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ASYMPTOMATIC PULMONARY SARCOIDOSIS WITH HYPOTHYROIDISM: A CASE REPORT

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ABSTRACT: Sarcoidosis is a granulomatous lesion affecting multi organs, mainly the lungs, kidney, skin, lymph nodes etc. occurring mainly in African American blacks and Nordics. A 45 year old female presented with progressively increasing generalised skin eruption, fatigue and joint pains. Further work up of the patient reveals Hypothyroidism, Rheumatoid factor positive and Lipid profile showed isolated hypertriglyceridemia. CXR-PAV showed bilateral hilar lymphadenopathy. Calcium profile was normal. Bone marrow examination for anemia showed non-caseating well formed epithelioid granuloma strongly suggestive of Sarcoidosis. High ACE level of 114 clinched the diagnosis for Sarcoidosis. The patient responded to steroid and is on remission.

KEYWORDS: Sarcoidosis, Epithelioid granuloma, ACE

INTRODUCTION: Sarcoidosis was first described by Jonathan Hutchinson in 1869. Sarcoidosis is literally taken from *sarc* meaning *flesh*, *-oid*, *like*, and *-osis*, *diseased or abnormal condition*, is also called sarcoid, Besnier-Boeck disease or Besnier-Boeck-Schaumann disease, is a disease in which abnormal collections of chronic inflammatory cells (granulomas) form as nodules in multiple organs.^[1] The cause of sarcoidosis is unknown. Granulomas of non-caseating type most often appear in the lungs or the lymph nodes, but virtually any organ can be affected. Normally the onset is gradual. Sarcoidosis may be asymptomatic or chronic. It commonly improves or clears up spontaneously.

Sarcoidosis most commonly affects young adults of both sexes, although studies have reported more cases in females. Incidence is highest for individuals younger than 40 and peaks in the age-group from 20 to 29 years; a second peak is observed for women over 50.^{[2][3]}

Sarcoidosis occurs throughout the world in all races with an average incidence of 16.5/100,000 in men and 19/100,000 in women. The disease is most prevalent in Northern European countries, and the highest annual incidence of 60/100,000 is found in Sweden and Iceland. In the United States, sarcoidosis is more common in people of African descent than Caucasians, with annual incidence reported as 35.5 and 10.9/100,000, respectively.^[4]

Granulomatous inflammation is characterized primarily by accumulation of monocytes, macrophages and activated T-lymphocytes, with increased production of key inflammatory mediators, TNF-alpha, IFN-gamma, and IL-12, characteristic of a Th1-polarized response (T-helper lymphocyte-1 response). Sarcoidosis has paradoxical effects on inflammatory processes; it is characterized by increased macrophage and CD4 helper T-cell activation resulting in accelerated inflammation, however, immune response to antigen challenges such as tuberculin is suppressed. This paradoxical state of simultaneous hyper- and hypo- activity is suggestive of a state of anergy. The anergy may also be responsible for the increased risk of infections and cancer. It appears that

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regulatory T-lymphocytes in the periphery of sarcoid granulomas suppress IL-2 secretion which is hypothesized to cause the state of anergy by preventing antigen-specific memory responses.^[5]

While it is widely believed that TNF-alpha plays an important role in the formation of granulomas, it was observed that sarcoidosis can be triggered by treatment with the TNF-alpha antagonist etanercept.^{[6][7]}

CASE REPORT: A 45 year old female presented with generalized skin eruptions which was progressive in nature for the past 3 months. The eruption was hyperpigmented, maculopapular in nature but with spiky feel on touch. She also complained of low grade fever, fatigue, lack of appetite and joint pains over Left ankle and Left 1st Metatarsal joint. Except for history of cholecystectomy 13 yrs back and Extraction of CBD stones by ERCP 3 yr back she did not have any significant illness in the past. On further work up the patient was also found to be hypothyroid, positive for rheumatoid Arthritis, anaemic and dyslipidemic. Skin biopsy showed chronic non-specific dermatitis. Bone marrow examination for anaemia revealed non-caseating epithelioid granuloma. Possibility of Sarcoidosis was considered and further work-up was performed.

INVESTIGATIONS AND FINDINGS: Preliminary routine investigations gave picture of anaemia (Hb: 7.4 gm%), normochromic normocytic on peripheral smear and for which further investigations; iron profile revealed raised ferritin level (1196 ng/ml) and bone marrow examination gave a non-caseating epithelioid granuloma. Bilateral hilar lymphadenopathy in chest X-Ray was noted. However Mantoux test was negative and sputum tests were also negative. Investigation for skin lesions gave chronic non-specific dermatitis in biopsy.

Bilateral hilar lymphadenopathy on CXR-PAV

**Non caseating epithelioid granuloma
In bone marrow**

Thyroid profile showed mild hypothyroidism (TSH=8.7 u IU/mL). Rheumatoid Factor was weakly positive (16.3 IU/L). Serum triglyceride was raised (204 mg/dl) and Serum Calcium was 8.3mg/dl and serum Albumin of 3.8mg/dl (corrected calcium=8.5mg/dl) ACE level was raised 114 U/L (8 – 65). Other systemic parameters were essentially normal. Stool for occult blood was negative.

DISCUSSION: The case was approached with step wise baseline investigations for fatigue. Investigations revealed anaemia of chronic disease and hypothyroidism which were appropriately

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managed. Raised ferritin was considered as acute phase reactant which explained its high level in the setting of acute inflammation/infections as clinically correlated with chronic fever. Non-caseating epithelioid granuloma in bone marrow examination raised a strong suspicion for Sarcoidosis. This was also complemented with the chest radiograph giving a bilateral hilar lymphadenopathy, a very common finding in Sarcoidosis. Tuberculosis was ruled out with proper investigations. Sputum and Mantoux test negativity were in favour of Sarcoidosis. The fever responded with an adequate dose of systemic oral antibiotic. Absence of chest symptoms and lack of any occupational exposure curtailed the differential diagnosis for other respiratory diseases. Raised ACE (Angiotensin Converting Enzyme) level when estimated confirmed the diagnosis of Sarcoidosis though ACE level may be normal in some cases of sarcoidosis. The serum calcium level was in the normal range which occurs in some cases of sarcoidosis. Skin lesions in our patient might not be related to sarcoidosis as the skin biopsy revealed only features of chronic non-specific dermatitis. Hypertriglyceridemia was considered as the cause for the skin lesion as the lesions subsided with statin therapy. Rheumatoid factor may be positive in Sarcoidosis often in low titre. As the cells that make up granulomas secrete large amounts of ACE, this enzyme level is often high in patients with sarcoidosis which was found in our patient. Final diagnosis of the patient was made as Sarcoidosis, Hypothyroidism and isolated hypertriglyceridemia. The patient was put on Prednisolone 30mg/day tapered within one month and maintained on 10 mg/day for another two months and withdrawn thereafter and kept on regular follow up.

CONCLUSION: Sarcoidosis has not been reported from the state of Manipur so far. This case proves the occurrence of Sarcoidosis in Manipur and reported because of the asymptomatic lung involvement which is most commonly associated. Upto 25% of the cases may involve skin manifestations but the skin lesion seen in the patient seems to be independent of Sarcoidosis as suggested by improvement of the lesion with statin therapy. Presence of granulomatous lesion in the bone marrow in this case suggests further inquest.

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