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A RARE CASE OF NEUROSARCOIDOSIS

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ABSTRACT

Sarcoidosis involving Central Nervous system is extremely rare. In nearly 5 to 10 percent of patients with sarcoidosis central nervous system involvement are seen. In contrast Sarcoidosis generally affects lungs in 90% of patient. Neurosarcoidosis affects age groups of 30 to 50 years and females are more affected than males. Neurosarcoidosis generally affects any part of central nervous system and pheripheral nervous system and diagnosis is extremely difficult as there is no definitive test to diagnose it. In treatment part corticosteroids are normally the main line of treatment and around half of patients have significant advantage. For patients who are found non beneficial to corticosteroid treatment, second-line treatment like incorporation of azathioprine, methotrexate, cyclosporine, cyclophosphamide, mycophenolate can be tried. The mix of infliximab and mycophenolate mofetil is under examination too. Here we are going to present a 46 year old male with bilateral lower limb weakness. . This disease can masquerade as many other diseases. Spontaneous improvement or remissions occur in about 60% of patients with neurosarcoidosis. There are no reliable biomarkers identified to monitor disease activity. Since it is rare but important cause of neurological morbidity, and neurological symptoms often herald the diagnosis. A systemic approach is needed for its diagnosis and prompt management.

Keywords: Sarcoidosis, Neurosarcoidosis, Granulomatous disease

INTRODUCTION

Neurosarcoisosis is rare manifestation of sarcoidosis involving 5 to 10% of patients with unknown etiology **[1]**. It is more normal in males in India, however there is a slight female transcendence in rest of the world **[2]**. Sarcoidosis is rare in countries like india **[3]**. The genuine incidence of sarcoidosis in India is unknown. It has been assessed that sarcoidosis established 10 to 12 cases for each 1,000 new enlistments in a respiratory unit at Kolkata and 61.2/100,000 new cases at a middle in New Delhi in a report distributed in 2002 **[4]**. Neurosarcoidosis generally affects all parts of cns and pheripheral nerves. Unconstrained improvement or abatements happen in about 60% of patients with neurosarcoidosis. The death rate in all types of sarcoidosis is from 1-5% and is because of extreme pneumonic, heart, or neurologic infection **[5]**.

Case report

A 46 year old male Patient was apparently asymptomatic before 4 months, then he developed complaints of fever, generalized weakness, easy fatiguability and loss of appetite. He took treatment in local hospital where he was treated on the lines of obstructive jaundice,? viral hepatitis, alcoholic liver disease associated with dimorphic anemia, thrombocytopenia, splenomegaly and T2DM.Patient then developed bilateral lowerlimb weakness following the treatment. He was then referred to a central institute, in view of severe anemia, thrombocytopenia, melena (without oral iron) and progressively increasing lowerlimb weakness.

At central institute hospital the patient was treated on lines of lymphoproliferative disorder under evaluation with autoimmune hemolytic anemia, ?TB vs lymphoma and freshly diagnosed t2dm. Investigations done there revealed normocytic normochromic anemia with lymphocytic predominance, reticulocytosis, raised LDH, positive direct and indirect coombs test, mild splenomegaly, generalized lymphadenopathy. NCS done there on showed asymmetrical sensorymotor axonal with demylinating polyradiculoneuropathy involving both lowerlimbs. In view of anemia patient was transfused with 3 units of whole blood and 3 units of p.RBCs. Patient was then started on oral steroids and was discharged.

patient was admitted to a private hospital for worsening of weakness and extension of weakness to all 4 limbs. The patient was treated on lines of GBS , autoimmune hemolytic anemia, alcoholic liver disease ,hiatus hernia, oral steroids were continued.

CT brain done and showed left occipital bone-? prominent arachnoid granulation ?hemangioma. MRI dorsolumbar spine with whole spine screening showed C5-C6, L5-S1 myelopathy. MRI pelvis and both hips (PBH) showed retroperitoneal bilateral inguinal and bilateral iliac lymphadenopathy with sclerotic lesion in left iliac bone. The patient was then referred to Sree Balaji Medical college and hospital for further management. Neurologist opinion was sought and was followed. After admission, all the routine investigations was done. Patient was treated for hypokalemia. With all the available previous medical records, conservative treatment was started on lines of provisional diagnosis of TB vs Follicular lymphoma vs GBS vs multiple myeloma with autoimmune hemolytic anemia with alcoholic liver disease with hiatus hernia with t2dm with lymphadenopathy with hypokalemia. Rheumatologist advised to continue the oral steroids. Serum protein electrophoresis was done and showed no M band and was suggestive of acute inflammation. Direct and indirect coombs test were negative and Viral markers were negative. Stool examination for occult blood, ova and cyst were negative. Hence oral steroids were resumed. ACE levels were found to be elevated. ANA titre done by immunoassay was negative. Insulin was added in view of raised sugars, other symptomatic treatment was also continued. patient had persistent fever, hence widal, smear for malarial parasite, stool culture sensitive test were done and was negative ,platelets counts were normal. Patient was catheterized in view of urinary retention. Urine culture sensitive showed isolated candida non-albicans. Parenteral antibiotics were started and fever subsided .On review with previous lymphnode biopsy showed follicular lymphoma and Pathologist raised the suspicion of POEMS syndrome.

3T-MRI DL spine with whole spine screening done and showed linear mildly interrupted long segment intra medullary T2 hyperintense signal in bilateral paramedian and peripheral region from C7-D12 level Features suggestive of neurosarcoidosis. Neurologist opinion was soughted and advised to restart oral steroids after short course of iv steroids. Ophthalmology opinion was sought, fundus examination was normal.

On Re-evaluation and IHC study of lymphnode biopsy slides suggested granulomatous inflammation with no definitive evidence of malignancy with CD20 highlighting B lymphocytes with CD68 highlighting histiocytes and epitheloid cells with CD3, CD10, BCL2 ,CD19,S-100 protein, CD30, CD23, MIB1 were in

conclusive and special stain with AFB /PAS/GMS do not highlight any microorganism.

Lumbar puncture performed for CSF analysis showed minimal raised proteins with normal glucose and ADA levels. No cells seen. No growth on CSF culture. CSF-CBNAAT also was negative.

On Rheumatologist review, diagnosis of neurosarcoidosis was made and tab. Mycofenolate mofetil (MMF) 500mg BD was started and the dose of oral steroids were increased. Meanwhile patients sugar levels were monitored and insulin dose were adjusted accordingly. ACE levels were repeated and found to be elevated. Hence dose of MMF was increased to 1gm BD. Gradually the power of bilateral lowerlimb increased from 1/5 to 2/5 on bilateral lowerlimb. On follow up the patient symptoms improved and on the last visit power improved to 4/5 in bilateral lowerlimbs and he is able to fulfil his daily needs.

DISCUSSION

Neurosarcoisosis is rare manifestation of sarcoidosis involving 5 to 10% of patients with unknown etiology **[1]**. It is more normal in males in India, however there is a slight female transcendence in rest of the world **[2]**. Sarcoidosis is rare in countries like india **[3]**. The genuine incidence of sarcoidosis in India is unknown. It has been assessed that sarcoidosis established 10 to 12 cases for each 1,000 new enlistments in a respiratory unit at Kolkata and 61.2/100,000 new cases at a middle in New Delhi in a report distributed in 2002 **[4]**. Neurosarcoidosis generally affects all parts of cns and pheripheral nerves. Unconstrained improvement or abatements happen in about 60% of patients with neurosarcoidosis . The death rate in all types of sarcoidosis is from 1-5% and is because of extreme pneumonic, heart, or neurologic infection **[5]**. Sarcoidosis can affect any cranial nerves and most commonly affected cranial nerve is facial nerve **[6]**. Meningeal invasion specially includes the basal leptomeninges. It has been accounted for in up to 40% of patients . It might show with cranial nerve paralyses. It can prompt hydrocephalous, ventricular framework granulomas, or choroid plexus invasion **[7]**. Hypothalamic and pituitary involvement is common , generally due to subependymal granulomatous penetration in the area of the third ventricle. Diabetes insipidus and hyperprolactinemia are the two most endocrine disorder alongside hypogonadism **[8]**. About 7 to 22% patients may present with seizures which may be focal or generalized onset **[9]**.

Neurosarcoidosis can cause arachnoiditis, cauda equina dysfunction, extradural and intradural, extramedullary and intramedullary lesions. Pheripheral neuropathy happens in 4-20% of patients with neurosarcoidosis and the Subtypes sensorimotor axonal polyneuropathy, various mononeuropathies, tangible polyneuropathy including little fiber neuropathy, AIDP and demyelinating polyneuropathies **[10]**. Myopathy is common in neurosarcoidosis and it can give polymyositis like picture. About 50% of muscle biopsy in sarcodosis shows features of myopathy **[11]**. For an unequivocal conclusion, there ought to likewise be "positive" histology. For a finding of plausible neurosarcoidosis, CSF or MRI evidence is needed just as proof of fundamental sarcoidosis. Histology, Kveim test, or potentially at least two circuitous pointers, Gallium filter, chest imaging, or serum ACE are used for the diagnosis **[12]**. Chest x-ray shows findings in up to 90% of sarcoidosis patients, and hilar adenopathy is the most widely recognized finding. High goal chest CT is more touchy, particularly for identifying knobs along the bronchovascular group and subpleural areas **[13]**. CT scan is less sensitive than MRI and MRI can recognize proof of meningeal irritation, diencephalic inclusion and parenchymal sores in about 40%. Vague white issue changes are generally seen, Specifically periventricular T2-hyperintensity is common **[14]**. In patients with leptomeningeal association, the CSF discoveries are as per the following: 40-70% display pleocytosis; 40-73% has a raised protein; and 10-20% has a low glucose.Oligoclonal groups and a raised IgG record are experienced in up to 53% **[15]**. The first line drug in management of neurosarcoidosis is corticosteroids.The second line drugs which are steroid sparing immunosuppressives are used such as methotrexate, cyclosporine, azathioprine, cyclophosphamide, chlorambucil, chloroquines, and mycophenolate.Biologics such as TNF alfa blockers are used. Infliximab is used in patients who are not improving on steroid theraphy shows a promising result **[16]**.

CONCLUSION

Neurosarcoisosis is rare manifestation of sarcoidosis involving 5 to 10% of patients. This disease can masquerade as many other diseases. Spontaneous improvement or remissions occur in about 60% of patients with neurosarcoidosis. There are no reliable biomarkers identified to monitor disease activity. Since it is rare but important cause of neurological morbidity, and neurological symptoms often herald the diagnosis. A

systemic approach is needed for its diagnosis and prompt management is very important to solve this interesting mystery.

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