Castleman Disease with Mesenteric Involvement

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Definition and Description of the Disease

Castleman disease (CMD) is the name given to a several types of benign, non-neoplastic lymphoproliferative disorders. CMD most commonly involves a single nodal group in the mediastinum. However, lymphoid involvement may also occur individually in other sites or in multiple locations. When a single nodal group is involved, the condition is called Unicentric CMD. If the disease assumes a form that involves multiple nodal locations it is called Multicentric CMD. CMD with mesenteric involvement is very rare.

Epidemiology

CMD in all forms is a very rare disorder. Unicentric disease restricted to one lymph node grouping is usually seen in young and middle-aged patients with no gender differences. To the present, 55 cases of CMD with mesenteric involvement has been described in the medical literature.

Patients at Risk

Several cases of CMD have been described in patients with Sjogren's Syndrome. Other autoimmune diseases occurring in patients with CMD include rheumatoid arthritis, systemic lupus erythematosus, myasthenia gravis, Evans' syndrome,

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vitiligo, Graves' disease, ulcerative colitis, celiac disease, immune-mediated thrombocytopenia. Two cases of CMD have been reported in patients with Crohn's disease. POEMS syndrome (polyneuropathy, organomegaly, endocrinopathy, M proteins, skin changes) has occurred in a number of patients with CMD. Some patients with CMD and TAFRO syndrome (thrombocytopenia, anasarca, fever, reticulin fibrosis, and organomegaly) have been described.

Cases of CMD have been reported as a complication of infection with the human immunodeficiency virus (HIV). Other patients have developed CMD de novo without the presence of underlying autoimmune diseases. It is presumed that the risk of CMD with mesenteric involvement is similar to other patients with CMD.

Pathophysiology

Because a number of cases of CMD occurring in patients with autoimmune and immunologically-mediated diseases, CMD is postulated to originate as an autoimmune disorder. Reports of CMD in patients with HIV infection, suggests a possible of a role of immunodeficiency in the development of CMD. It has now been determined that symptoms experienced by patients with the plasma cell histologic subtype of CMD are related to excessive production of IL-6 by affected lymph nodes resulting in direct systemic overactivity of IL-6.

Signs and Symptoms

Patients with symptoms generally fall into two categories; those that develop symptoms at the site of the lesion due to local mass effect, and those that develop systemic symptoms. The severity and types of symptoms occurring in patients with CMD depend on the location, muticentricity and histologic subtype of the disease. In general, patients with unicentric disease, (especially if it is of the hyaline vascular histologic subtype, see below) are asymptomatic or have mild symptoms, while multicentric disease and plasma cell histologic subtype disease are associated with more severe systemic symptoms. Typical systemic symptoms of CMD include fever, night sweats, weight loss, fatigue and anemia. Signs and symptoms in patients with CMD and mesenteric involvement that have been described in the literature have included lack of symptoms, vague abdominal pain, nausea, acute abdominal pain, obstructive symptoms and tenderness, the presence of a palpable abdominal mass, and the signs and symptoms associated with systemic disease.

Diagnosis

In asymptomatic patients, the diagnosis of CMD is generally based on an incidental finding on imaging. The presentation of patients with CMD are dependent on disease location, the presence of multicentricity and the histologic subtype.

Physical Findings

The physical examination in patients with CMD requires a thorough palpation of the lymph node chains to assess the extent of muticentricity of the disease. Specific physical findings are dependent on disease location, and the presence of multicentricity. Cases of CMD with mesenteric involvement that are described in the literature have demonstrated normal examinations, abdominal tenderness and the presence of a palpable abdominal mass.

Laboratory Findings

These are nonspecific. Anemia is a cardinal finding in multicentric CMD. Hypoalbuminemia has been linked to a poorer prognosis of the disease.

Imaging

Some reported cases of CMD with mesenteric involvement have initially been diagnosed on abdominal ultrasound. Small intestinal radiography with barium contrast has been used to demonstrate extrinsic compression and displacement of small bowel loops. Abdominal CT and MRI are the radiographic tests of choice to identify and characterize CMD with mesenteric involvement. Findings on abdominal CT and/or MRI that have been described in the literature include a localized solid mass (some with calcification and various degrees of contrast enhancement), a mass effect with small intestinal displacement, mesenteric nodal enlargement, fascial thickening around the mass and satellite lesions. Pelvic and retroperitoneal lesions have also been described. Hepatosplenomegaly may also be present (Fig. 34.1a, b).

Histologic Findings

CMD can be classified based on two specific histologic subtypes. The most common of these is the hyaline vascular form of the disease, which occurs in 80–90% of cases. Most of these cases are unicentric disease and present as a single mass on imaging. On microscopic examination, excised specimens of the hyaline vascular

subtype show a lymphoid tissue mass containing very large lymphoid follicles, capillary proliferation and hyalinization. The plasma cell histologic subtype occurs in the remaining 10–20% of cases. The plasma cell variant of CMD demonstrates architecturally recognizable lymph node containing solid sheets of plasma cells in various forms of differentiation. These patients generally have multicentric disease.

Treatments

Most treatments used for patients with CDM are based on individual case reports and case series. Some patients with asymptomatic unicentric CMD may be monitored without treatment. However, surgical resection is usually performed for solitary mesenteric lesions, as enlarging and increasingly symptomatic mesenteric masses have been described. Complete surgical excision is generally curative of the CDA including cases with mesenteric involvement. Since multicentric CDA is representative of a systemic lymphoproliferative disorder and carries a poorer prognosis, treatment consists of anti-inflammatory and antineoplastic medications. Reported treatments include rituximab, combination chemotherapy, autologous stem cell transplantation, bortezomib, thalidomide, anakinra (an IL1-antagonist), interferon-a, and all-trans retinoic acid.

Improvement of CMD symptoms and abnormal laboratory results following administration of anti-IL-6 antagonists has been recently demonstrated. A recent randomized, placebo-controlled trial of siltuximab, a chimeric monoclonal neutralizing antibody against IL6, was performed in 79 patients with multicentric CMD. In that study, sustained tumor and symptomatic responses occurred in 18 (34%) of 53 patients in the siltuximab group and none of 26 in the placebo group (difference = 34.0%, 95% CI 11.1–54.8%, p = 0.0012).

Prognosis

Surgical resection of solitary lesions is curative of the disease. Recently, a retrospective analysis of 113 patients with CMD evaluated at the Mayo Clinic and University of Nebraska was performed. This study demonstrated a 65% 5-year overall survival in patients with multicentric disease and a 91% overall survival for patients with unicentric disease. Other cofactors that influenced prognosis included the presence of POEMS. Patients with multicentric CMD with POEMS syndrome and no osteosclerotic lesions had the lowest overall survival (27%). The presence of HIV infection is an additional confounding factor affecting prognosis of CMD. It is assumed that similar prognostic indicators occur patients with CMD with mesenteric involvement.

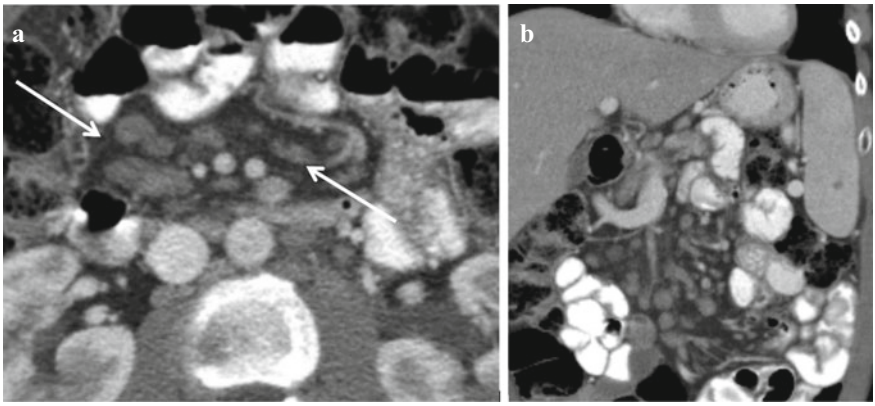

Fig. 34.1 Castleman disease with mesenteric involvement. Contrast-enhanced axial (**a**) and coronal (**b**) CT images showing numerous enlarged mesenteric lymph nodes (arrows), hepatomegaly and mild (14 cm) splenomegaly. In themselves, these are non-specific findings. This case was histologically-proven multicentric Castleman disease. With permission from Dr. Scott Sorensen and Dr. Abraham Dachman

Suggested Reading

1. Bracale U, Pacelli F, Milone M, et al. Laparoscopic treatment of abdominal unicentric castleman's disease: a case report and literature review. BMC Surg. 2017;17(1):38.
2. Lv A, Hao C, Qian H, Leng J, Liu W. Castleman disease of the mesentery as the great mimic: incidental finding of one case and the literature review. BioScience Trends. 2015;9(3):198–202.
3. Dei-Adomakoh YA, Quarcoopome L, Abrahams AD, Segbefia CI, Dey DI. Sjögren's and plasma cell variant Castleman disease: a case report. Ghana Med J. 2018;52(1):61–5.
4. Papaziogas B, Chatzimavroudis G, Koutelidakis I, Grigoriou M, Atmatzidis K. A rare form of isolated mesenteric Castleman's disease presenting as an abdominal mass (isolated mesenteric Castleman's disease). J Gastrointestin Liver Dis. 2006;15(2):171–4.
5. Caroline Ribeiro Sales A, Romão de Souza Junior V, Iglis de Oliveira M, Azevedo Braga Albuquerque C, de Barros Campelo Júnior E, Sérgio Ramos de Araújo P. Multicentric Castleman's disease in human immunodeficiency virus infection: two case reports. J Med Case Rep. 2018;12(1):117.
6. Yoshizaki K, Murayama S, Ito H, Koga T. The role of interleukin-6 in Castleman disease. Hematol Oncol Clin North Am. 2018;32(1):23–36.
7. van Rhee F, Greenway A, Stone K. Treatment of idiopathic Castleman disease. Hematol Oncol Clin North Am. 2018;32(1):89–106.
8. van Rhee F, Wong RS, Munshi N, Rossi JF, Ke XY, Fosså A, et al. Siltuximab for multicentric Castleman's disease: a randomized, double-blind, placebo-controlled trial. Lancet Oncol. 2014;15(9):966–74.