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Case Report

Sarcoidosis presenting as Lofgran's syndrome

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ABSTRACT

A 40 year old male, first presented with erythema nodosum, fever, weight loss and joint pains and did not respond to anti-tubercular treatment. One year later he came back with joint pains, erythema nodosum, fever and dry cough. He also had weakness in distal right lower limb more than left limb. He had raised ESR, hypocalcaemia, raised ACE levels and lymphnode involvement on HRCT, with skin biopsy suggestive of sarcoidosis. This time patient responded to treatment and is on regular follow up.

Keywords: Erythema nodosum, Hypercalcemia, ACE levels, Sarcoidosis

INTRODUCTION

Sarcoidosis is a chronic inflammatory disease characterized by the presence of noncaseating granulomas, hence can also be included in granulomatous diseases. It is often multisystemic and requires the presence of involvement in two or more organs for a specific diagnosis. Sarcoidosis can affect every organ of the body; the lung (95%) is most commonly affected. Other organs commonly affected are the skin (24%), eye (12%). Extrathoracic lymphnode (15%), liver (12%), spleen (7%), neurologic (5%) and cardiac (2%).

Because of granulomas and its chronic nature, and lung involvement, in an endemic region like India, it is often misdiagnosed as tuberculosis, and vice-versa. Besides sarcoidosis and tuberculosis may co-exist.

Investigations like: serum calcium levels, ACE levels, CT thorax for pulmonary lymph-node involvement, and FDG pet scan, joint X-rays, skin biopsy, MRI brain and NCV studies for neurosarcoid are carried out to know the extent of multisystemic involvement and later for follow-up glucocorticoids form the mainstay and most often used immunosuppressive treatment. Methotrexate, azathioprine, and in refractory cases biologicals like adalimumab, rituximab, infliximab can be tried. In endemic area, it is a must to rule out tuberculosis before starting treatment

CASE REPORT

40 year old male came to OPD with c/o fever since 2-3 months dry cough and multiple joint pains since 1-2 years. Rash over lower limbs.

One year ago patient developed painful eruptions over lower limbs diagnosed as erythema nodosum. He also had weight loss of 6 kg and was put on Anti-tubercular treatment for 6 months which he completed. On general examination, pulse 90 bpm regular blood pressure, 110/70 mmhg, SpO2 92% on room air. Pallor and bilateral pitting pedal edema were present upto knee joints. An erythematous rash seen on shin of tibia diagnosed as erythema nodosum and over the nose and cheeks, diagnosed as lupus pernio.

Systemic examination

Musculoskeletal examination, joints involved; b/l knee joints, b/l elbow joint, b/l wrist joints, were red, swollen, tender with restriction of movement.

CNS Motor system, distal weakness power 4/5 at knee and ankle more on right. Side suggestive of motor peripheral neuropathy, other systems were normal.

Lab parameters, hemoglobin; 7.7 gm%, TLC; 4500/ul, platelet count; 2 lakh, total bilirubin; 0.80 mg/dl, SGOT/SGPT; 50/54 ualp; 635 u/l (n=46-116), serum protein; (t/a/g 5.7/1.4/4.3) g/dl, urea/creatinine; 40/2.2 g/dl, urine routine protein ++, urine protein; 0.59gm/day, Esr/crp; 55/12, serum calcium; 14 mg/dl (n=8.5-10.5), 24 hour urinary calcium; 202 mg/dl (n=10-100), serum ace level; 130 u/l (n=8-52), serum parathormone; less than 10 pg/ml (n=10-65), p-anca, c-anca, asora factor, anti-ccp, ana and ana blot were negative. HIV, HepB and C were negative. Suputum for afb as well as cbnnat was negative. Ultrasonography abdopelvis s/o grade 1 fatty liver. NCV study s/o mixed demyelinating axonal sensory motor polyneuropathy more on right side. EMG was normal. Nerve biopsy of left sural nerve s/o chronic mild asymm-etrical axonal neuropathy. MRI brain s/o periventricular calcifications. Skin biopsy section was taken over lesion over shin of tibia.

Diagnosis

Panniculitis with non-caseous granulomas s/o erythema nodosum.

Treatment

Tablet prednisolone 40 mg/day later reduced to 20 mg/day and tablet hydroxychloroquine 200 mg twice a day. Later azathioprine was added.

Follow up

Patient showed improvement in the form of good appetite, no fever, regressed skin lesions, normal calcium levels, decreased joint pain and significant improvement in neurological deficit and renal function tests became normal.

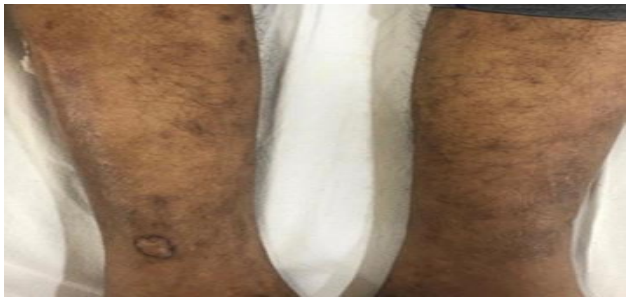

Figure 1: Rythema nodosum.

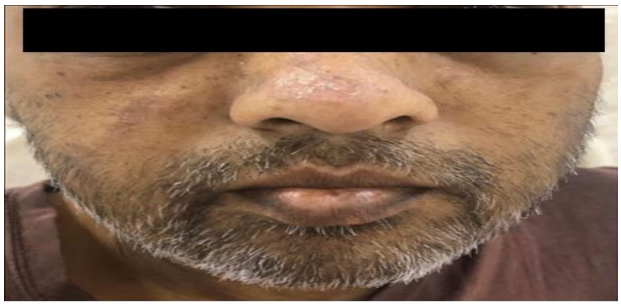

Figure 2: Lupus pernio.

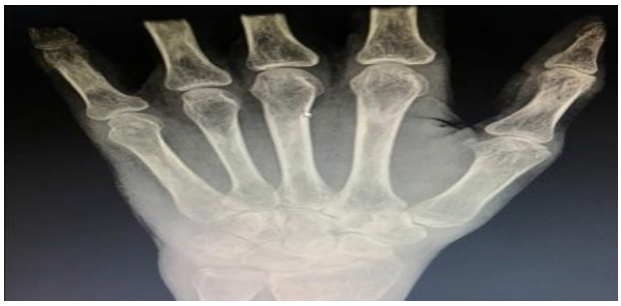

Figure 3: X-Ray of left hand joint involvement.

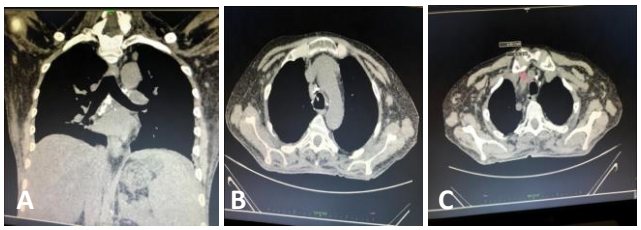

Figure 3: HRCT thorax with multiple calcified LN seen in A) pre tracheal, B) carinal, C) aorto-pulmonary, bilateral hilar, peri hilar regions, largest measuring 22x12 mm at aortopulmonary window.

DISCUSSION

Sarcoidosis etiologyis mainly unknown but some autoimmune association in the form of environmental exposures to insecticides and mold have been associated with an increased risk for disease.[1-4] Nonspecific constitutional symptoms include fatigue, fever, night sweats and weight loss. Commonly involved organs [are] pulmonary involvement (70-90%), bilateral hilar adenopathy, which in the current case patient had, restrictive and obstructive disease, reticulonodular infiltration.[5-10] Ocular involvement (20-30 %) a/w anterior and posterior uveitis, optic neuritis, chorioretinitis, glaucoma. Cutaneous (20-30%), erythema nodosum, lupus pernio cutaneous, subcutaneous nodules and alopecia, again seen in current case patient and biopsy proved. Haematological (20-30%), peripheral lymphadenopathy, splenomegaly, anemia andthrombocytopaenia. Musculoskeletal joints (10-20%), arthralgias, bone cysts and myopathy. Neurological (5-15%), cranial neuropathy (first, seventh cranial nerve involvement more common), aseptic meningitis, myelopathy, peripheral neuropathy andmononeuritis

multiplex. Cardiac (5-10%), arrythmias, heart block-cardiomyopathy andsudden death. Endocrine, hyper-calcemia hypopituitarism and diabetes insipidus. renal acute renal injury. Liver, hepatomegaly, raised alp due to obstruction. Tuberculosis often overlaps with sarcoidosis.[11-13]

Agarwal et al and Gupta et al stated that tuberculous sarcoidosis: Is not a separate entity, and many a times a physician encounters situations wherein sarcoidosis may precede, follow or present concurrently with TB.[15,16] According to an official American thoracic society clinical practice guideline.[17] Lymph node sampling, screening for extrapulmonary disease diagnostic evaluation of suspected extrapulmonary disease are must for diagnosing sarcoidosis. Glucocorticoides are the first line drugs which can be started after ruling out active tuberculosis.

Patompong in Thailand uses methotrexate as the first DMARD for pulmonary sarcoidosis.[18] The usual dose is between 10 and 25 mg weekly, either orally or intramuscularly. Methotrexate has a slow onset of action, and maximal efficacy will not be observed until at least 2 to 3 months after initiation of the therapy. Less commonly used DMARDs with less evidence to support their efficacy include azathioprine, leflunomide, mycophenolate, chloroquine/hydroxychloroquine.

Biologic agents are considered third line therapy for patients with refractory disease that do not respond to glucocorticoids and DMARDs or for those who cannot tolerate these agents. The most commonly prescribed class of biologic agents is tumor necrosis factor α (TNF-α) inhibitor; infliximab.[14] In a randomized controlled study of patients with chronic refractory pulmonary sarcoidosis comparing low-dose intravenous infusion of infliximab (3 mg/kg) and high dose intravenous infusion of infliximab (5 mg/kg body weight) and refractory FDG-PET, positive pulmonary sarcoidosis given the 5 mg/kg body weight infliximab dose was found effective. Adalimumab is another TNF-α inhibitor with some data to support its efficacy. Rituximab, a monoclonal antibody to CD20, is the only non TNF-α inhibitor biologic agent for which there is some published evidence of efficacy.

Cottin et al reported sarcoidosis from bench to bedside: a state of the art series for the clinician suggest that fluorodeoxyglucose positron emission tomography (PET) scanning identifies areas with active metabolic (inflammatory) activity, which can be targeted by biopsies, and suggests the presence of disease in organs that are difficult to access and with potential morbidity.[19] Sauer et al, Stern et al classify patients with severe cardio-pulmonary sarcoidosis, especially with high degree of pulmonary arterial hypertension as high risk sarcoidosis. These patients have to be on very regular and frequent follow-up.[1,20]

Clinical implications

Erythema nodosum along with fever, polyarthritis, uveitis and hilar lymphadenopathy can be a part of acute presentation of sarcoidosis known as Lofgren's syndrome. Thus every patient coming with fever cough and weight loss and skin eruptions even in an endemic area of tuberculosis, should be investigated for sarcoidosis.

CONCLUSION

Case report presents patient with joint involvement, skin eruptions in the form of erythema nodosum and lupus pernio, like Lofgren's syndrome, but on investigations also had lung involvement, neurological involvement and an AKI and hepatopathy in the beginning. Hence diagnosed as a case of sarcoidosis treated with glucocorticoides and azathioprine, to which he has responded

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