Original Research Paper

Volume - 13 | Issue - 04 | April - 2023 | PRINT ISSN No. 2249 - 555X | DOI : 10.36106/ijar

Haematology

CASTLEMAN DISEASE : A CASE REPORT OF RARE CAUSE OF CERVICAL LYMPHADENOPATHY

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ABSTRACT Castleman disease (CD) is a rare lymphoproliferative disorder characterized by enlargement of lymph nodes with two primary subtypes that vary in presentations and course. Unicentric Castleman disease (UCD) presents as a solitary mass, most commonly in the mediastinum, and rarely in the head and neck . In contrast to multicentric Castleman disease (MCD),which features generalized lymphadenopathy and numerous systemic symptoms, a more aggressive clinical course and relatively poorer prognosis .The most common histopathological subtype is the hyaline vascular variant .We present the case of an 14 years old female presented with a slowly expanding painless left sided neck swelling. Physical examination, coagulation tests, infectious disease screening (HIV, HCV and HBsAg), ESR test and chest X-ray were all normal. Both computed tomography (CT) and Ultrasonography (USG) findings showed a well-defined solid enhancing mass lesion in the left supraclavicular fossa, which was completely excised and diagnosed to have hyaline vascular variant of unicentric Castleman disease .This disorder carries a an excellent prognosis and does not require further therapy if complete excision of the involved lymph node has been done. We report a case of unicentric Castleman disease is a rare cause of cervical lymphadenopathy , diagnosis by excision biopsy and surgical resection is curative. However ,Histopathological examination rules out lymphoma and concluded that it is unicentric Castleman disease, hyaline-vascular variant .

KEYWORDS : lymphnode, plasma cell, hyaline vascular, multicentric castleman disease (mcd), unicentric castleman's disease

Introduction

Castleman disease (CD) was originally identified by Benjamin Castleman ,who described a cohort of patients with solitary hyperplastic mediastinal lymph nodes which demonstrated small, hyalinized follicles and interfollicular vascular proliferation on histopathology. Years later, Castleman and colleagues distinguished this hyaline vascular type of CD from other variants of this disorder, namely the plasma cell variant and the much rarer mixed variant[1]. Castleman disease (CD) is a rare, poorly understood lymphoproliferative disorder that share common lymph node histological features. The disease was first described in 1954. Followed by small case series in 1956.There are several forms of idiopathic Castleman's disease that can be classified either anatomically (unicentric or multicentric) or by morphology (hyaline-vascular, plasma cell, or mixed histology). With the discovery of KSHV, it was recognized that this virus causes a plasmablastic variant of multicentric Castleman's disease(MCD). Unicentric Castleman's disease (UCD) most often presents as a localized disease with a solitary, slow-growing lymph node.This is the most common type of Castleman disease which only affect a single region of lymph nodes. Mostly lymph nodes in chest or abdomen are affected. The patient is mostly asymptomatic with a single site lymph node enlargement. The disease has three histological subtypes of unicentric Castleman's disease (i) the hyaline vascular variant, characterized by lymphoid follicular proliferation at different levels of maturity, often forming a layered or 'onion skin' pattern surrounding a hyalinized vessel at the center of the follicle. Most seen in UCD(90%). (ii) the plasma cell variant, characterized by Interfollicular plasmacytosis with hyperplastic germinal centers and has significantly less vascularity.(iii) Mixed type-shows both characteristics of hyaline vascular and plasma cell type.Most of the previous cases are of hyaline vascular type and the most common sign is asymptomatic neck mass. The hyaline vascular form is much more common and almost always involves only one site. It accounts for around 90% of all unicentric cases [2]. In contrast to multicentric Castleman's disease, which is most commonly seen in the setting of immunocompromise (usually in HIV infected patients); unicentric Castleman's disease is seen in immunocompetent patients. Multicentric with generalized lymphadenopathy and more aggressive clinical course This form is more serious than UCD that affects multiple regions of lymph nodes and is characterized by generalized lymphadenopathy. Symptoms of MCD are often non specific and may include serious infections, fever, fatigue, excessive sweating, weight loss, skin rash and more aggressive clinical course. Elevated interleukin6 (IL-6) production can be seen in MCD patients.

Multicentric is further classified into two categories: HHV-8 positive Multicentric Castleman disease which often occurs in immunocompromised individuals, such as those with human immunodeficiency virus(HIV) infection and idiopathic Multicentric Castleman disease which is negative for HHV-8 and HIV. Also, UCD canbe treated with simple excision alone and usually does not require systemic therapy[1,2,3]

Case Presentation

A 14 year old female with no co-morbidities presented with swelling in the left side of the neck since birth, which had increased in size proportionally with her age. There was no pain over the swelling, no complaints of difficulty in eating or swallowing food. There was no history of fever, night sweats, or weight loss. There was no history of any other such swellings in any part of her body. Physical examination revealed a firm level II,III,IV cervical lymph node in the left side of her neck, which was multiple non matted , non fixed, left lateral neck masses were found. On Ultrasound neck, showed multiple enlarged reactive lymph nodes with maintained hilum and showing internal vascularity are seen in bilateral level IB, II,III and IV region, with largest size 4.1 x 1.4 cm in left level IV. FNAC was done. Cytological report s/o scantily cellular smear with moderate infiltrate against a hyaline background. Contrast enhanced CT scan of the neck was done. s/o multiple enlarged reactive lymph nodes in left cervical III, IV and V , with largest measuring 4.2 x 2.7 cm in cervical level V. She underwent excision biopsy of the lymph node in surgery department and was referred to our department for further evaluation and management. Computed tomography scan of the thorax, abdomen and pelvis showed no other significant lymphadenopathy to rule out multicentric CD. HIV, HBsAg and Anti-HCV antibodies were negative. Histopathology of the lymph node showed a characteristic onion skin appearance of follicles seen scattered in cortex and medulla, with single to multiple germinal centre with thickened mantle zone . There was also presence of the pathognomonic “Lollipop Lesions” which are formed due to penetration of sclerotic blood vessels into the atrophic germinal centers.no R-S cells seen.

These features were consistent with the diagnosis of the hyaline vascular variant of unicentric Castleman's dis ease. As whole node excision was done and she had no evidence of disease elsewhere in the body, she was kept under follow-up.

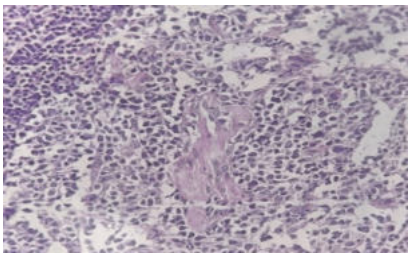

FIGURE 1: Homogenous lymphocyte population with few centroblasts in between & Presence of hyalinized germinal centre

DISCUSSION-

CD is a heterogeneous group of non-neoplastic lymphoproliferative disorders that can be clinically classified into localized or unicentric and disseminated or multicentric.The clinicopathological features of Castleman's disease were described by Benjamin Castleman in 1956.He reported a series of 13 patients with hyperplastic lymph nodes in the mediastinum which contained small,hyalinized follicles and increased vascular proliferation between the lymph node follicles [2]. It is a rare tumor that usually presents as a slowly growing, solitary painless mass [4]. The most common site involved is the mediastinum and involvement of cervical lymph nodesis rare. In an early series by Kelleret al., 86% of cases were confined to the mediastinum and only 6% of cases involved the neck . A recent series, in 2003, by Bond et al. showed that the neck was involved in only 14% of all cases, with the mediastinum being the most common site, accounting for 60% of cases [4]. Within the head and neck region, the most common sites were cervical and submandibular areas. Unicentric Castleman's disease: It most commonly occurs in young adults with a median age of 35 years [2,4]. In most series, there was an equal incidence seen in males and females [2, 4]. The most common histological variant was that of hyaline vascular variant which was seen in around 90% of all unicentric Castleman's disease. Of those patients with the plasma cell variant, 50% had systemic findings of anemia, an elevated ESR count, hypergammaglobulinemia, and marrow plasmacytosis [2]. Multicentric Castleman's Disease:It is a systemic disease with multiple sites of involvement. Almost all cases are that of the plasma cell variant. It may be associated with or without HHV-8 infection. There was a male preponderance, and occurs in older patients [2].It is most commonly seen in the setting of HIV infection[4]. MCD usually presents with constitutionalsymptoms like fever, night sweats and arthralgia as well as peripheral lymph node enlargement and hepatosplenomegaly [2, 4].The histopathological features of Castleman's disease like increase in plasma cells and immunoblasts, germinal centre hyperplasia and increased vascularity are seen as exaggerations of responses to normal antigenic stimuli. Studies in the early 1990's have found a correlation between the systemic manifestations of unicentric Castleman's disease and local production of Interleukin-6[2]. The exact cells which seem to produce IL-6 has not been elucidated yet [2] but candidate cells include follicular dendritic cells, germinal centre B cells or the interfollicular cells [2]. Also, IL-6 receptor polymorphisms have been identified in HIV-negative CD and are associated with increased soluble IL-6 receptor levels [6]. Most patients with unicentric Castleman's disease (UCD) are asymptomatic and are diagnosed when an enlarged lymph node was noted on physical examination or imaging. Unicentric Castleman's disease may be suspected when there is a single persistently enlarged mass, especially a nodal mass associated with moderate to intense post-contrast enhancement on CT scan. The hyaline vascular variant of Castleman's disease is characterized by the presence of abnormal follicles with atrophic germinal centers surrounded by wide mantle zones consisting of small lymphocytes [2]. A characteristic feature is the presence of two adjacent germinal centers surrounded by a single, wide mantle zone. These are called double germinal centers. The germinal centers are usually depleted of lymphocytes and are replaced with follicular dendritic cells arranged in a concentric manner producing an onion-skin appearance .The interfollicular tissue contains many small sclerotic blood vessels These are often seen penetrating up to the centre of the regressed germinal centers, producing a pathognomonic “lollipop lesion” [2] However, in this case, the patient showed an enlarged lymph node in the right supra-clavicle region associated with a mild pain which is a rare presentation. Further laboratory investigations showed increased levels of AST and ALT which is not related to the Castleman disease. CT scan and USG findings showed a well-encapsulated solid mass with no significant cervical lymphadenopathy suggesting lymphoma. There are various unusual sites of presentation like peripancreatic and retroperitoneal11, mesocolon and infraclavicular region.As in any neck mass, radiological investigations were done. Both lymphoma and neurogenic tumor were considered because they are common in this site. A reactive lymphadenopathy was seen in FNAC slides. There was no evidence of lymphoma in FNAC. However FNAC cannot reliably distinguished Castleman disease from other lymphadenpathies such as HIV- associated lymphadenopathy, Dermatopathy, lymphadenopathy, and progressively transformed germinal center. Thus, histopathological examination was required to confirm the diagnosis of Castleman Disease. Grossly, CD in our case appeared as encapsulated homogenous mass with a grey-white color. Histopathological examination showed a well-encapsulated lymph node tissue with an expanded mantle zone (paler areas), regressed follicles with radially penetrating sclerotic blood vessels (lollipop-like appearance).The prognosis for patients with unicentric disease, regardless of the histologic variant,is generally excellent, as surgical excision is curative [2].There has been no reported recurrence of the hyaline vascular variant in literature following complete excision. In my Patient did not have recurrence of swelling after 3 month and 6 month follow up .Multicentric disease is more aggressive and carries a poorer prognosis and shorter survival [2]. Treatment recommendations for multicentric Castleman's disease have been difficult to establish because the literature contains mostly small series. Patient did not have recurrence of swelling after 3 month and 6 month follow up .

Conclusions

Unicentric Castleman disease is a rare benign condition, surgical resection is curative. Histopathological examination rules out lymphoma and concluded that it is Unicentric Castleman disease, hyaline-vascular type case. No further therapy is required after complete excision of the lymph node.

Additional Information

Disclosures-

Human subjects: Consent was obtained or waived by all participants in this study.

Conflicts of interest: In compliance with the ICMJE uniform disclosure form, all authors declare the following: Payment/services info: All authors have declared that no financial support was received from any organization for the submitted work.

Financial relationships: All authors have declared that they have no financial relationships at present or within the previous three years with any organizations that might have an interest in the submitted work. Other relationships: All authors have declared that there are no other relationships or activities that could appear to have influenced the submitted work.

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