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RESEARCH ARTICLE

HYALINE VASCULAR CASTLEMAN'S DISEASE PRESENTING AS AXILLARY MASS: A DIAGNOSTIC DILEMMA ON FINE NEEDLE ASPIRATION CYTOLOGY

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ABSTRACT

Castleman's disease (CD) is an uncommon lymphoproliferative disorder typically presenting as 'Mediastinal' lymph node swelling. Clinical presentation can range from asymptomatic to generalised lymphadenopathy and hepatosplenomegaly. Two histological variants are hyaline vascular type and plasma cell type. Hyaline vascular type CD presents as unicentric mass mimicking various infectious and malignant causes of lymphadenopathy. Cytological features vary depending upon the extent of the lesion, thus, fine needle aspiration cytology (FNAC) is not always conclusive and histopathology is required to reach a definitive diagnosis. Here we present a case of unicentric castleman's disease (UCD) diagnosed on FNAC with histological correlation.

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INTRODUCTION

Castleman's disease (CD), also known as giant lymph node hyperplasia, angiofollicular lymph node hyperplasia, was first described in 1956 by Benjamin Castleman and his colleagues as benign localised follicular hyperplasia of mediastinal lymph nodes (Castleman *et al*., 1956). It is a rare lymphoproliferative disorder of unknown etiology. Clinically, CD may be unicentric (UCD) presenting as a solitary mass with no other symptoms, or it may be multicentric (MCD), a generalized symptomatic disease presenting with generalised lymphadenopathy and associated symptoms of fever, weight loss, anemia and hepatosplenomegaly (Norbert Wagner and Zerrin Maden, 2013). MCD is frequently associated with HHV8 infection (Du *et al*., 2007). Two distinct variants are identified on histology; hyaline vascular variant, which is more common and plasma cell variant (Norbert Wagner and Zerrin Maden, 2013). Here, we present a case of UCD-hyaline vascular type, presenting as axillary swelling. Cytological features were studied and were correlated on histology.

Case report

A 35 year old female with a solitary axillary swelling was referred to the FNAC department with clinical suspicion of extrapulmonary tuberculosis. There was no history of fever, fatigue or weight loss. Also there was no significant past or family history. On examination, there was a well defined, mobile, non tender, soft to firm mass measuring 4x5 cm in right axilla. No other lymph node was palpable. Ultra sonography revealed a hypoechogenic swelling with well defined margins in right axilla. Chest x-ray was also clear of any signs of tuberculosis. Peripheral blood counts were within normal limits. CRP was mildly elevated. FNAC was perfomed and slides were stained with May-Grunwald-Giemsa (MGG) stain. Smears were moderately cellular with a predominance of small lymphoid cells. Few small foci suggestive of germinal centres were noted. Some large tissue fragments consisting of lymphoid cells and few plasma cells were noted. Eosinophilic granular material with lymphocytes adhered to it was also seen (Fig.1). Hyalinised blood vessels were also seen (Fig.2). Differential diagnosis of CD of hyaline vascular type along with Hodgkin's lymphoma and HIV lymphadenopathy was given. Excision biopsy was performed for confirmation and was sent for histopathological examination. Grossly, a well defined, encapsulated mass of 5x5x6 cm was received. Cut surface was grey white and homogenous. Microscopic examination revealed lymph node with thickened capsule, variable sized, enlarged lymphoid follicles surrounded by normal mantle zone. Small capillaries were seen penetrating the follicles and also in parafollicular area. Medullary sinuses

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were not seen. Histological features conformed to diagnosis of hyaline vascular type CD. (Fig.3)

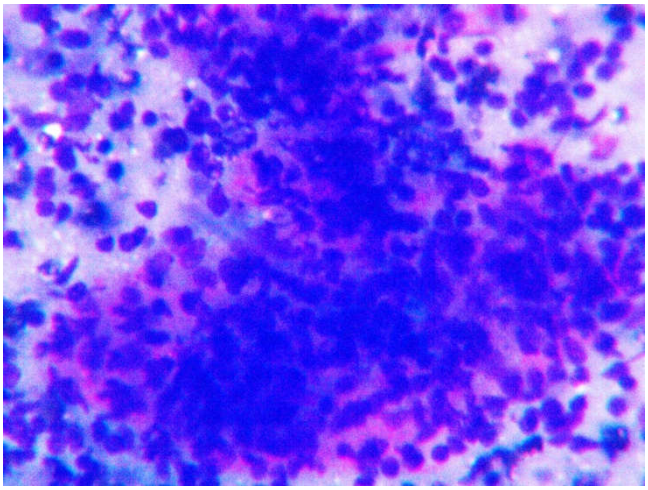

Fig. 1. Photomicrograph showing eosinophilic granular material with adherent lymphocytes (MGG;100X)

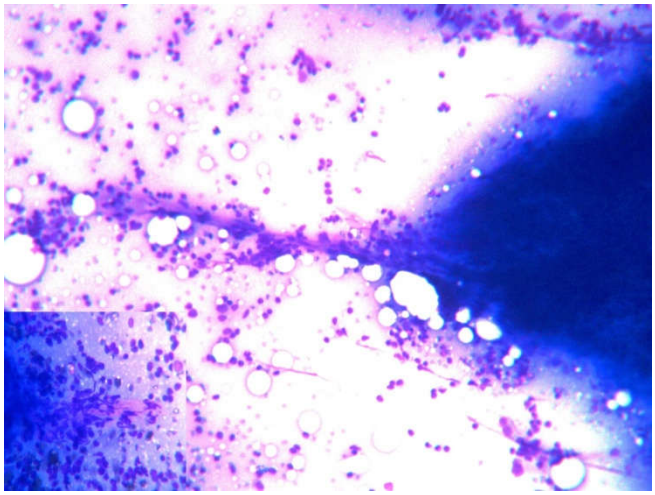

Fig. 2. Hyalinised blood vessel entering a cluster (MGG;100X). Inset shows high power view of hyalinised capillary entering a follicle (MGG;400X)

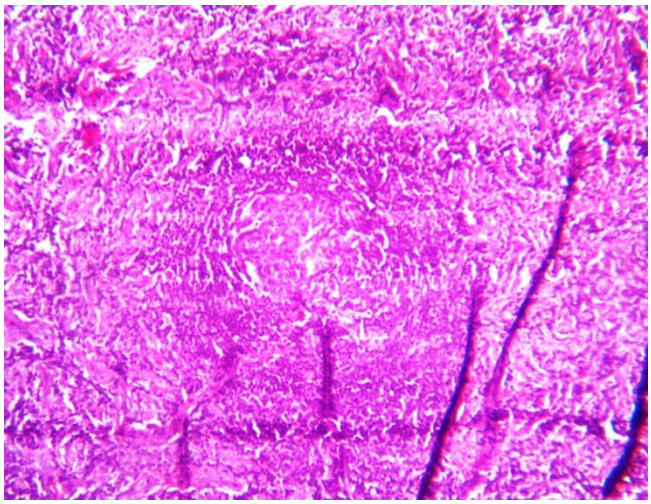

Fig. 3. Reactive follicle with lollipop appearance. Hyalinised capillary entering the follicle (arrow) (H&E, 100X)

DISCUSSION

CD is a rare benign lymphoproliferative disorder that may present as a nodal or extra nodal mass (Rosai *et al*., 2003). Majority (around 90%) of the localized type belongs to the hyaline vascular subgroup, as seen in our patient, and almost all of the multicentric type belongs to the Plasma Cell type. CD can develop in any of the lymphoid tissue of the body, most commonly in the mediastinum (60%), followed by abdomen, neck, lung, and retroperitoneum. Less than 4% of cases present as solitary axillary lymph node swelling. Patients with the hyaline vascular type are usually asymptomatic, as was also seen in the present case (Norbert Wagner and Zerrin Maden, 2013). The aetiology of CD is not completely understood yet. Various hypotheses are suggested based on clinical evidences: chronic stimulation by a viral antigen (human herpes virus 8 or Kaposi sarcoma-associated herpes virus) (Du *et al*., 2007), chronic inflammation (Castleman *et al*., 1956), immunodeficient state (Oksenhendler *et al*., 1996) and autoimmunity (Hsu *et al*., 1993). Fine Needle Cytology (FNAC) is a quick, cost-effective and safe diagnostic procedure, which can be highly useful for diagnosis of various surgical and non-surgical diseases. Also, it is very useful for the discrimination between reactive lymphadenopathies and other malignant conditions, thereby avoiding unnecessary surgical procedure. Cytodiagnosis of CD is often difficult because of many overlapping features with various malignant and non-malignant conditions. Only few case reports are available describing cytological features of the disease. In the present study the predominant cytological feature was a polymorphous population with predominance of small lymphocytes and few capillary fragments. Deschenes studied cytomorphological features of three cases of hyaline vascular CD with histopathological correlation to set cytomorphological criteria that could help in the identification of this condition on aspirate smears. The following cytomorphological indicators pointed towards the lesion: presence of large oval to round cells having ill-defined cytoplasmic margins and large nuclei with irregular nuclear outlines, fine or coarse chromatin, giving a crumpled tissue paper appearance in background of polymorphous population of lymphoid cells predominantly small lymphocytes (Deschenes *et al*., 2008).

Mallik suggested that the most striking cytological feature of CD is "the presence of large atypical cells with "crumpled tissue paper" like chromatin, occasional multinucleation, nuclear indentations and nuclear grooves" (Mallik *et al*., 2007). CD can mimic Hodgkin's lymphoma due to the presence of Reed-Sternberg like cells in a polymorphous background. Large atypical/dysplastic follicular dendritic cells were first described in association with CD in 1991. Identification of these dysplastic follicular dendritic cells within aspirates of CD may help to avoid the possibility of misdiagnosing CD as Hodgkin's lymphoma. Thus, in appropriate clinical context, a mature small lymphoid population associated with larger atypical cells which are consistent with dysplastic follicular dendritic cells can be suggestive of CD (Taylor *et al*., 2000; Meyer *et al*., 1999). However, we did not identify these dysplastic follicular dendritic cells, cells with crumpled tissue paper appearance and Reed Sternberg-like cells in our aspirates. Similar findings were also reported by Ayyagri

(Ayyagari Sudha and Namala Vivekanand, 2010). The first cytological case report of CD by Hidvegi and his collaborators described the presence of capillary vessels in their aspirate. We also found capillary fragments in our case, which directed towards possibility of CD (Hidvegi *et al*., 1982). On histopathology, HV type is further subdivided into "lymphoid subtype" which have a marked mantle zone hyperplasia, merging with mantle zone hyperplasia and "stroma rich subtype" which have prominent vascular and associated myoid component merging with angiomatoid proliferative lesion and angiomatoid hamartomas. Histopathological differential diagnosis includes follicular lymphoma, mantle zone lymphoma, AIDS related complex and thymoma. Immunohistochemistry aids in reaching a definitive diagnosis (Ghosh *et al*., 2010). Thus we can conclude that definitive diagnosis of CD on cytology samples is difficult, the presence of branching hyaline capillaries penetrating reactive follicular germinal centres should at least raise the suspicion. After exclusion of other reactive and malignant lymphoproliferative disorders, a careful review of the cytomorphology and clinical features should be carried out. Excisional biopsy should be always recommended.

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