Case Report

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Castleman disease of the mesentery as the great mimic: Incidental finding of one case and the literature review

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Summary **Castleman disease is an uncommon benign lymphoproliferative disorder characterized by hyperplasia of lymphoid follicles. More commonly described in the mediastinum, its occurrence in the mesentery is exceedingly rare, which is easily to be ignored in differential diagnosis when an abdominal mass is found. We report the case of an asymptomatic 71-year-old woman with a homogenous and hypervascular mass at the inner side of duodenojejunal junction. Based on the clinical suspicion of a gastrointestinal stromal tumor, a surgical resection was performed. Final diagnosis of the mass was hyaline vascular variant of Castleman disease. Here, we summarize the clinicopathological and radiological features of this disease by literature review, which may be helpful to bring awareness of this entity and improve the clinical decision making when similar scenarios are encountered.**

Keywords: Differential diagnosis, clinicopathological, radiological, treatment decision

1. Introduction

Castleman disease (CD), also known as benign giant lymph node hyperplasia, was first described as benign, localized mediastinal lymphadenopathy by Dr. Benjamin Castleman in 1956 (*1*). Subsequently it was expanded to represent a diverse group of nonneoplastic lymphoproliferative disorders involving a variety of nodal and extranodal sites with various histologic patterns (*2*).

The usual location of this disease is the mediastinum (70%). Although extrathoracic sites have been reported in the neck, axilla, pelvis, and retroperitoneum, CD located in the mesentery is very rare (*2-4*), and the etiology is still unclear.

Based on the histopathologic features, Castleman disease is classified as 2 types, the hyaline vascular (HV-CD) and plasma cell (PC-CD) variant, representing 80%-90% and 10%-20% of CD cases, respectively. Clinically and radiologically, CD can also be classified as unicentric type and multicentric type. The unicentric type is a localized disease, usually asymptomatic and most often seen in HV-CD. The multicentric type, which is characterized by disseminated lymphadenopathy, is almost always associated with systemic symptoms, and is dominated by PC-CD. Nevertheless, HV-CD and PC-CD can exhibit considerable clinical and histologic overlap, and a so-called mixed variant of CD is occasionally seen (*5*).

Mesenteric CD is a rare disease easily to be ignored in differential diagnosis when an abdominal mass is found. As a result of nonspecific symptoms and shared radiologic features with other entities by imaging, it is very difficult to differentiate mesenteric CD from other neoplastic diseases preoperatively, such as gastrointestinal stromal tumor (GIST), ectopic pheochromocytoma, and lymphoma. To our knowledge, only 53 cases of mesenteric CD have been reported worldwide in the English literature (*6-17*), and most of the cases were under other clinical suspicion and were definitively diagnosed as CD following surgical resection and histopathologic examination. With different clinical diagnosis, the optimal treatment decision or surgical approach may vary, therefore a correct preoperative diagnosis is preferred.

In this article, we report one case of hyaline vascular

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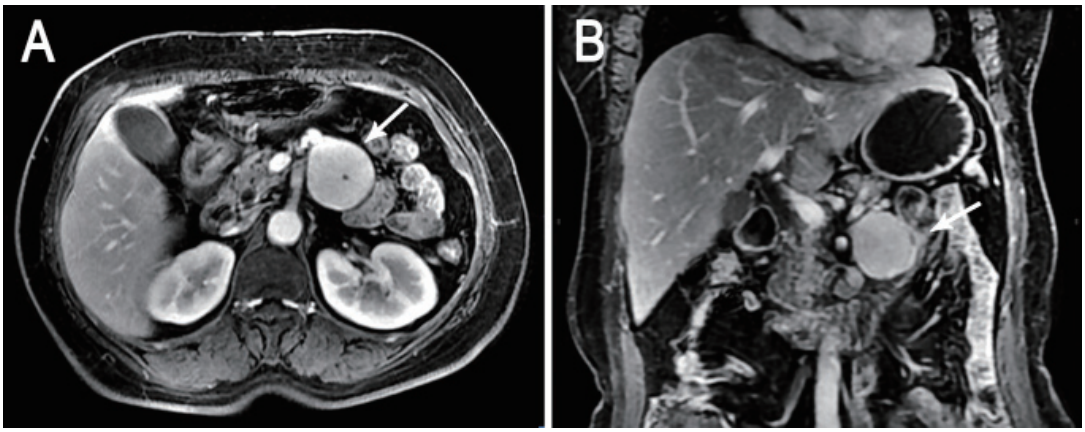

Figure 1. MRI images of the lesion. Abdominal MRI showing a sharply demarcated soft tissue mass located at the inner side of duodenojejunal junction, just beneath inferior border of pancreas, and adjacent to the left side of superior mesenteric artery. The mass was homogeneous and moderately enhanced in arterial phase and portal venous phase.

variant CD in the mesentery of the duodenojejunal junction, where this disease has not been reported previously in literature. We also summarize the clinicopathological and radiological features of this disease by comprehensive literature review, which may be helpful to improve the clinical decision making when similar scenarios are encountered.

2. Case report

A 71-year-old female patient was admitted to a local hospital due to osteoarthritis of her right knee. A 4 × 5 cm hypoechoic mass was incidentally found by a routine abdominal ultrasound examination.

After the patient was transferred to our hospital, further investigation with abdominal contrast-enhanced magnetic resonance imaging (MRI) showed a sharply demarcated soft tissue mass measuring 4.5 × 4.1 cm, with slightly low and high signal intensity on T1- and T2-weighted images, respectively. The mass was located at the inner side of duodenojejunal junction, just beneath the inferior border of the pancreas, and adjacent to the left side of superior mesenteric artery (SMA). After the contrast medium was injected, the mass appeared to be homogeneous and moderately enhanced in both the arterial phase and portal venous phase (Figure 1).

Her past medical history included hypertension and coronary heart disease. Physical examination, routine laboratory tests including C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), as well as computed tomography (CT) of the thorax revealed no obvious abnormalities. In addition, the levels of tumor markers including a-fetoprotein (AFP), carcinoembryonic antigen (CEA), carbohydrate antigen 19-9 (CA 19-9) and carbohydrate antigen 125 (CA 125) were all within the normal limits.

Based on imaging findings, a GIST was highly suspected with differential diagnosis including a leiomyoma or neurogenic tumor. Thus, the patient

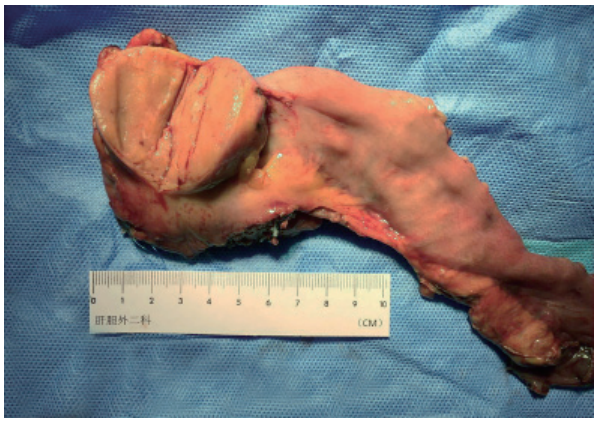

Figure 2. Resected specimen. Resected specimen showing the cut surface of a 4 × 4 cm mass (left) and adjacent duodenum.

underwent laparotomy. During the operation, the tumor was confirmed to derive from the mesentery of the duodenojejunal junction. After the tumor was carefully separated from the superior mesenteric vein (SMV), SMA and the pancreas, the segment of the mesentery containing the mass was resected along with the transverse portion of duodenum and initial part of jejunum (pancreas-sparing segmental duodenectomy). A duodenojejunal side-to-side anastomosis was performed to reconstruct the alimentary tract.

Grossly, the mass measured 4 × 4 × 3.5 cm, was firm and well-demarcated from surrounding tissue. The cut surface was grey-yellow, homogeneous and firm (Figure 2). Microscopic examination showed a large lymph node with preserved architecture and numerous follicles throughout the cortex and medulla. The lymphoid follicles were surrounded by a broad mantle zone composed of concentric rings of small lymphocytes forming the so-called "onion skin" pattern (Figure 3). The follicles contained a small germinal center that is lymphocyte depleted with prominent dendritic cells and hyaline deposits on Periodic Acid-Schiff (PAS) stain. The interfollicular areas were composed of numerous high endothelial venules with plump endothelial

cells and were associated with small lymphocytes, eosinophils and plasma cells. The histologic findings were diagnostic of Castleman disease, hyaline vascular variant.

The postoperative course of the patient was uneventful and she was discharged on the 14th postoperative day.

3. Discussion

3.1. *Clinicopathological features*

We reviewed the English literature of mesenteric Castleman disease through a search on Pubmed database, and the clinicopathological findings of 53 cases of mesenteric CD reported previously were summarized in Table 1. Histologically, the HV and PC variants constituted 26 and 21 of all cases, respectively, and 6 cases were of the mixed variant. Interestingly, the proportion of HV variant in mesenteric CD (49%) is significantly lower than traditionally reported 80%-90% in mediastinal CD cases. All cases presented as solitary lesions (unicentric type), and there was a female predominance with thirty-eight (71.7%) female patients. This predominance was most prominent in HV variant patients with 88.5% of them female (23/26), while no fender difference in PC variant or mixed variant. The average age of reported patients was only 27.5 years (range: 2-77 years) with about half patients (47.2%) under 20, and only five patients over 60 years. The present patient was the second oldest one compared to all previously reported HV-CD patients. The average mass size was 5.8 cm (2 cm to 17 cm), and 90% of cases were within a range from 3 cm to 7 cm.

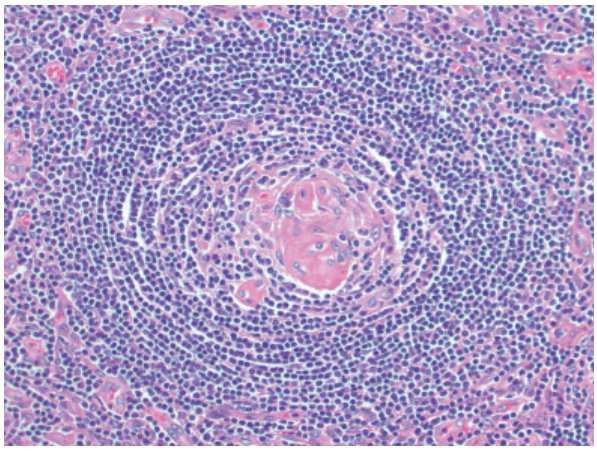

Figure 3. Microscopic findings. Microscopic view of the specimen showing the typical appearance of the hyaline vascular variant of Castleman disease, with a broad mantle zone composed of concentric rings of small lymphocytes surrounding a lymphocyte-depleted small lymphoid follicle forming so-called "onion skin" appearance.

Clinically, over half of reported patients were asymptomatic or with complains of nonspecific symptoms, such as abdominal pain and an abdominal mass. A small portion of patients experienced constitutional symptoms such as weight loss, fever or growth retardation. It is worth noting that laboratory findings in most patients with the PC variant showed systemic manifestations including anemia, an elevated sedimentation rate, and hypergammaglobulinemia, while only a small portion of the patients with the HV variant presented these abnormalities.

3.2. *Radiological features*

Mesenteric CD often presents as a homogeneous, hypoechoic mass on ultrasound. The most characteristic feature of mesenteric CD at computed tomography (CT) scan is a well-defined, homogeneous, single intraabdominal mass of soft tissue attenuation with or without satellite nodules. The enhanced CT and angiography findings usually demonstrate the homogeneity and hypervascularity of the mass (*18*). On MRI, the lesion could be isointense or slightly hypointense compared with that of normal muscle on T1-weighted images and hyperintense on T2-weighted images. After intravenous injection of contrast

Table 1. Clinicopathological findings of mesenteric Castleman disease reported previously

Items	HV-CD (n = 26)	PC-CD (n = 21)	Mixed CD (n = 6)	Overall (n = 53)
Gender				
Female	23	12	3	38
Male	3	9	3	15
Mean age (yrs)	33.0	24.3	13.8	27.5
(range)	(9-74)	(8-77)	(2-29)	(2-77)
Mean tumor size (cm)	5.9	5.7	4.9	5.8
(range)	(2-17)	(3-10)	(4-6.5)	(2-17)
Symptoms				
Constitutional symptoms (fever, weight loss, growth retardation, *etc*)	7	13	4	24
Local or no symptoms (abdominal pain, abdominal mass, asymptomatic)	19	8	2	29
Laboratory findings				
Abnormal (anemia, elevated ESR/CRP, hypergammaglobulinemia, *etc*)	12	19	6	37
Normal	14	2	0	16

HV, hyaline-vascular; PC, plasma cell; ESR, erythrocyte sedimentation rate; CRP, C-reactive protein.

medium, the enhancement of mesenteric HV-CD was characterized by homogeneous high enhancement in the early phase of dynamic enhancement, persistent enhancement in the delayed phase, with the enhancement mode similar to that of large arteries. But in some cases with tumors larger than 5 cm, during early stage of enhancement, the interior of the tumor could be seen to have distinct radial or fissured non-enhanced areas. The non-enhancement areas were reduced or vanished in delayed scan on CT, and MRI scans of corresponding areas gave low signals on the non-enhanced T2-weighted images (*19*). Pathologic examinations of the areas revealed abundance of parallel fibrous tissue. In the present case, the 4 cm isolated mass was found incidentally without any abdominal and systemic symptoms, and the ultrasonography, enhanced CT and MRI revealed a homogenous and hypervascular mass, which was in accordance to above radiological features.

3.3. *Differential diagnosis*

For abdominal soft tissue mass showing a clear boundary, homogenous and hypervascular imaging features, and with or without systemic manifestations, Castleman disease should be included in the differential diagnosis, especially for female patients. However, the above radiological features are not specific for CD, and the most commonly stated preoperative radiologic differential diagnosis are hypervascular mesenchymal tumor, such as GIST, and neurogenic tumor, such as ectopic pheochromocytoma.

GISTs are the most common mesenchymal neoplasms with varying malignant potential based on the risk-stratification scheme. The gold standard for treatment of localized primary GIST is complete excision with negative margins. Small GISTs often appear as round tumors with strong and homogeneous arterial enhancement and a persistent enhancement pattern. However, large GISTs (> 5 cm) appear as lobulated tumors with mild heterogeneous gradual enhancement, and they frequently exhibited intratumoral cystic changes (*20*). Most of mesenteric CD have a higher enhancement than that of GIST, but if mesenteric CD gives a moderate or a mild enhancement, it is difficult to distinguish it from hypervascular mesenchymal tumors including GIST. Another distinguishing radiological finding is the absence or rare presence of cystic necrotic degeneration in the mesenteric CD. This might be attributed to abundance of blood supply, good collateral circulation and low susceptibility of lymphatic follicles to necrosis. However, one study reported cystic necrotic degeneration were found in about 20% of the CD cases (*19*).

Ectopic pheochromocytoma comprises approximately 10-25% cases of pheochromocytoma, 30% of which could be malignant, and surgical resection is still the most effective treatment (*21*). The enhancement mode of ectopic pheochromocytoma may also be similar to those of mesenteric CD. However, the signal intensity of ectopic pheochromocytoma on T2-weighted image is usually stronger than that of CD, and the interior of the lesions may reveal highly uneven density and signals accompanied by cystic central necrosis (*19*). The clinical and laboratory examinations can also contribute to the differentiation of these two diseases. Most patients with functional ectopic pheochromocytoma show paroxysmal hypertension clinically, and in laboratory examination show elevation of catecholamine and its metabolic product 3-methoxyl-4-hydroxyl mandelic acid.

On the other hand, based on microscopic findings, mesenteric CD should be differentiated from a number of benign and neoplastic conditions particularly neoplastic lymphoproliferative disorder. The hyalinied follicles in CD may mimic early follicular lymphoma. The prominent mantle zone in CD may also mimic mantle zone lymphoma. Rare cases of early interfollicular Hodgkin lymphoma may show CD-like changes including the regression of residual germinal centers and hypervascularity. However, CD lacks Reed-Sternberg cells. Immunophenotyping, in situ hybridization, and PCR for immunoglobulin heavy chain rearrangements aid in the evaluation of B-cell clonality and are helpful in differentiating CD from a lymphoma.

3.4. *Treatment decision*

Due to lack of specific radiographic feature for CD, an endoscopic or ultrasound-guided fine-needle biopsy should be recommended when CD is suspected, as the optimal treatment decision or surgical approach may vary with different clinical diagnosis.

Irrespective of the histopathologic subtype, the unicentric type CD always shows a benign biologic behavior. For cases with symptoms such as anemia, the symptoms may show complete reversal after surgical resection of the tumor (*15*). For asymptomatic unicentric mesenteric CD, the necessity of surgical resection remains unclear. Complete surgical excision is usually curative of the mesenteric CD, since there is no reported case of recurrence after total excision of the solitary mass.

On the contrary, the multicentric type Castleman disease follows a more aggressive course and is associated with poor prognosis. The therapeutic approach of the multicentric type remains controversial, as many treatment regimens have been proposed, including surgery, chemotherapy, corticotherapy or combination of these (*22,23*). Although all cases of mesenteric CD reported previously were unicentric type, an accurate staging of the disease, including a thorough clinical examination for the detection of suspicious lymph nodes in the axilla, neck or groin and CT of the thorax should be performed in order to exclude the presence of extra-mesenteric disease.

For a benign tumor, a surgical approach balancing complete resection and organ-preserving may be more beneficial for patients. For the present case, if the diagnosis of mesenteric Castleman disease was made preoperatively, a surgical procedure preserving mesenteric vessels and duodenum may be possible, and the duodenojejunal anastomosis may be avoided. Considering that the patient was without symptoms, close follow-up may also be an electable alternative. However, because the endoscopic or ultrasound-guided approach had difficulty in pointing out the tumor location, and a fine-needle biopsy for a hypervascular tumor is regarded as potentially dangerous, a definitive preoperative diagnosis was not made.

In summary, for abdominal soft tissue mass showing a clear boundary, homogenous and hypervascular imaging features, and with or without systemic manifestations, mesenteric Castleman disease should be included in the differential diagnosis, especially for female patients. GIST, ectopic pheochromocytoma and lymphoma could be top differential diagnosis from this disease. Endoscopic or ultrasound-guided fine-needle biopsy should be recommended to further clasify the tumor so an optimal treatment decision can be recommended to the patient.

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