gammopathy, skin changes. It usually manifests in the 5th to 6th decade of life, more common in males (M:F=2.5:1) with prevalence of ~0.3 per 100,000.[1] Since only a several hundred cases have been described in literature as it easily goes unrecognised, it poses a great diagnostic challenge and needs a high index of suspicion. Pulmonary manifestations of POEMS syndrome include pulmonary hypertension, restrictive lung disease, respiratory muscle weakness and pleural effusions.[2] The treatment with immunosuppressants reduces the resistance to infections caused by intracellular pathogens causing opportunistic infections like tuberculosis, which increases the mortality and morbidity.[3]

II. CASE REPORT

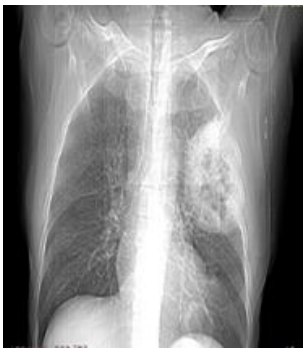
A 52 year old male, office clerk by occupation presented in Pulmonary Medicine outpatient department of SMS Medical College, Jaipur with 2 months history of dyspnoea on exertion, cough with mucopurulent expectoration, loss of weight and loss of appetite. His past history revealed left cervical lymphadenopathy diagnosed as Castleman disease on excisional biopsy 5 years ago. He also gave a history of tingling sensation and numbness of both feet with gradual onset, progressive weakness of both lower limbs since 2 years, which was diagnosed as chronic inflammatory demyelinating polyneuropathy. The patient was on treatment with oral steroids and immunosuppressant (Azathioprine) for 2 years. He is a chronic smoker, non-alcoholic and known hypothyroid on treatment since 2 years. Physical examination revealed bilateral cervical lymphadenopathy, clubbing, pedal edema, hyperpigmentation and hypertrichosis. Respiratory examination revealed decreased breath sounds in left mammary, inframammary, axillary and inter scapular areas with crepitations on auscultation. CNS examination revealed bilateral lower limb proximal muscle power 4/5 and distal muscle power 0/5 with absent deep tendon reflexes and bilateral flexor plantar reflex. Sensory system examination suggestive of impaired sensation of pain, touch, temperature and vibrations bilaterally below knee.

Complete blood counts was suggestive of leucocytosis and elevated ESR. Blood sugar levels were elevated with normal HbA1C. Other blood investigations like serum vitamin B12, liver, renal and thyroid function tests were normal, along with negative viral markers. Chest x-ray at the time of admission showed two cavitating lesions in mid and lower zones of left lung. Sputum was negative for mycobacteria on both smear by Ziehl-Nielson method and CBNAAT. Sputum microbiology showed few gram positive cocci and no fungal elements. CECT thorax showed large thick walled cavity in anterior segment of left upper lobe with surrounding ground glass haziness and septal thickening and another small thick walled cavity in left lower lobe of lung. CT guided biopsy of the cavitating lesion revealed tubercular pneumonia.

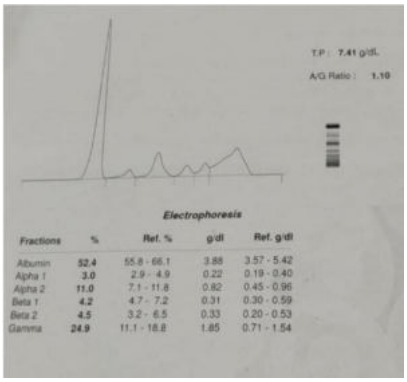
Further workup was done to diagnose POEMS syndrome. USG and CECT abdomen revealed hepatosplenomegaly. USG, CECT and MRI neck showed bilateral cervical lymphadenopathy (L>R). Cervical lymph node excision biopsy done 2 years ago was suggestive of Castleman disease- plasma cell variant. Four limb nerve conduction study showed sensori-motor axonal affection of bilateral tibial and peroneal nerves and sensori-motor demyelinating affections of right median and ulnar nerves. CSF examination revealed albumin-cytological dissociation. Serum protein electrophoresis showed distorted gamma region. X-ray hip joints showed mixed lytic osteosclerotic bone lesions. Serum immunofixation, VEGF levels and bone marrow biopsy were not done due to non-affordability.

He was started on anti-tubercular treatment and improved symptomatically after a month. Other medications like thyroxine were continued along with lifestyle modifications and regular blood sugar monitoring. Patient is currently in outpatient check-ups for haematology, neurology, endocrinology and pulmonary medicine.

(Fig.- 1)

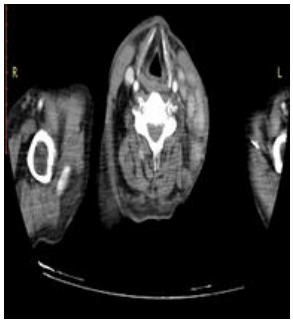


(Fig.- 2)

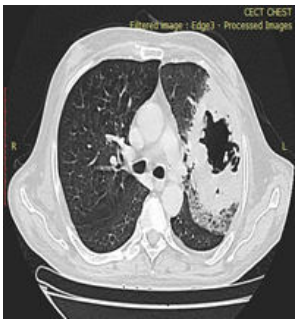


(Fig.- 3)

Fig.- 1 Hypertrichosis and hyperpigmentation of right forearm, Fig.- 2 Chest x-ray showing thick walled cavities in left lung, Fig.- 3 Serum protein electrophoresis showing distorted gamma region



(Fig.- 4)



(Fig.- 5)

Fig.- 4 CECT neck showing left cervical lymphadenopathy, Fig.-5 CECT thorax showing left upper lobe thick walled cavity with surrounding ground glass haziness

III. DISCUSSION

POEMS syndrome, also known as osteosclerotic myeloma, Takatsuki syndrome and Crow-Fukase syndrome, is a rare paraneoplastic syndrome associated with multisystem involvement like polyneuropathy, organomegaly, endocrinopathy, monoclonal gammopathy and skin changes. The syndrome is a manifestation of an underlying plasma cell disorder and its pathogenesis remains unclear. The acronym POEMS was coined by Bardwick in 1980. The three important points related to this acronym are- not all features are required for diagnosis, there are other features not included in the acronym and there is a variant associated with Castleman disease.[1]

Diagnosis of this syndrome can be made when both mandatory major criteria, one of the three other major criteria and one of the six minor criteria are present. Mandatory major criteria include polyneuropathy, typically demyelinating and monoclonal plasma cell proliferative disorder, almost always λ. Other major criteria include sclerotic bone lesions, Castleman disease and elevated levels of vascular endothelial growth factor (VEGF). Minor criteria include organomegaly (splenomegaly, hepatomegaly, lymphadenopathy), extravascular volume overload (edema, pleural effusion or ascites), endocrinopathy (adrenal, thyroid, pituitary, gonadal, parathyroid and pancreatic), skin changes (hyperpigmentation, hypertrichosis, glomeruloid hemangiomata, plethora, acrocyanosis, flushing and white nails), papilledema, thrombocytosis/ polycythemia. Other symptoms and signs are clubbing, weight loss, hyperhidrosis, pulmonary hypertension/ restrictive lung disease, thrombotic diatheses, diarrhoea, low vitamin B12 values.[1]

Castleman disease (CD or angiofollicular lymph node hyperplasia), a rare lymphoproliferative disorder, is characterised by three histological varieties- hyaline vascular, plasma cell or mixed form and two clinical forms- localized and multicentric. It occurs in around 11-30% of patients with POEMS syndrome.[4] Multicentric Castleman disease (MCD) develops around 40-50 years of age, with systemic symptoms, multiple nodal and organ involvement. Castleman disease variant of POEMS syndrome has no clonal plasma cell disorder and typically little to no peripheral neuropathy.[5] Our patient belongs to this variant as a monoclonal plasma cell disorder could not be confirmed.

The mainstay of POEMS syndrome therapy target to plasma cell disorder or local lesions, dependent on the status of bone marrow infiltration. Various treatment modalities include autologous hematopoietic stem cell transplantation, radiation, systemic chemotherapy, lenalidomide or thalidomide, steroids, immunosuppressants like azathioprine, bortezomib, bevacizumab (anti VEGF antibody). Although azathioprine is not considered as the mainstay therapy, its combination with steroids have shown promise with managed toxicity.[6] These drugs suppress immune system causing emergence of undue infections. Thiopurines (azathioprine), corticosteroids and anti-TNF agents alone or in combination are associated with higher incidence of tuberculosis. Patients presenting with nonspecific symptoms like cough, fever, weight loss should be considered at risk of tuberculosis, especially when immunosuppressed and in high prevalence countries like India.[3]

The diagnosis is very challenging and often delayed due to its rarity and multisystem involvement. Patients have an excellent prognosis if diagnosed early and given appropriate treatment. The main causes of death are cardiorespiratory failure, renal failure, infection and stroke.[7] This case throws light not only on the importance of evaluating for this rare syndrome in patients presenting with multisystem involvement, but also for tuberculosis caused by underlying immunosuppression.

IV. CONCLUSION

The diagnosis of POEMS syndrome is based on a cluster of clinical manifestations and laboratory investigations. Therefore, a detailed history collection and physical examination in addition to essential laboratory tests are necessary to rule in the diagnosis.[6] The multimodal approach with immunosuppressive therapy significantly changes the overall immunity of patients, increasing their risk for opportunistic infections like tuberculosis- the most common in our country. Hence patients considered for immunosuppressive therapies should be evaluated and protected against opportunistic infections.

ABBREVIATION

POEMS syndrome- Polyneuropathy, Organomegaly, Endocrine abnormality, Monoclonal gammopathy, Skin changes
CD- Castleman disease
CIDP- Chronic Inflammatory Demyelinating Polyneuropathy

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