‘Red Herring’ in the Pathology of Cervical Lymph node

Veena.G1, V.Rajalakshmi2*, K.Meenakshisundaram3, Sathish Selvakumar4, K.Rajeswari5

1Senior Resident,2Professor & HOD,3Associate Professor,4&5Assistant Professors, Department of Pathology, ESIC Medical college & PGIMSR, K.K.Nagar, Chennai-78.

ABSTRACT

The causes of cervical lymphadenopathy can be multiple from reactive, infectious to neoplastic. Rarely a combination of infective and neoplastic process can be the cause of lymphadenitis. One may distract the presence of other and hence a careful evaluation is essential not to miss both the lesions. Neoplastic process can be of primary or metastatic deposit from a malignant tumor. We report a case of Hodgkin lymphoma and tuberculosis coexisting in a 30 years old female patient. Both Hodgkin lymphoma (HL) and tuberculosis (TB) can share the same clinical and laboratory findings. Few studies show misdiagnosis of Hodgkin as tuberculosis and were started on antituberculosis treatment. In countries where tuberculosis is endemic, the association between Hodgkin and tuberculosis must always be considered.

A 30 years old female presented with cervical lymphadenopathy of one year duration. She was diagnosed to have tuberculosis and was started on antituberculosis treatment. She completed the course of treatment and there was no regression in the size of the lymph node. Then repeat FNAC followed by biopsy of the lymph node was done. The diagnosis of Hodgkin lymphoma and tuberculosis was made on both FNAC and histopathology which was confirmed with immunohistochemistry. Quantiferon test for tuberculosis was found to be positive. The case is presented to highlight the importance of diagnosing the coexisting Hodgkin lymphoma with tuberculosis.

KEYWORDS: Co-existence, Lymphoma, Tuberculosis.

INTRODUCTION

Cervical lymphadenopathy has multiple causes from reactive to infective to malignancy. The co-existence of infective etiology and malignancy is very rare, for example malignant lymphoma with tuberculosis infection. Hodgkin lymphoma is a malignant neoplasm originating in lymphoid tissue that features presence of characteristic Reed-Sternberg cells. It was first described by Thomas Hodgkin in 1832 [1]. It constitutes 30% of all lymphomas. The immunophenotype of the neoplastic Reed-Sternberg(RS) cell is unique. Single cell experiment has conclusively proven that RS cell represents clonal expansion of a pre-apoptotic germinal centre B-cell. Tuberculosis caused by mycobacterium tuberculosis, is characterized by presence of granuloma composed of epithelioid cells with caseous necrosis.

CASE REPORT

A 30 years old female had fever with chills of 5 months duration with swelling in the right cervical region of one year duration. FNAC done in outside hospital and an impression of granulomatous lymphadenitis was made and she was started on anti-tuberculous treatment. The swelling persisted with fever. A clinical diagnosis of Multidrug-resistant TB lymphadenitis was then made. She came to our institution and on examination, she was moderately built and nourished. Multiple nodes were palpable in the right cervical region ranging in size from 2x1 cm to 5x3cm. Few nodes were discrete and few were matted. They were firm in consistency. Chest X ray showed no pulmonary involvement. Serological investigations showed she was HIV negative. Repeat Fine needle aspiration of the node was done.

On microscopy, smears showed numerous clusters of epithelioid cells in a background containing lymphocytes. Scattered atypical, mononuclear and binucleate cells were also seen. A diagnosis of Granulomatous Lymphadenitis was made and in view of the atypical cells an excision biopsy was suggested to rule out Hodgkin lymphoma(Fig 1).

Excision of cervical lymph node was done. We received multiple grey brown soft tissue pieces together measuring...
2x1.5x1cm. Microscopy showed lymph node with effacement of architecture by sheets of lymphoid cells admixed with large atypical cells with large nucleus and prominent nucleoli. Many binucleate cells and scattered mononuclear cells (Fig 3) with prominent nucleoli in the background containing eosinophils were seen. Granulomas composed of epithelioid cells (Fig 2) were also seen. The diagnosis of Hodgkin lymphoma with tuberculous lymphadenitis was made. Immunohistochemistry confirmed the diagnosis of Hodgkin lymphoma, with Hodgkin cells positive for CD 15 (Fig4) and CD 30. Quantiferontest for tuberculosis was found to be positive. This test is used as an aid in the diagnosis of latent tuberculosis infection.

Figure 1: FNAC Smear showing mononuclear large cells with large nucleus containing prominent nucleoli (40x,pap stain)

Following the diagnosis, the patient was further evaluated. CT abdomen showed ill-defined non enhancing calcified lesion in liver(calcified granuloma). Mesenteric lymph node of 7 mm seen with mild puckering of lateral wall and pulled up caecum. Ileocaecal mucosal thickening of 10 mm –all suggestive of tuberculosis abdomen. CT neck showed multiple enlarged conglomerate matted poorly enhancing posterior group of cervical lymph nodes on right side. Multiple bilateral anterior cervical lymph nodes and nodes in supraclavicular region more on right side comparing with left, features suggestive of tuberculous lymphadenitis.

Figure 2: Photomicrograph showing a granuloma composed of epithelioid cells (40x,H&E)

Figure 3: Photomicrograph showing effacement of lymphnode architecture with scattered mononucleate and binucleated RS Cells (40x,H&E)

Figure 4: IHC CD 15: Photomicrograph showing tumour cells positive for CD 15 (40X)
DISCUSSION

Hodgkin lymphoma (HL) accounts for 8.2% of lymphoid malignancies and is more common in whites than in blacks. Hodgkin lymphoma has bimodal distribution of age with one peak incidence occurring in patients in their 20’s and other in their 80’s. Clinically, in Hodgkin lymphoma, the swelling is painless, firm and free, mobile. It does not fuse together and breakdown and suppurate as in tuberculosis (TB).

There is prevalence of tuberculosis in 96 cases /10000 patients with HL[2]. In countries where tuberculosis is endemic, the association between HL and tuberculosis must be considered[3]. The similarity in clinical course, laboratory and imaging procedures make the diagnosis difficult. In a study with 201 cases, Kaplan et al found out that tuberculosis infection with high mortality occurs in patients with TB occurring after antineoplastic therapy[2]. Hodgkin lymphoma is the most common cause of progressive lymph node enlargement next to tuberculosis. Melero et al [4] reported six TB cases in lymphoma patients and described the higher incidence of tuberculosis in these patients than in general population.

Tuberculosis occur in Hodgkin lymphoma patients due to the immunologic changes that accompany HL. Hodgkin has been attributed with complex cellular immunodeficiency. The IL 5 and IL 10 levels are increased by TH2 cellular response and this is attributed to the delay of response in hypersensitivity skin tests, eosinophils increase in circulation, reduced activity of NK cells and increased IL 2 levels[5].

In a study, Bhattacharya et al [6] described that HL is associated with immunodeficiency and it may be preceded by chronic inflammatory disease. Tuberculosis is chronic infectious disease which is promoted by cell mediated immunodeficiency.

The pathogenesis is that, tuberculosis infection directly damages the DNA [7,8,9] and inhibit apoptosis, thus increasing the mutagenesis of progeny cells. This along with angiogenesis favour tumorigenesis. Few mycobacterial cell wall components induce the formation of nitric oxide [10,11]and reactive oxygen species[12], involved in mutagenesis.

Further evaluation of the patient is essential if there is initial therapeutic failure during the treatment of HL/TB, because further introduction of immunosuppressive chemotherapy where immunological changes already present in patients with HL may worsen the clinical course of Tuberculosis[6]. Gamma interferon assay was found to be positive. Interferon gamma release assay (IGRA) are diagnostic tool for latent TB infection. It is not affected by BCG vaccination status. IGRA have higher sensitivity and specificity for detecting TB infection than conventional TST(Tuberculin skin test) as they utilize antigen specific for MTB complex.

In our case, she did not respond to ATT treatment alone, so the patient was referred for repeat FNAC and biopsy of the node. The diagnosis of HL and TB was made. She was started on CHOP regimen. Now, the size of the cervical swelling regressed and she is symptomatically free after 8 cycles of chemotherapy.

CONCLUSION

Neoplastic and infective process can present in the same patient and can be the cause for lymphadenopathy. Both processes can present with the same clinical and laboratory findings. Extensive clinical examination, with careful evaluation of the tissue is essential. One process can hide or distract the feature of the other. So this case poses the difficulty and stresses the importance in diagnosing two lesions in the same patient, as the treatment is different for both the conditions. We report this case for its rarity and therapeutic importance.

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*Corresponding author: Dr V. Rajalakshmi. E-Mail: raji_path @rediffmail.com