Unicentric-mesenteric Castleman disease in a child: an unusual presentation

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Introduction

Castleman disease (CD) is a rare non-malignant lymphoproliferative disorder first described by Dr. Benjamin Castleman in 1956[1,2]. The overall incidence of CD is less than 1/100,000[3,4]. Histological subtypes are hyaline vascular (80–90%), plasma cell (10%), and mixed type (2%)[3]. The most common site of CD is the mediastinum (70%), other common sites being neck, axilla, pelvis, and retroperitoneum[1].

Case report

A 12-year-old boy, without any significant past medical history, presented with a one-month history of generalized abdominal pain along with dyspeptic symptoms, weight loss, and anorexia. There was no history of low-grade fever, night sweats, or contact history of chronic cough. He did not have joint pain or swelling, skin rashes, or any alteration in bowel habits. He did not have a past history of recurrent infections. The patient was in discomfort and was noted to be pale. Apart from angular stomatitis, no other features of nutritional deficiency were noted. There was generalized lymphadenopathy, the nodes being less than 1 cm each (shotty nodes) noted in cervical and inguinal areas on presentation. There was a firm palpable mass in the left hypochondriac area. There was no hepato-splenomegaly.

The blood picture showed hypochromic microcytic anaemia; haemoglobin was 7.5 g/dL, mean corpuscular volume was 58fl, serum iron was low (2.22 µmol/L), transferrin saturation was very low (4.24%), serum ferritin was low (20 ng/ml) and total iron binding capacity was high (54 µmol/L). All this suggested an iron deficiency anaemia. He had elevated erythrocyte sedimentation rate (62mm first hour) and C-reactive protein (84mg/L). Other baseline investigations were normal. Human immunodeficiency virus and human herpesvirus-8 antibodies were negative. Ultrasound scan of the abdomen showed a highly vascular hypoechoic mass measuring 3.5cm x 2.6cm x 2.5cm on the left side of the abdomen, medial to the kidney. Contrast-enhanced computed tomography of the abdomen confirmed a well-defined mass anterior to the left renal hilum (2.5cm x 3cm x 4cm) arising from the root of the small intestinal mesentery (Figure 1).

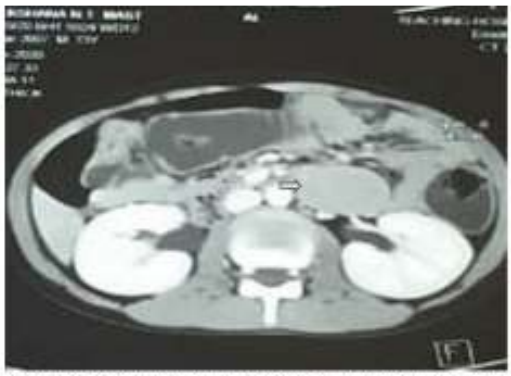

Figure 1: ***Contrast enhanced computed tomography of abdomen showing well-defined mass anterior to left renal hilum (shown by arrow) arising from root of small intestinal mesentery***

Fine needle aspiration was not attempted as the mass was in very close proximity to the renal vessels. A laparoscopy and biopsy of the node was attempted but was converted to an open surgical biopsy as the mass was located near the root of mesentery causing difficulty in identification and resection. The postoperative period was uneventful. Histology showed a significantly enlarged lymph node with regressive follicles and concentric onion skin appearance of the mantle zone suggestive of hyaline vascular CD. No atypical cells or granulomas were seen. Immunohistochemistry studies showed lymph node with preserved architecture. There were many reactive follicles of varying sizes distributed throughout the cortex and para cortex, surrounded by a mantel layer. Some regions showed areas of regressive follicles with features of Castleman disease. Granulomata were not seen. Evidence of lymphoma was not present (Figures 2 and 3).

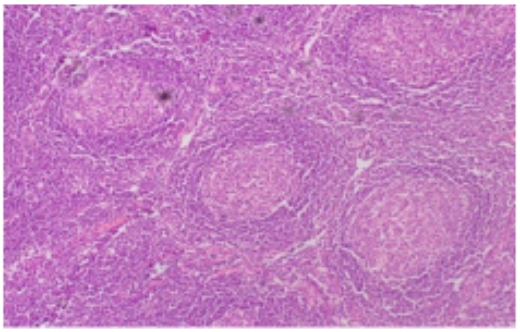

Figure 2: ***Histology of resected lymph node showing lymphoid follicles with depleted germinal centres and hyalinized central vessels***

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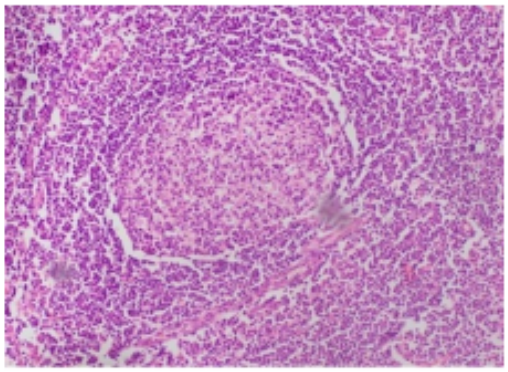

Figure 3: ***showing specific features of a lymphoid follicle. Mantle zone is expanded forming an onion skin appearance and sinuses are expanded with hyaline material between increased vessels***

Bone marrow aspiration was not performed as the histology of resected lymph node confirmed the diagnosis without ambiguity and patient did not fulfill the criteria for multicentric Castleman disease. His blood picture did not show any abnormal cells and immunohistochemistry excluded features of haematological malignancy.

The patient had hyaline vascular UCD with some constitutional symptoms and anaemia which responded to surgical removal. His initial inflammatory markers were high. After surgical resection, inflammatory markers came down to baseline values and his symptoms settled. The generalized lymph node enlargement regressed gradually postoperatively. There was no evidence of recurrence during his follow-up at 3 and 6 months and inflammatory markers remained normal.

Discussion

The case described was a diagnostic quandary to the team that managed this patient, as the patient presented with long-term dyspeptic symptoms and an abdominal lump. According to the site, CD is divided into unicentric CD (UCD) where one lymph node or group of lymph nodes in one site of the body are involved and multicentric CD (MCD) where lymph node groups in 2 or more sites are involved[1]. UCD is commoner than MCD[1] and hyaline vascular type is seen in UCD in nearly 90% of patients[3]. In our case, the patient had unicentric hyaline vascular CD. CD is characterized by B cell lymphoid hyperplasia and hypervascularity[2,3]. CD can occur along the pathway of the lymphatic system and around 20% of the time, it presents as a mass in the abdomen[3]. Our patient presented with an abdominal mass and was found to have an enlarged lymph node in the root of the mesentery.

The aetiology of CD is multifactorial including viral infections, abnormality of the lymphoid tissue growth, chronic low-grade inflammation, hamartomatous process, immunodeficiency, and autoimmunity[3]. HHV-8 and HIV are well known to be associated with MCD[3,5]. The illness results mainly due to overproduction of interleukin-6 causing lymphoid hyperplasia and systemic manifestations[3,5]. According to the histology, the hyaline vascular type shows marked proliferation of hyalinized follicles with interfollicular vascular proliferation[2] while the plasma cell type shows hyperplastic germinal centres and sheets of plasma cells in the interfollicular region, with blood vessel proliferation and persistent sinuses[2]. A small percentage of the population shows a mixed histologic appearance with the features of both hyaline vascular (HV) and the plasma cell subtypes[2,3]. In contrast-enhanced imaging, HV type is more contrast-enhanced than the plasma cell type[2].

In UCD, around 90% are asymptomatic but can have symptoms due to the site and the size of the node[2]. UCD can present in many ways including localized and generalized symptoms. They can have associated anaemia probably due to underlying inflammation. However, our patient developed some constitutional symptoms and anaemia in addition to localized symptoms. Unicentric mesenteric CD of HV type, associated with inflammatory anaemia/ non-iron deficiency anaemia/ iron refractory microcytic anemia has been previously reported[6,7,8]. Surgical removal of the node is the mainstay of treatment in UCD even though there are reported cases of recurrences[3,9]. Usually, HV-CD has a good prognosis once complete surgical resection is performed[10,11,12]. Rarely, a UCD lymph node may be unresectable due to its location or size. In such instances, pre-surgical embolization, medical management with immunomodulators, or ultimately radiotherapy, are considered for symptomatic UCD[9].

UCD is associated with an increased risk of lymphoma[2] and therefore, regular follow-up is important. Symptoms of Hodgkin's disease and lymphoma can mimic CD[2]. Paediatric CD is usually favoured by primary activation of innate immunity when compared with adults. Thus, the effect on life expectancy is also less than in adults[13]. Inflammatory conditions with adenopathy need to be considered when the condition mimics malignancy-lymphoma, metastasis, or infections, and the diagnosis is confirmed by histopathology[14].

As this is one of the differentials of pyrexia of unknown origin[15] and affects the overall health of the patient by involving multiple systems, early identification of the type of CD will help early intervention and clinical improvement. In children, anaemia and iron deficiency cause developmental delay, poor school performance, and poor growth[8]. Thus, in any patient with iron refractory anaemia or anaemia without any significant cause, CD should be considered as one of the differentials[6,7,8] even though it is rare in the paediatric population.

Conclusion

Our patient was diagnosed with unicentric - hyaline vascular Castleman disease (UHV-CD) at the root of the small intestine mesentery, which is a very rare occurrence. It is mandatory to arrive at a correct diagnosis, as this entity can give rise to different clinical outcomes. UCD needs long-term follow-up due to the increased risk of lymphoma, a rare possibility of recurrence, and anaemia. However, UHV-CD demonstrates a good prognosis following complete surgical resection.

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