Extremely Rare Concomitance Of Tubercular Lymphadenitis With T Cell Non Hodgkin's Lymphoma – A Diagnostic Challenge For Clinician

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Abstracts: Tuberculosis (TB) presenting with Non Hodgkin's Lymphoma is an extremely rare clinical presentation and is quite difficult to diagnose because of similar signs & symptoms including lymphadenopathy, weight loss, anorexia and generalised weakness. Herein we report a case of 40 year old male who presented with enlarged cervical and axillary lymph nodes, diagnosed and initiated on therapy for TB based on the axillary node FNAC that showed granulomatous lymphadenitis suggestive of TB but was later confirmed to be a case of non Hodgkin's lymphoma by excisional biopsy followed by histopathology and immunohistochemistry . [Anand A NJIRM 2016; 7(5):95-97]

Key Words: Tuberculosis, Non Hodgkin's lymphoma, lymphadenitis.

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Introduction: Primary pulmonary as well as extra-pulmonary tuberculosis is quiet common in India. Tuberculous lymphadenitis is the commonest form of extra-pulmonary tuberculosis with special affinity for cervical, mediastinal, and axillary lymph-nodes[1]. Although several factors contribute to treatment failure of tuberculosis and significant morbidity and mortality, the most common causes in the "Third World" include poor compliance, late presentation, improper therapy, development of drug resistance, and erroneous diagnosis of this disease however the coexistence of Non Hodgkin's Lymphoma (NHL) and TB in the same organ is very rare and only few such cases have been reported till now. Here we report a rare concomitance of NHL preceded by tuberculosis and proved by excision biopsy & immunohistochemistry.

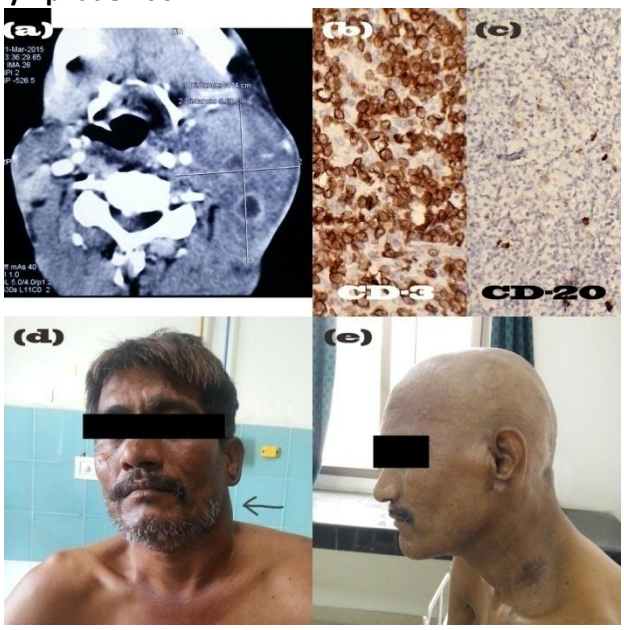
Case Report: A 40 year old male presented to the outpatient department with complaints of fever and painless lymphadenopathy of bilateral inguinal and left axillary nodes. The swellings were initially about pea in size and had been present for around a month before the patient first presented to the hospital. The patient was asymptomatic 3 months before he presented to the hospital following which he developed fever, which occurred during the evening each day. It was accompanied with sweating. One and a half months ago he noticed swellings in bilateral inguinal regions and left axilla. The swellings were 1cm by 1cm in size and non-tender. There was no history of tuberculosis in the patient, nor a history of contact with a known case of tuberculosis. There was no history of weight loss or decreased appetite. The labs were as follows: Hb - 11.2 gm/dL; Total Leucocyte count - 15900 cells/mm3; DLC – Neutrophil 80%,Lymphocyte 15% ,Monocyte 3%, Eosinophil 2%. ; Platelets - 3 lakh/mm3; Elisa for HIV - Negative; HBsAg - Negative. FNAC of the axillary node showed features suggestive of Tuberculosis with granulomatous inflammation with giant cells, though Acid fast bacilli (AFB) staining was negative. The patient was therefore put on Category-I Anti Tubercular Therapy (RHEZ) under RNTCP programme, following which he showed symptomatic improvement and there was a decrease in size of left axillary lymph node. He was advised fortnightly follow up with continuation of ATT.

However, 4 months after the initiation of ATT, the lymph nodes were bigger in size than earlier. In addition to the axillary and inguinal lymphadenopathy, now there was cervical, right axillary and bilateral supraclavicular lymphadenopathy as well. The enlarged nodes were now much larger in size, with the axillary ones almost 3cm by 3cm. A repeat FNAC was done to rule out Multi drug resistance tuberculosis (MDR TB), reactive lymphadenitis or lymphoma. The repeat FNAC was positive for AFB, following which Category-II ATT(SHREZ) was started. An ultrasound of the abdomen was also done to rule out any other enlarged nodes, and it came out normal without any features of organomegaly or abdominal lymphadenopathy.

In spite of aggressive anti tubercular treatment with 5 first line drugs, the swellings continued to increase in size. A repeat FNAC was done. This FNAC (from submandibular, cervical and left axillary node) showed features of atypia and the absence of AFB on ZN staining. An excision biopsy was therefore planned to solve the diagnostic dilemma. The excision biopsy showed features of Non-Hodgkin's Lymphoma. CT of neck & thorax and an ultrasound of the abdomen was then done to stage the disease. Findings in the neck

were suggestive of cervical lymphadenopathy with extra-nodal spread (Figure 1a).

Fig1a.CECT Neck shows large mass of lymph node with extra nodal spread shown by arrow. b&c. Tumor cell showing strong cytoplasmic CD3 positivity. (CD3; x400) and tumor cells negative for CD 20 (CD20; x200). d&e.Pre and post chemotherapeutic improvement in cervical lymphadenitis.



The chest CT was clear. Ultrasound of the abdomen showed splenomegaly and enlarged nodes in left peri-aortic and left common iliac areas, along with the bilateral inguinal lymphadenopathy already present. This was in huge contrast to the USG abdomen done 3 months ago which did not show any organomegaly or lymphadenopathy. The histopathology of the biopsy specimen revealed the presence of non Hodgkin's lymphoma , which was further confirmed by immunohistochemistry which was found to be strongly positive for CD3 (figure 1b-c) and negative for CD20 stain, suggestive for T-cell type Non Hodgkin's Lymphoma . Patient was referred to Oncologist and CHOP(Cyclophosphamide, Doxorubicin, Oncovin , and prednisolone) regimen was started . Patient get drastic improvement clinically as well as symptomatically in follow up after completion of three cycles (Fig 1 d-e)

Discussion: Concomitant Tuberculosis & Non Hodgkin's lymphoma is a rare presentation and it is very difficult to diagnose the same because of similar clinical features such as cough, fever, loss of appetite, weight loss, night sweats, hepatosplenomegaly and lymphadenopathy. Furthermore, in countries with a high tubercular burden, such as India, it becomes even more difficult to make a diagnosis of unusual combination of diseases.

T-cell NHLs are uncommon malignancies that represent approximately 12% of all lymphomas. Various geographic frequencies of T-Cell NHL have been documented in the range of 1.5-18.3% and it often expresses CD3, CD4, CD25, and CD52 antigens[2.]

It has been hypothesized that Mycobacterium tuberculosis infection causes direct DNA damage and apoptosis inhibition, which increases mutagenesis of progeny cells, combined with angiogenesis favoring tumorigenesis. Specifically, various mycobacterial cell wall components are hypothesized to induce the production of nitric oxide and reactive oxygen species which are involved in mutagenesis. It should also be noted that both nitrative-DNA damage as well as oxidative-DNA damage have been implicated in inflammation-related carcinogenesis[J]. It has been also proposed that low secretor genotype of TNF alpha are associated with increased susceptibility to NHL[4].In the other hand it was also proposed that the risk of NHL is significantly increased (Odds Ratio 1.8) in individuals with a history of severe forms of tuberculosis who have not received curative chemotherapy[5]. In the present case, however, there was no previous history of ATT intake by the subject.

In other direction it was also postulated that the incidence of TB lymphadenitis in lymphoma patients is much higher than in the patients without a malignancy and the presence of TB may be the main factor contributing to the death of the patient. However researchers suggest that the chronic inflammation of TB lymphadenitis may actually precede and accelerate the onset of the lymphoma[2].

Such a rare concomitance frequently precipitate the diagnostic dilemma among clinician and misdiagnosis and treatment delay may result in worsening of symptoms in a patient[6]. However a definitive diagnosis can only be achieved by histopathology, In obtaining biopsy specimens, pitfalls of FNAC must be realized in present case , especially when a lymphoproliferative disorder is in the differential. Hence Performing excisional or incisional lymph node biopsy is preferred with immunohistochemistry when

lymphoma is suspected or there is slightest confusion in the histopatology of granulomatous inflammation , as the characteristic histopathologic features of both disease processes can be easily delineated by this method.

Conclusion: Although tubercular lymphadenitis is the commonest type of extra-pulmonary presentation of tuberculosis worldwide, in this part of world a corroborative FNAC report suggestive of granulomatous inflammation is enough to commence the anti-tubercular regimen because of paucibacillay nature of lesion. The key message delivered in the present case to all clinicians is to advise biopsy to all such cases where there is no improvement after commencement of ATT.

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