

Castleman's Disease and Superior Vena Cava Thrombosis:

A Rare Presentation and a Review of the Literature

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Abstract

Castleman's disease is a clinicopathological entity in which growth of lymphoid tissue is unregulated. It may present as asymptomatic involvement of one lymph node group or as a multicentric disease with systemic symptoms. Unlike localized disease, for which surgical excision is curative regardless of the histological type, multicentric disease often necessitates aggressive systemic therapy and portends a poor outcome. Superior vena caval thrombosis is an uncommon manifestation associated with Castleman's disease.

We describe a patient with this rare manifestation and present a systematic survey of the disease, based on the current literature.

Key Words: Castleman's disease, Kaposi's sarcoma, superior vena cava thrombosis.

Introduction

CASTLEMAN'S DISEASE is also known as angio-follicular lymphoid hyperplasia or giant lymph node hyperplasia, lymph nodal hamartoma and benign giant lymphoma (1, 2). It was first described in 1956 in a group of patients with localized mediastinal lymph node enlargement characterized by (1) "hyperplasia of lymphoid follicles with or without germinal center formation and capillary proliferation with endothelial hyperplasia." It is currently classified into two major subgroups: localized Castleman's disease and multicentric (disseminated) Castleman's disease (3). There are three histologic variants: hyaline-vascular, plasma cell and transitional (mixed type) (3, 4). In this article, we present a case of the hyaline-vascular type of Castleman's disease (localized) presenting with superior vena cava thrombosis, and review the literature.

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Case Report

A 47-year-old woman from Guyana with no significant medical history was hospitalized because of a right lung mass on her chest roentgenogram (Fig. 1). The patient had a dry cough for two months but denied fever, shortness of breath, expectoration, chest pain, palpitation, loss of weight, loss of appetite, hemoptysis, smoking, alcohol and recreational drug use.



Fig. 1. Chest roentgenogram showing a suprahilar mass lateral to azygos vein.

The physical examination was unremarkable. The patient was in no apparent distress, normotensive, afebrile, in regular sinus rhythm, and breathing normally. There was no evidence of superior vena caval obstruction. The complete blood count, routine serum chemistries and liver profile were normal. Protein C and S deficiencies, anticardiolipin antibodies and factor 5 Leiden were not found. The serum angiotensin converting enzyme (ACE) level was normal. Room air arterial blood gases (ABG) were normal. The PPD test was negative with a positive anergy panel.

The CT scan of the chest revealed a 4–5 cm mass representing extensive lymphadenopathy in the right hilum compressing the medial segment of the right middle lobe (Fig. 2). A large thrombus was also seen in the superior vena cava. The patient was anticoagulated with heparin (80 units/kg, followed by 18 units/kg/min) so as to maintain the PTT at 1.5–2 times the control value.

Heparin was withheld when it was decided that a mediastinal biopsy should be performed. Unfortunately, the tissue obtained from this biopsy attempt was not diagnostic. Heparin was then restarted after this procedure. On day 12 of heparin therapy, a superior vena caval venogram showed small round filling defects in the superior vena cava (Fig. 3). A filling defect in, and dilation of, the right brachiocephalic vein were also seen.

Heparin was discontinued in order to perform an open lung biopsy. The histopathology of this tissue was consistent with Castleman's disease of the hyaline-vascular type. Surgical resection of the right middle and upper lobe was followed by uneventful recovery. The patient is now well. No further therapy was administered.

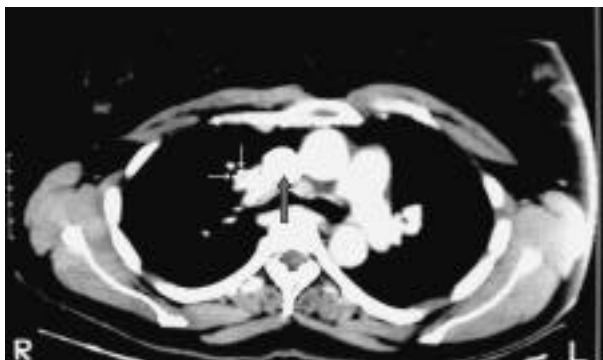


Fig. 2. Computed tomographic scan of the chest showing a mass on the right side representing lymphadenopathy (narrow arrows) and a superior vena caval thrombus (wide arrow).

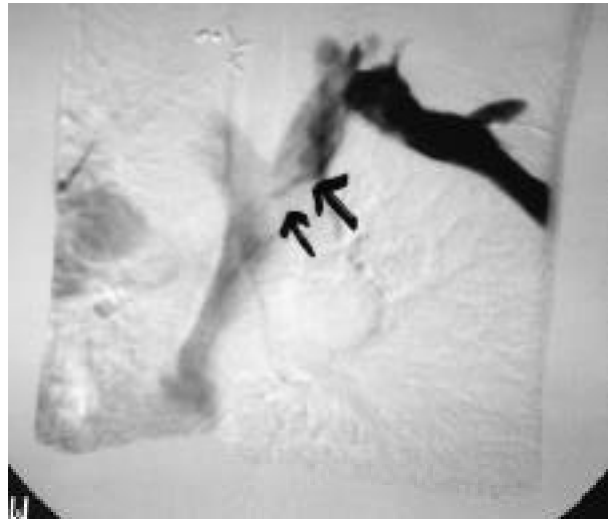


Fig. 3. Superior vena caval venogram showing a thrombus (defect) in the right brachiocephalic vein extending into the superior vena cava.

Discussion

Castleman and his colleagues (1, 5) first reported a group of patients who presented with mediastinal masses that were thought to be thymomas. Light microscopy revealed striking lymph node hypertrophy with hyalinized foci that resembled Hassall's corpuscles. In 1969, Flendrig and Schillings (6) described two histologic variants of Castleman's disease: hyaline-vascular and plasma cell. In a large review, Keller et al. (4) found that 91% of all cases of this disorder were hyaline-vascular and 9% were of the plasma-cell variety. They also described a third type: mixed cell type or hyaline-vascular plasma-cell type. These histopathologic types typically present as indolent disease confined to a single site. A more generalized lymphadenopathy (multicentric) form, accompanied by systemic symptoms, organomegaly and laboratory abnormalities, has a progressive clinical course (7).

Pathogenesis

The underlying cause of Castleman's disease is unknown; however, several theories have been formulated to account for the spectrum of associated pathologic and clinical features (8). Proposed pathogenetic mechanisms include chronic, low-grade inflammation (4), immunodeficiency (9–12) or autoimmunity (11) and Epstein-Barr virus (9, 13, 14), Toxoplasma, or *Mycobacterium tuberculosis* infec-

tions (2, 4). Although the evidence to support these hypotheses is scanty and speculative, the search for a unifying model of Castleman's disease has led to new insights into its pathogenesis.

Accumulating data suggest that overproduction of IL-6 by the hyperplastic lymph node plays a central role in the development of both localized and multicentric variants of Castleman's disease (15, 16). IL-6, a soluble protein secreted by several cell types, has modulating effects on immune function and hematopoiesis. It is necessary for the proliferation and maturation of B-lymphocytes into immunoglobulin-secreting plasma cells. In animal models, dysregulated production of this cytokine causes abnormal plasma cell proliferation in lymph nodes and other lymphoid organs in conjunction with polyclonal hypergammaglobulinemia, a syndrome clinically and histologically indistinguishable from Castleman's disease in humans (17).

In addition, lymph nodes from patients with Castleman's disease (12) excrete large amounts of IL-6, suggesting that the inappropriate synthesis of IL-6 plays a role in the pathogenesis of this syndrome (18). Furthermore, IL-6 induces proliferation of normal endothelial cells (19) and AIDS-Kaposi sarcoma derived cell lines (20). Lastly, systemic manifestations such as fever, weakness, anemia hypergammaglobulinemia, and the acute phase response in the plasma-cell variant, can be explained on the basis of increased blood level of IL-6 (10).

The lymphoplasmacytic proliferation driven by abnormal IL-6 production may set the stage for the development of malignant lymphomas. Similarly, continued stimulation of endothelial cells through release of angiogenic factors could promote vasoproliferation and ultimately lead to the emergence of a vascular neoplasm (21).

Multicentric Castleman's disease (MCD) is associated with human herpes virus 8 (HHV-8) (22). This virus is also associated with AIDS, and AIDS-related Kaposi's sarcoma (KS), as well as primary effusion lymphoma (23). HHV-8 encodes a functional analogue of IL-6, a cytokine that promotes the growth of KS and myeloma cells. IL-6 levels are increased in the sera and lymph nodes of patients with MCD. In those patients with Castleman's disease who do not have HIV infection, HHV-8 may explain the development of Kaposi's sarcoma (24).

Histologic Features

Histologically, Castleman's disease is divided into hyaline-vascular and plasma-cell

types (4). A clear separation of the two variants is not always possible, and cases with mixed histologic features occur. The hyaline-vascular type is characterized by the proliferation of small, distinctive follicles that obscure the underlying nodal architecture (4).

The follicles are surrounded by circumferentially arranged layers (onion skin) of small lymphocytes in the mantle zone, with peripherally arranged capillaries penetrating the germinal center. Frequently, the germinal centers have a characteristic whorled appearance (4). The interfollicular stroma has marked proliferation of capillaries, varying numbers of lymphocytes, and occasional plasma cells. The plasma-cell type of Castleman's disease (CD) also has numerous lymphoid follicles, but they tend to be larger, and prominent germinal centers are more typical of reactive follicular hyperplasia (2, 7).

The expanded interfollicular zones of the plasma-cell type of CD are filled with mature plasma cells which form broad sheets (2, 4). The interfollicular stroma tends to be less vascular and is mainly populated by endothelial venules. Lymph nodes may be only partially involved, and areas of uninvolved nodes show patent sinuses. Although immunohistologic staining in most cases of plasma-cell CD shows polyclonal expression of light chains in the plasma cells, a monoclonal component associated with a serum M protein occurs in rare cases (25).

Although these histologic features are characteristic, they are not specific, and "Castleman's disease-like" changes have been reported in a wide range of conditions (2), including rheumatoid arthritis, Sjögren's syndrome, phenytoin hypersensitivity, lymph node draining carcinomas, iatrogenic immunosuppression (12), and congenital or acquired immunodeficiency states, including the acquired immunodeficiency syndrome (AIDS) (2, 13, 26). Similar histologic changes reported in lymph nodes in patients with Hodgkin's disease have led to diagnostic errors (14).

Hyaline-Vascular Castleman's Disease

Most patients with the hyaline-vascular variant are asymptomatic. Some patients have compression of the tracheobronchial tree, causing dry cough and dyspnea. Recurrent infections may occur, due to local mass effect (1, 4). About 70% of the lesions are intrathoracic (4), the anterior mediastinum being the most common site. One study showed a distribution of

46% of cases in the mediastinum, 39% in the abdomen, 15% in the periphery (27). Rarely, lesions which simulate lung cancer are found within the lung fissures (4). There may be recurrent pleural effusions (4, 28). Extrathoracic lesions have been reported in the retroperitoneum, mesentery, central nervous system, orbit, and pelvis, neck, axilla, and skeletal muscles (29–32). Localized hyaline-vascular Castleman's disease appears on chest radiographs as a sharply marginated smooth or lobulated mass.

Pleural effusion is uncommon, and calcification in the mass is rare (33). On unenhanced CT images, a homogeneous or heterogeneous mass of soft-tissue attenuation is seen. Although calcification is uncommon, occurring in only 5–10% of cases (34, 35), when it is present, it is typically coarse and central in location. On CT scan or MRI, involved lymph nodes typically demonstrate homogeneous contrast enhancement (36, 37). This feature may prove helpful in distinguishing the Castleman's-disease mass from other mediastinal masses such as lymphomas or thymomas, which generally do not show any enhancement on a CT scan.

Surgical resection is the primary treatment of the hyaline-vascular variant (32), and is curative in virtually all cases. However, local recurrence has been reported after subtotal resection of the tumor. Radiation therapy has been used with varied success in patients who are poor surgical candidates or in those with unresectable lesions (38). Hyaline-vascular CD is considered benign and self-limited, with 5-year survival approaching 100% (2, 4). In very rare instances, vascular neoplasms that resemble KS develop (21). KS is more typically associated with the multicentric variant of the disease (8, 39, 40). Rarely, malignant lymphoma may occur in patients with hyaline-vascular CD. Vascular neoplasms such as KS and lymphomas may develop as long as eight years after the initial diagnosis of CD. Thus, long-term follow up is necessary (41).

Plasma-Cell Castleman's Disease

The plasma-cell type of Castleman's disease usually presents as multiple, discrete, enlarged lymph nodes (4). Patients are likely to experience fever, weight loss and pruritus during the course of their illness (4). Although such symptoms are common in the plasma-cell variant, both types of Castleman's disease may

be associated with numerous clinical conditions not directly related to the tumor mass (Table 1).

Surgical resection of the hyperplastic lymph nodes often results in complete resolution of constitutional symptoms. Plasma-cell lesions are likely to occur in extrathoracic sites such as the mesentery and retroperitoneal space, or involve multiple lymphoid organs concurrently (2, 4, 8). The mediastinal masses may invade the bronchi as friable endobronchial lesions that cause bleeding during biopsy or other instrumentation (37).

Multicentric Castleman's Disease

Disseminated or multicentric Castleman's disease is currently regarded as a potentially malignant lymphoproliferative disorder associated with POEMS (polyneuropathy, organomegaly, endocrinopathy, monoclonal proteinemia, and skin changes) syndrome, osteosclerotic myeloma, KS, and AIDS (3, 42–44). It affects individuals of all ages, but the peak incidence is in the fifth decade of life. Women are more commonly affected than men by a ratio of 2:1. Most patients present with fever, weight loss, and weakness (3) (Table 2).

TABLE 1

Clinical Conditions Associated with Castleman's Disease

Dermatologic	Hematologic
Pemphigus vulgaris (PC)	Refractory anemia (PC)
Cutaneous Kaposi sarcoma (HV) #	Lupus anticoagulant (PC)
Glomeruloid hemangioma (PC) #	Autoimmune cytopenias (PC)
	Thrombotic thrombocytopenic purpura (HV)
	Myelofibrosis (HV)
Renal	Neurological
Nephrotic syndrome (PC)	Peripheral neuropathy (PC)
Acute renal failure (PC)	Pseudotumor cerebri (PC, HV) #
Glomerulonephritis (PC)	Myasthenia gravis (HV)
Oncologic	Miscellaneous
Malignant lymphoma (PC, HV)	Temporal arteritis (HV)
Osteosclerotic myeloma (PC)	Pericardial effusion (HV)
Extramedullary plasmacytoma (PC)	Bronchiolitis obliterans (HV)
Nodal Kaposi sarcoma (PC)	Recurrent pleural effusion (HV)
Gamma heavy chain disease (HV)	Amyloidosis (PC)
	Growth retardation (PC)
	POEMS syndrome (PC)*
	Peliosis hepatis (PC)

PC = plasma-cell type; HV = hyaline-vascular variant

* POEMS syndrome = polyneuropathy, organomegaly, endocrinopathy, Monoclonal (M) protein, and skin changes

Associated with multicentric Castleman's disease.

(Refs. 2, 4, 7, 8, 27, 40, 49, 55–71).

TABLE 2
Comparison between Clinical Features of the Localized Variant and Multicentric Variant of Castleman's Disease.

Factor	Localized	Multicentric
Age range (yr)	12–72	19–85
Median age (yr)	23.5	56
Manifestation	Incidental, "mass effect"	Fever, weight loss, pruritus
Histologic features	HV, PC, HV-PC	PC, HV, HV-PC
Lymph node distribution	Central	Peripheral
Organomegaly	Absent	Present
Premalignant potential	Occasionally	Frequently
Clinical course	Benign	Aggressive
Treatment	Surgical excision	Chemotherapy
Prognosis	100% 5-yr survival	Guarded, 26-mo median
Differential diagnosis	Follicular lymphomas, other causes of adenopathy, AIDS, KS.	Follicular lymphoma, AIL, POEMS, Osteosclerotic myeloma, AIDS, KS.

AIDS = acquired immunodeficiency syndrome; AIL = angioimmunoblastic lymphadenopathy; HV = hyaline-vascular variant; PC = plasma-cell variant; HV-PC = mixed-cell variant; POEMS = polyneuropathy, organomegaly, endocrinopathy, M protein, and skin changes; KS = Kaposi sarcoma.

References (1, 2, 4, 7–10, 13, 14, 26, 27, 45, 49, 51–53).

Laboratory studies commonly reveal anemia, an increased erythrocyte sedimentation rate, polyclonal hypergammaglobulinemia, granulocytosis, and bone marrow plasmacytosis (42). The multicentric variant of CD is clinically more aggressive than the localized variant and follows one of four courses: relapse and remission, stable and persistent, rapidly fatal, or transformation into malignant lymphoma (40).

Historical, clinical and laboratory findings are not useful in predicting the outcome or clinical course of individual patients. One study suggests that the presence of peripheral neuropathy is associated with resistance to therapy and a poor prognosis (45). Most patients with multicentric Castleman's disease have the plasma-cell form (3, 40, 46).

Disseminated thoracic Castleman's disease appears on chest radiographs as bilateral mediastinal widening (35, 43, 47). Focal mediastinal masses are rare. The anterior mediastinum is commonly effected. CT scanning reveals diffuse adenopathy involving multiple mediastinal compartments. The nodes typically are 1–6 cm in diameter and of homogeneous attenuation on unenhanced images (33). Associated findings such as splenomegaly or ascites are common (47). Multicentric plasma-cell Castleman's disease rarely presents with reticulonodular opacities on chest radiographs (48). Unlike the localized plasma-cell type of Castleman's disease, which is amenable to surgical excision and has a favorable prognosis (4), the multicentric variant necessitates systemic therapy and is associated with a poor outcome (40, 45, 49). The overall mortality rate is about 50%, with a median survival of 26 months (40). The most common cause of death is sepsis or lymphoma. Patients with multicentric Castleman's disease of either histological type have a poor prognosis (40, 46, 49, 50) in spite of treatment with a combination of radiation therapy, corticosteroids, and chemotherapy. Several immunosuppressive agents (cyclophosphamide, azathioprine) have been used in the treatment of multicentric disease, with anecdotal reports of efficacy (40, 51–53).

No regimen is consistently effective in achieving durable remission (40). Radiotherapy alone has been used in isolated cases (53). In view of the poor prognosis of multicentric Castleman's disease, an aggressive management approach with intensive chemotherapy is recommended (52).

After extensive review of the literature, this appears to be the first report in English of a patient with both Castleman's syndrome and superior vena cava thrombosis. Aiba et al. reported, in Japanese, a case of Castleman's disease and superior vena cava syndrome (54). Their patient received chemotherapy and irradiation. The exact cause of the association between the two conditions is not clear. We speculate that the large right hilar mass compressed the superior vena cava, which induced the intravascular thrombosis. Further progression of the thrombotic process in the adjacent veins did not occur when the hilar mass was removed. Repeat CT scan 6 months later showed no evidence of disease and the patient is clinically well.

The various hematological and coagulation disturbances described in relation to Castleman's disease are: autoimmune cytopenias (55),

refractory anemia (56), thrombocytopenic purpura (57), lupus anticoagulant (58), and myelofibrosis (59). These manifestations are usually associated with the plasma-cell variant of Castleman's disease. In our case, no coagulation abnormality was detected.

Conclusion

Castleman's disease is an uncommon cause of lymphadenopathy, and must be considered after all other causes have been eliminated. Several neoplastic, autoimmune, infectious diseases can mimic Castleman's disease. Follow-up and periodic evaluation is necessary to detect the malignant lesions. Close communication between the clinician and the pathologist is essential to arrive at the correct diagnosis. The malignant potential of the disease and its possible multicentricity must be kept in mind in order to plan appropriate treatment. The optimal therapeutic regimen for Castleman's disease is unknown. Local disease can be cured with local resection, with an excellent prognosis. For individuals who are poor surgical candidates, radiation therapy can be used. MCD of either histological type has a poor prognosis. Treatment in this situation consists of combination chemotherapy, radiation, and corticosteroids. The finding of thrombi within the superior vena cava and the right brachiocephalic vein is extremely unusual and was thought to be related to compression of these vessels by a large right hilar mass.

References

- Castleman B, Iverson L, Menendez VP. Localized mediastinal lymph-node hyperplasia resembling thymoma. *Cancer* 1956; 9:822–830.
- Frizzera G. Castleman's disease: More questions than answers. *Hum Pathol* 1985; 16:202–205.
- McCarthy MJ, Vukelja SJ, Banks PM, Weiss RB. Angiofollicular lymph node hyperplasia (Castleman's disease). *Cancer Treat Rev* 1995; 21:291–310.
- Keller AR, Hochholzer L, Castleman B. Hyaline-vascular and plasma-cell types of giant lymph node hyperplasia of the mediastinum and other locations. *Cancer* 1972; 29:670–683.
- Castleman B. Case records of the Massachusetts General Hospital: Weekly clinicopathologic exercise (case 40011). *N Engl J Med* 1954; 250:26–30.
- Flendrig JA, Schillings PHM. Benign giant lymphoma. *Folia Medica Neerlandica* 1969; 12:119–120.
- Gaba AR, Stein RS, Sweet DL, Variakojis D. Multicentric giant lymph node hyperplasia. *Am J Clin Pathol* 1978; 69:86–90.
- Frizzera G, Banks PM, Massarelli G, Rosai J. A systemic lymphoproliferative disorder with morphologic features of Castleman's disease: Pathological findings in 15 patients. *Am J Surg Pathol* 1983; 7:211–231.
- Case records of Massachusetts General Hospital. *N Engl J Med* 1987; 316:606–618.
- Issacson PG. Castleman's disease. *Histopathology* 1989; 14:429–432.
- Stansby G, Hillson A, Hamilton G. Gallium scintigraphy in the diagnosis and management of multifocal Castleman's disease. *Br J Radiol* 1991; 64:165–167.
- Francis ND, Hollowood K, Gaberial R. Angiofollicular lymph node hyperplasia [letter]. *J Clin Pathol* 1988; 41:353–354.
- Racz P, Tenner-Racz K, Van Volten F, et al. Classification of histopathological changes of lymph nodes in HIV infection: Significance of Castleman's disease like lymph node lesion concerning the diagnosis of HIV-1 related Kaposi sarcoma. *Antibiot Chemother* 1991; 43:210–213.
- Zarate-Osorno A, Medeiros LJ, Danon AD, et al. Hodgkin's disease with coexistent Castleman-like histologic features: A report of three cases. *Arch Pathol Lab Med* 1994; 118:270–274.
- Yoshizaki K, Matsuda T, Nishimoto N, et al. Pathogenic significance of interleukin-6 in Castleman's disease. *Blood* 1989; 74:1360–1367.
- Yabuhara A, Yanagisawa M, Murata T, et al. Castleman's disease with spontaneous production of high levels of B cell differentiation activity. *Cancer* 1989; 63:260–265.
- Brandt SJ, Bodine DM, Dunbar CE, et al. Dysregulated IL-6 expression produces the syndrome resembling Castleman's disease in mice. *J Clin Invest* 1990; 86:592–599.
- Leger-Ravet MB, Peuchmaur M, Devergene O, et al. IL-6 expression in Castleman's disease. *Blood* 1991; 78:2923–2930.
- Motro B, Itin A, Sachs L, et al. Pattern of interleukin-6 expression in vivo suggests a role for this cytokine in angiogenesis. *Proc Natl Acad Sci U S A* 1990; 87:3092–3096.
- Miles SA, Rezaifar, Salazar-Gonzalez JF, Vander Meyden M, et al. AIDS Kaposi sarcoma-derived cells produce and respond to interleukin 6. *Proc Natl Acad Sci U S A*. 1990; 87:4068–4072.
- Gerald W, Kostianovasky M, Rosai J. Development of vascular neoplasia in Castleman's disease: Report of seven cases. *Am J Surg Pathol* 1990; 14:603–614.
- Soulier J, Grollet L, Oksenhendler E, et al. Kaposi's sarcoma-associated herpes virus-like DNA sequence in multicentric Castleman's disease. *Blood* 1995; 86:1276–1280.
- Briz M, Martin T, Yebra M, et al. Detection of human herpes virus 8 in patients with Kaposi's sarcoma or Castleman's disease associated with AIDS. *Med Clin (Barc)* 1998; 110(17):662–664.
- Herrada J, Cabanillas F, Rice L, et al. The clinical behavior of localized and multicentric Castleman's disease. *Ann Intern Med* 1998; 128:657–662.
- York JC, Taylor CR, Lukes RJ. Monoclonality in giant lymph node hyperplasia [abstract]. *Lab Inv* 1981; 44:77A.
- Lacinate NA, Sun NC, Long LA, et al. Multicentric Castleman's disease followed by Kaposi sarcoma in two homosexual males with the acquired immunodeficiency syndrome. *Am J Clin Pathol* 1985; 83:27–33.
- Frizzera G. Castleman's disease and related disorders. *Semin Diagn Pathol* 1988; 5:346–364.
- Reynolds SP, Gibbs AR, Weeks R, et al. Massive pleural effusion: An unusual presentation of Castleman's disease. *Eur Respir J* 1992; 5:1150–1153.
- Humpherys SR, Holley KE, Smith LH, McIlrath DC. Mesenteric angiofollicular lymph node hyperplasia (lymphoid hamartoma) with nephrotic syndrome. *Mayo Clin Proc* 1975; 50:317–321.

30. Gianaris PG, Leestma JE, Cerullo LJ, Butler A. Castleman's disease manifesting in the central nervous system: A case report with immunological studies. *Neurosurgery* 1989; 24:608–613.
31. Snead MP, James JN, Snead DR, et al. Orbital lymphomas and Castleman's disease. *Eye* 1993; 7:84–88.
32. Samuels TH, Hamilton PA, Ngan B. Mediastinal Castleman's disease: Demonstration with computed tomography and angiography. *Can Assoc Radiol J* 1990; 41:380–383.
33. McAdams HP, Rosado-de-Christenson M, Fishback NF, Templeton PA. Castleman's disease of the thorax: Radiologic features with clinical and histopathologic correlation. *Radiology* 1998; 209:221–228.
34. Kim JH, Jun TG, Sun SW. Giant lymph node hyperplasia in the chest. *Ann Thorac Surg* 1995; 59:1162–1165.
35. Moon WK, Im JG, Kim JS, et al. Mediastinal Castleman's disease: CT findings. *J Comput Assist Tomogr* 1994; 18:43–46.
36. Ferreiros J, Gomez L, Mata MI, et al. Computed tomography in abdominal Castleman's disease. *J Comput Assist Tomogr* 1989; 13:433–466.
37. Hsieh ML, Quint LE, Faust JM, Turner JE. Enhancing mediastinal mass at MR: Castleman's disease. *Magn Reson Imaging* 1993; 11:599–601.
38. Stokes SH, Griffith RC, Thomas PR. Angiofollicular lymph node hyperplasia (Castleman's disease) associated with vertebral destruction. *Cancer* 1985; 56:876–879.
39. Weisenburger DD, Nathwani BN, Winberg CD, Rappaport H. Multicentric angiofollicular lymph node hyperplasia: A clinicopathologic study of 16 cases. *Hum Pathol* 1985; 16:162–172.
40. Moon WK, Im JG, Han MC. Castleman's disease of the mediastinum: MR imaging features. *Clin Radiol* 1994; 49:466–468.
41. Shahidi H, Myers JL, Kvale PA. Castleman's disease. *Mayo Clin Proc* 1995; 70:969–977.
42. Krishnan J, Danon AD, Frizzera G. Reactive lymphadenopathies and atypical lymphoproliferative disorders. *Am J Clin Pathol* 1993; 90:385–396.
43. Kirsch CF, Webb EM, Webb WR. Multicentric Castleman's disease and POEMS syndrome: CT findings. *J Thorac Imaging* 1997; 12:75–77.
44. Ceaserman E, Knowles DM. Kaposi's sarcoma-associated herpes virus: A lymphotropic human herpes virus associated with Kaposi's sarcoma, primary effusion lymphoma and multicentric Castleman's disease. *Semin Diagn Pathol* 1997; 14:54–66.
45. Menke DM, Camorinano JK, Banks PM. Angiofollicular lymph node hyperplasia: Comparison of unicentric, multicentric, hyaline-vascular, and plasma cell type by morphometric and clinical analysis. *Mod Pathol* 1992; 5:525–530.
46. Kessler E. Multicentric giant lymph node hyperplasia. *Cancer* 1985; 56:2446–2451.
47. Libson E, Fields S, Strauss S, et al. Widespread Castleman's disease: CT and US findings. *Radiology* 1988; 166:753–755.
48. Barrie JR, English JC, Muller N. Castleman's disease of the lung: Radiographic, high resolution CT and pathologic findings. *AJR Am J Roentgenol* 1996; 166:1055–1056.
49. Frizzera G, Peterson BA, Bayrd ED, et al. A systemic lymphoproliferative disorder with morphologic features of Castleman's disease: Clinical findings and clinicopathological correlation in 15 patients. *J Clin Oncol* 1985; 3:1202–1216.
50. Peterson BA, Frizzera G. Multicentric Castleman's disease. *Semin Oncol* 1993; 20:636–647.
51. Pavlidis NA, Skopouli FN, Bai MC, et al. A successfully treated case of multicentric angiofollicular hyperplasia with oral chemotherapy. *Med Pediatr Oncol* 1990; 18:333–335.
52. Repetto L, Jaiparkash MP, Selby PJ, et al. Aggressive angiofollicular lymph node hyperplasia treated with high dose melphalan and autologous bone marrow transplantation. *Hematol Oncol* 1986; 4:213–217.
53. Bartoli E, Massarelli G, Soggia G, Tanda F. Multicentric giant lymph node hyperplasia: A hyperimmune syndrome with rapidly progressive course. *Am J Clin Pathol* 1980; 73:423–426.
54. Aiba M, Takaba T, Takamiya Y, et al. A case report of mediastinal Castleman's lymphoma associated with superior vena cava syndrome. *Kyobu Geka* 1988; 41(7):585–589.
55. Burgert EO, Jr., Gilchrist GS, Fairbanks VF, et al. Intra-abdominal, angiofollicular lymph node hyperplasia (plasma-cell variant) with an antierythropoietic factor. *Mayo Clin Proc* 1975; 50:542–546.
56. Neerhout RC, Larson W, Mansur P. Mesenteric lymphoid hamartoma associated with hypoferrremia, anemia, growth failure, and hyperglobulinemia. *N Engl J Med* 1969; 280:922–925.
57. Couch WD. Giant lymph node hyperplasia associated with thrombotic thrombocytopenic purpura. *Am J Clin Pathol* 1980; 74:340–344.
58. Rizzo SC, Balduini CL, Gamba G, et al. Castleman's disease with coagulation defect: A case report. *Blut* 1984; 49:107–109.
59. Bleiweiss IJ, Dumitrescu OL, Jagirdar J. Angiofollicular lymph node hyperplasia associated with myelofibrosis: Case report and immunological marker studies. *Hematol Oncol* 1988; 6:275–284.
60. Okuda K, Himeno Y, Toyama T, et al. Gamma heavy chain disease and giant lymph node hyperplasia in a patient with impaired T cell function. *Jpn J Med* 1982; 21:109–114.
61. Monpoint S, Frappier JM, Petibon E, et al. Pemphigus associated with Castleman's pseudolymphoma. *Dermatologica* 1989; 178:54–57.
62. Rywlin AM, Rosen L, Cabello B. Coexistence of Castleman's disease and Kaposi's sarcoma: Report of a case and speculation. *Am J Dermatopathol* 1983; 5:277–281.
63. Chan JK, Fletcher CD, Hicklin GA, Rosai J. Glomeruloid hemangioma: A distinctive cutaneous lesion of multicentric Castleman's disease associated with POEMS syndrome. *Am J Surg Pathol* 1990; 14:1036–1046.
64. Kondo M, Matsuda N, Chiyotani A, et al. A case of broncho-bronchiolitis obliterans with Castleman's lymphoma. *Nihon Kyobu Shikkan Gakkai Zasshi* 1989; 27:735–741.
65. Yu GS, Carson JW. Giant lymph node hyperplasia, plasma cell type, of the mediastinum, with peripheral neuropathy. *Am J Clin Pathol* 1976; 66:46–53.
66. Perfetti V, Bellotti V, Maggi A, et al. Reversal of nephrotic syndrome due to reactive amyloidosis after excision of Castleman's disease. *Am J Hematol* 1994; 46:189–193.
67. Lenner P, Lundgren E. Giant lymph node hyperplasia (Castleman's disease) associated with temporal arteritis. *Scand J Haematol* 1981; 27:263–266.
68. Nicolosi AC, Almassi GH, Komorowski R. Cardiac tamponade due to Castleman's disease. *Chest* 1994; 105:637–639.
69. Weisenburger DD, DeGowin RL, Gibson P, Armitage JO. Remission of giant lymph node hyperplasia with anemia after radiotherapy. *Cancer* 1979; 44:457–462.
70. Bosco J, Pathmanthan R. POEMS syndrome, osteosclerotic myeloma and Castleman's disease: Case report. *Aust N Z J Med* 1991; 21:454–456.
71. Bardwick PA, Zvaifler NG, Gill ZN, et al. Plasma cell dyscrasia with POEMS syndrome: Report of two cases and review of the literature. *Medicine* 1980; 59:311–322.