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Hodgkins lymphoma masquerading as Granulomatous Lymphadenitis – A perilious diagnostic dilemma

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Abstract

Presence of granulomas in Hodgkin lymphoma is a sporadic finding, which is often a source of diagnostic dilemma.

Case report: We reported a case of 30-year-old woman who presented with left axillary swelling, fever and weight loss. Fine needle aspiration from the left axillary lymph node was performed,

Cytology report: the cytological examination of which showed granulomatous inflammation and associated findings of occasional binucleated cells, the latter being present is of less common occurrence. This unusual finding of led to ambiguous interpretation of cytological findings which were to be mandatorily confirmed by histopathological examination.

Histopathology report: Histopathological examination, along with ancillary techniques, was conclusively diagnostic of Hodgkin lymphoma with co-existence of non-caseating epithelioid granulomas, a rare and interestingly uncommon finding.

Conclusion: Granulomatous reaction in a lymph node with Hodgkin lymphoma can have dubious distinction of masking the primary and crucial diagnosis of lymphoma, which often can be, in the hands of those not fully well-versed with working in the field of lymphoproliferative disorders, easily misdiagnosed as granulomatous inflammation of lymph node including tuberculosis, particularly in endemic countries, and other granulomatous lesions. References to the fact that epithelioid cell granulomatous reaction can occur, apart from the conventional reactive changes, in lymph nodes draining malignancies, do exist in English medical literature. It is also notable that a variant of Hodgkin lymphoma, Nodular sclerosis, does have a histologic variant, epithelioid cell variant, a fact which might further confound the well-established granulomatous reaction occurring in lymph nodes draining areas of malignant neoplastic lesions.

Keywords: Hodgkin lymphoma, Nodular sclerosis, granulomatous reaction, non-caseating epithelioid cell granulomas, lymphoproliferative lesions,

Introduction

Hodgkin lymphoma is a malignant neoplasm arising from the B lymphocytes (germinal or post germinal) and it accounts for 0.7 per cent of all new cancers [1]. It is mainly characterized by the presence of neoplastic lymphoid cells admixed with inflammatory cells comprising small lymphocytes, eosinophils, neutrophils, histiocytes and plasma cells as well as stromal fibroblasts [2]. Hodgkin lymphoma differs from non-Hodgkin lymphoma by the presence of distinct binucleated giant cells with prominent eosinophilic nucleoli, Reed-Sternberg (RS) cells which are considered pathognomonic and of diagnostic value to Hodgkin lymphoma [3]. Reed-Sternberg cells contain abundant pale basophilic cytoplasm and contain two near identical (mirror-image) nuclei with prominent acidophilic or amphophilic nucleoli, covering more than 50% of the nuclear area. RS cells, albeit considered to be of 'diagnostic value', are not unique as their mimics or RS-like cells are can be seen in reactive lymph node lesions (such as infectious mononucleosis, B and T cell lymphomas, certain carcinomas, melanomas, and sarcomas). Presence of epithelioid cell granulomas often lead to diagnostic predicament and hamper or cause delay in the accurate diagnosis and result in uncalled for treatment with antibiotics or antitubercular drugs with undesirable associated complication.

Case Report

30-year-old female presented with complaints of left axillary swelling since three months. The swelling was painful with restriction of movement of the left shoulder and, of late, was accompanied with fever for the last one month. Patient had also history of significant weight loss during the last three months. Overall, the varied symptoms lead to malaise, lethargy and disruption of her participation in routine physical activities. She also had a past history of having tuberculosis two years back for which she had undergone successful clinical treatment. Her recent past history revealed that she had undergone Fine Needle Aspiration Cytology (FNAC) of left axillary lymphadenopathy at a private clinical laboratory facility and cytological findings were of granulomatous lymphadenopathy. The patient was non-reactive for HIV and serology for auto-immune disorders was negative. As the patient was on antibiotic and/or anti-tubercular therapy, there was transient improvement in her clinical condition. After few days, she presented again with relapse in clinical features including enlargement of left axillary lymph nodes for which she came to the present tertiary care hospital for further clinical investigations. On examination….. Fine needle aspiration cytology of the lymph node revealed moderate cellularity consisting of polymorphous population of lymphoid cells with scattered epitheliod cells scattered poorly formed non-caseating epithelioid cell granulomas without any atypical cells. Few binucleate cells with nuclei showing granular chromatin and prominent nucleoli were also noted. Differential diagnosis of Hodgkins lymphoma (HL) with granuloma and tuberculosis were made. Lymph node biopsy was done to confirm the cytological diagnosis, which showed diffuse effacement of lymph node architecture characterized by sheets of mononuclear cells with irregular nuclear margin, vesicular nuclei with prominent nucleoli with some cells showing clustered nuclei along with numerous giant cells, some showing multilobated and pleomorphic nuclei displaying prominent nucleolus surrounded by lymphoid cells

admixed with few polymorphonuclear cells and eosinophils. Focal areas of delicate fibrosis and hypocellularity are also noted. Overall, the histological findings are suggestive of Hodgkin lymphoma. Further laboratory work-up with immunohistochemical studies showed the lesion to be positive, with high expression, for CD30 and negative for CD45. Ancillary clinical imaging studies revealed lymph nodes expressing focal uptake on PET/CT. Finally, on the basis of histological and immunohistochemical findings, the condition was conclusively diagnosed as classic Hodgkin lymphoma.

Discussion

Diagnosis of granulomatous inflammation is common in clinical practice [4]. In some of these malignancies for example, Hodgkin's disease the granuloma may be the dominant presentation of the primary disease [5] The present case describes an approach for diagnosing Hodgkin lymphoma with co-occurrence of granulomas by comprehensive evaluation using FNAC and histopathology. Six to nine percent of cases of Hodgkin lymphoma may have granuloma formation. [6] Hodgkin lymphoma mostly affects the age group of 20-34 years with median age of diagnosis 39 years.[4]. Usually, it presents as low grade fever, weight loss and/or multiple lymphadenopathy. Granulomas have been well-recognized histologically as discrete nodules composed of epithelioid histiocytes or multinucleated giant cells that are commonly accompanied by small lymphocytes. Epithelioid cell granuloma is histologically seen as a focal collection of inflammatory giant cells, macrophages, mononuclear cells and fibroblasts with or without caseous necrosis in the centre. These granulomas may form at the primary site of tumor or may develop at distant organs/ draining lymph nodes even without any evidence of malignancy.(7)(8)(9)

Khurana et al described six malignant cases who presented with granulomatous reaction on cytology. (10).The subsequent histologic findings in 2 cases revealed Hodgkin's disease with the exuberant granulomatous response, and the remaining 3 cases were found to be malignant neoplasms with epithelioid morphologic features and included one example of each diffuse large cell lymphoma, anaplastic carcinoma of the thyroid, and lymphoepithelial carcinoma(11). The ideal approach to diagnosis in such patients is not clearly defined in literature. It has been seen that the morphology of the granuloma does not differ between benign and malignant causes either on light or electron microscopy. However in most cases the granulomas are non-caseating in nature with many foreign body and Langhan's type giant cells. Their resemblance to sarcoid granulomas has prompted some authors to label them as sarcoid like granulomas or tumor related sarcoid reaction (12). In the present patient also, FNAC revealed non-caseating granulomas which prompted us to perform excision biopsy from the lymph node. Besides histopathology and IHC, the tissue was also subjected to Cartridge based nucleic acid amplification test (CBNAAT) that virtually excluded the diagnosis of tuberculosis.(13)

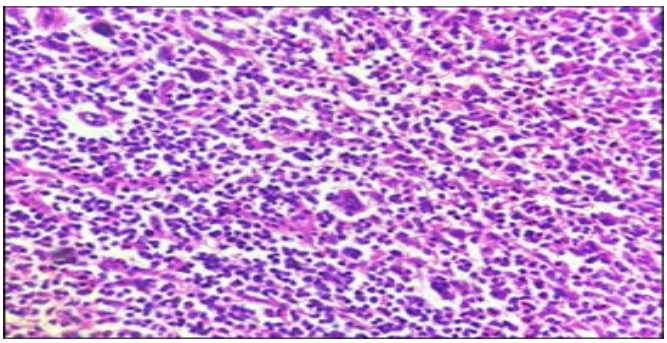

Fig.1: Showing Lymph node architecture with characteristic 'Reed Sternberg' cell.

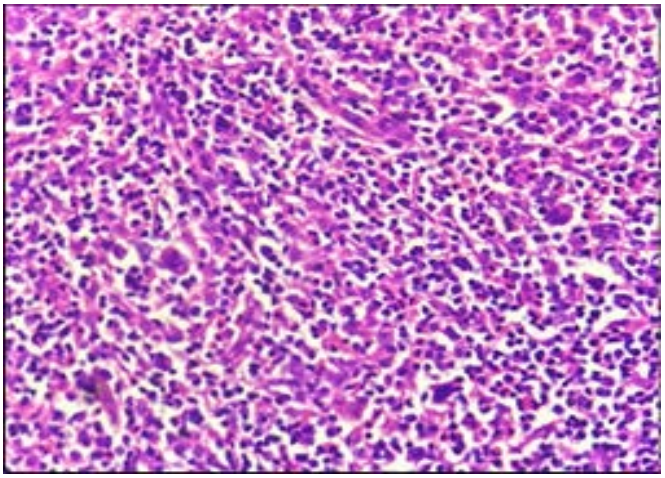

Fig.2: Showing lymphocyte predominant type of Hodgkin lymphoma.

Classification

HL is subdivided into classical Hodgkins Lymphoma (HL) and nodular lymphocyte-predominant HL (NLPHL) based on morphology and immunohistochemistry. NLPHL comprises a small percentage (about 5%) of the total number of patients diagnosed with HL. It is generally a much more indolent lymphoma, is usually asymptomatic, and is always negative for EBV (5)

Nodular Sclerosis

Nodular sclerosis (NSCHL) is the most common subtype, accounting for about 70% of CHL cases in the developed world and characterized by neoplastic lacunar-type HRS cells in an inflammatory background of band-forming sclerosis (5). Mediastinal adenopathy is seen in 80% of cases, and bulky nodes (>10 cm in diameter) are present in about one-half of patients.

Mixed Cellularity

Mixed-cellularity CHL (MCCHL) comprises 20% to 25% of CHL in the United States but is more frequent in patients with HIV infection and in developing countries. The HRS cells are scattered in a diffuse, mixed, inflammatory background without sclerosing fibrosis.

Lymphocyte Rich

Lymphocyte-rich CHL comprises about 5% of all CHL; specimens have scattered HRS cells within a nodular or diffuse cellular background of small lymphocytes and without neutrophils or eosinophils. Patients tend to have peripheral adenopathy without bulky mediastinal involvement and usually present with early-stage disease. Treatment outcomes are excellent using modern combination chemotherapy regimens, with rare treatment failures.(17)

Conclusion

Hodgkin lymphoma is a malignant neoplasm. Its diagnosis may be confused by the presence of granulomatous reaction and creates a diagnostic dilemma. A prognostic relevance of the granulomatous reaction in Hodgkin's lymphoma is not clear.(6) , it appears that distinguishing reactive or granulomatous lesions from those that are truly neoplastic occasionally may be difficult or impossible based on cytologic findings alone. Thus, in most such instances, excisional biopsy may be appropriate(17) Hence, it seems pertinent to perform biopsy in such cases.

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