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An Unusual Case of Hodgkin's Lymphoma with Initial Presentation of Fever, Mediastinal Lymphadenopathy and Disseminated Nocardiosis

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Abstract: ***We report an unusual case who presented with fever and mediastinal lymphadenopathy. He was extensively investigated, but all tests were normal. A few months later he developed disseminated Nocardiosis involving lung parenchyma and brain. He responded well to treatment. Some months later he was noted to have cervical lymphadenopathy, which on biopsy was found to be Hodkins lymphoma. He was also treated for the latter also and has now completely recovered from the lymphoma as well as Nocardiosis. We note that this form of presentation is extremely rare.***

Keywords: Lymphadenopathy, Nocardiosis, Hodgkin's Lymphoma

1. Introduction

When a patient presents with fever and mediastinal adenopathy the most common diseases that need to be kept in mind are tuberculosis, sarcoidosis, lymphoma and metastasis. To this one may add 'Reactive nodes' as the threshold of performing EBUS-TBNA for enlarged lymphnodes has decreased (1). However if all tests are persistently negative in a presumed immunocompetent patient making the correct diagnosis becomes a challenge. We present a patient who initially came with cough and mediastinal lymphadenopathy, later developed fever, followed by disseminated Nocardiosis. It was only after almost a year that he developed Hodgkins lymphoma of mixed cellularity.

2. Case Report

A Fifty three year old never smoker non diabetic gentleman with past history of Ulcerative colitis (UC) presented in March 2018 with complaints of cough not responsive to conventional therapy. The UC was in remission. He was only on Sulphasalazine for UC and had not received any immunosuppressive for more than 5 years. He was found to have enlarged mediastinal lymph nodes on CXR and CECT thorax (Fig 1). His haematological and biochemical profile was normal. An EBUS FNAC was performed which showed only reactive lymphnodes. A lymph node aspirate was negative for MTB DNA by PCR. The tuberculin skin test with 1TU was also negative.He was given symptomatic treatment and kept under observation.

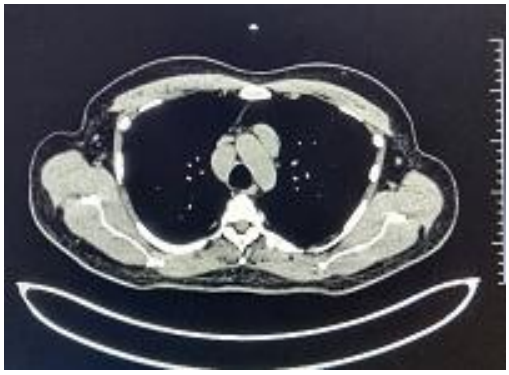

Figure 1

He developed Fever of 99-100 F in April 2018 andthere was an increase in the mediastinal lymph node size. A PET CT was performed which showed enlarged hilar lymphnodes, all lymphnode stations showed high FDG uptake. FDG uptake was also seen in multiple ribs, scapula, dorsal vertebra, left iliac bone, right sacrum and iliac bone. A bone biopsy was done from the iliac crest, and a simultaneous bone marrow biopsy was performed. Both biopsies were reported as normal. An immunoglobulin electrophoresis revealed no M spike. Immunoglobulin levels and Serum ACE was in the normal range.

In the meantime the patient developed high fever. Blood cultures were negative for bacteria and fungus. Procalcitonin and galactomanan were negative. ESR and C -reactive protein were raised. A serological study for Typhoid, Typhus and Rickettsial fevers was negative. Brucella antigen was also negative. An antinuclear antibody, P-ANCA and C-ANCA profile were negative. RA Factor was normal and serum Ferritin was marginally raised. He was HIV negative. The routine urine tests and cultures were negative. Trans-esophageal and 2-D Echocardiography was normal. AFB culture from the lymphnode aspirate was negative after 6weeks.

Over a period of 3 months the patient had lost 5 kg weight and developed recurrent normocytic normochromic anaemia for which packed red cell transfusion were given. A repeat EBUS from the mediastinal nodes revealed adequate smears that were reactive; however there was no granuloma or abnormal cells seen. In view of the history of UC he was investigated for occult colonic malignancy by colonoscopy and occult blood studies of stool both of which were negative. The patient refused a mediatinoscopic biopsy of the lymphnodes.

At this stage it was decided to empirically start anti-tubercular treatment. He was given the standard EHRZ treatment but the fever was persistent even after one month of ATT.

At this point a routine chest CT done showed diffuse bilateral infiltrates. (FIG 2) A trans-bronchial biopsy was done which revealed gram positive filamentous bacteria

identified on Modified ZN stain to be consistent with Nocardia.

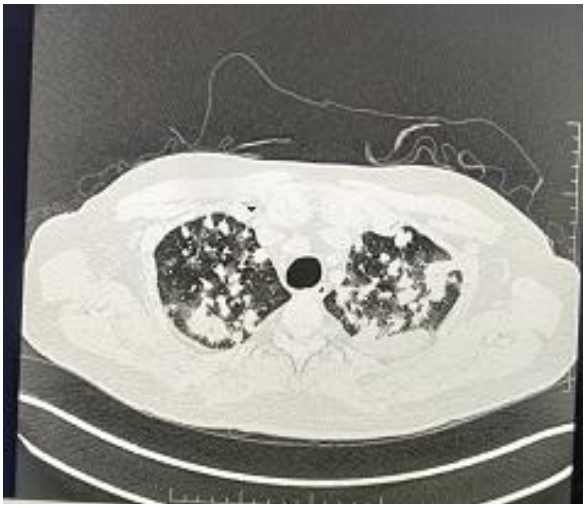

Figure 2

He was started on Trimethoprim and Sulfamethoxazole (TMP-SMX) combination. ATT was stopped. The patient became a febrile but then began to complain of unsteadiness of gait and giddiness. A MRI brain was done which showed multiple lesions in the brain and cerebellum. (FIG 3) These lesions were considered to be a part of disseminated Nocardiosis.

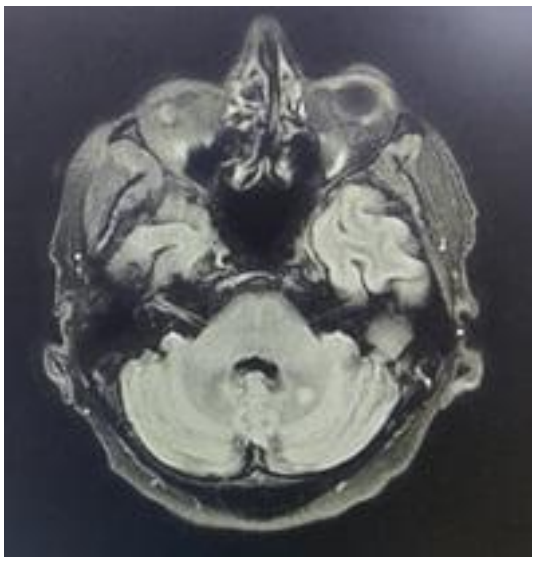

Figure 3

He was placed on Meropenem, Minocycline, and Linzolid.

After four weeks of this treatment his symptoms began to resolve and he felt better. A repeat MRI showed regression of the lesions. A CD4 and CD8 count was done which showed CD4 to be below 100cells /dl. In view of the low CD4 counts and disseminated Nocardiosis it was decided to continue treatment for one year. The patient developed thrombocytopenia for which Linizolid was stopped. He was continued on Minocycline along with TMP-SMX.

The response to therapy was satisfactory, the patient regained his lost weight, became afebrile and began to feel well. There was resolution of lung infiltrates and regression of mediastinal adenopathy. (FIG 4)

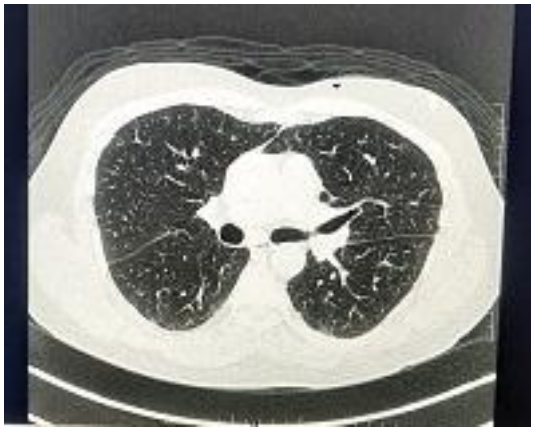

Figure 4

In January 2019 he developed an enlarged lymph node on the left side of neck which was biopsied and showed Mixed Cellularity Hodgkin's Lymphoma with CD30, PAX07 Positivity, but CD 15, 20, 3, 5, EBV and ALK was negative. He received five cycles of ABVD Chemotherapy and finally went into remission in July-August 2019 with repeat PET CT showing near complete resolution. (FIG 5) A repeat bone marrow biopsy also showed complete remission of lymphoma.

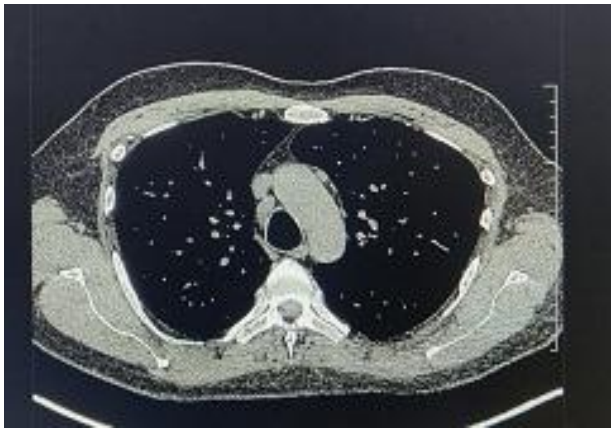

Figure 5

The PET CT also showed complete resolutions of the chest lesions and mediastinal nodes. A MRI brain showed the brain lesions to have resolved completely.

The CD4 and CD8 counts had improved to normal. The treatment for Nocardiosis was stopped in July 2019. He is now asymptomatic on regular follow up.

3. Discussion

Norcardiosis usually occurs in the immunocompromised host, it may also affect previously damaged lungs. The usual infection is through the pulmonary route from airborne particles. Human to human transmission has not been described. The most common extrapulmonary site of infection is CNS which also signifies dissemination and low immunity. (2)

Nocardiosis is known to occur in T-cell lymphomas where T –cell immunity is compromised. (3) But if the lymphoma itself is not manifest, the detection of the cause of immune compromise becomes challenging.

Nocardiosis per se does not give rise to mediastinal lymphadenopathy. Bone involvement may occur but is relatively rare. Thus there was suspicion in this case that Nocardiosis was not the primary pathology. The CD-4 counts were low despite the patient being HIV negative, and with no recent history of immunosuppressive therapy. This was another clue that there may as yet be another occult disease present. Though the patient refused a mediastinoscopic biopsy of enlarged nodes, it is pertinent to note that during treatment of Nocardiosis, there was regression of the mediastinal nodes.

It was almost a year later that the patient manifested with cervical lymphadenopathy that on biopsy proved to be Hodgkins Lymphoma. Thus unusual infections in a seemingly immunocompetent host may signify a latent malignancy which may manifest later.

Fortunately the patient has responded well to treatment with resolution of Nocardiosis, restoration of CD-4 count to normal, and remission of the Hodgkin's lymphoma.

Hodgkin's lymphoma by itself is the most common cause of fever of unknown origin (FUO) among haematological malignancies.(4) However it may be noted that the patient's fever subsided once he was adequately treated for Nocardiosis. Colonic inflammatory disease and malignancy are other causes of FUO that were considered and ruled out by colonoscopy.(5)

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