

# Unicentric Mixed Variant Castleman Disease Associated with Brachiocephalic Vein Thrombosis: A Rare Presentation

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**Abstract** Castleman disease (CD) is an uncommon lymphoproliferative disorder occurring mostly in patients presenting with mediastinal lymphadenopathy. Predominant phenotypes are categorized as localized hyaline vascular or multicentric plasma cell variants. Localized form of CD is usually asymptomatic and rarely associated with deep venous thrombosis. We report an exceptional case of mediastinal CD, which presented as retrosternal chest pain, in a 42-year old man. Imaging and pathological examination showed an atypical, mixed and localized form of CD. Thoracic CT scan revealed brachiocephalic vein thrombosis. Investigations didn't reveal other risk factors for deep venous thrombosis. Deep venous thrombosis is an exceptional complication of localized variants of CD. Therefore, it seems worth looking carefully for this last type of benign lymphopathy when an unusual thrombosis is found.

**Keywords:** *castleman disease, venous thrombosis, lymphadenopathy*

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## 1. Introduction

A Castleman disease (CD) is a rare lymphoproliferative disorder of unknown etiology. Two clinical types (localized and multicentric) and three histopathological types (hyaline vascular, plasma cell, and mixed) have been described [1]. Mixed variant is rare and mainly described in multicentric form of CD. Localized or unicentric form is generally asymptomatic and compression signs are exceptionally revealing. Thrombosis is rarely described in CD [2,3,4]. It is generally seen if the disease is associated with another thrombophilic state such as Behcet disease [5,6]. We report an exceptional unicentric mixed variant CD with brachiocephalic vein thrombosis.

## 2. Case Report

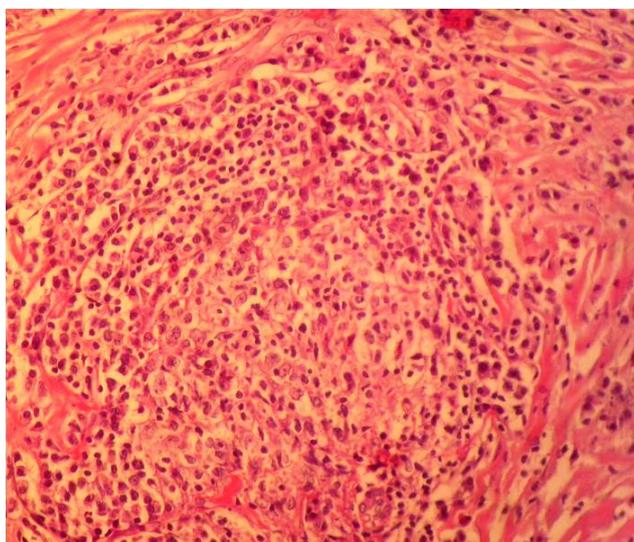
A 42-year-old man, with no past medical history presented with recent and atypical retrosternal chest pain. Physical examination showed no fever, no general state impairment and no respiratory distress. Cardiovascular examination revealed a blood pressure at 120/70mm Hg, a heart rate at 75 bpm and a normal cardiopulmonary auscultation. The patient did not show enlargement of peripheral lymph

nodes or organomegaly. Electrocardiogram was normal. Chest X ray showed an homogenous and well limited right parahilar opacity, with a mediastinal widening suggesting the presence of lymphadenopathies. Laboratory findings were within normal range and there was no increase in inflammatory markers. Calcemia and lactic deshydrogenase were normal. Viral serologies (VHB, VHC, CMV, EBV, HSV and HIV) were negative. There was no evidence of tuberculosis as bacilloscopies and intradermal tuberculin test were negative.

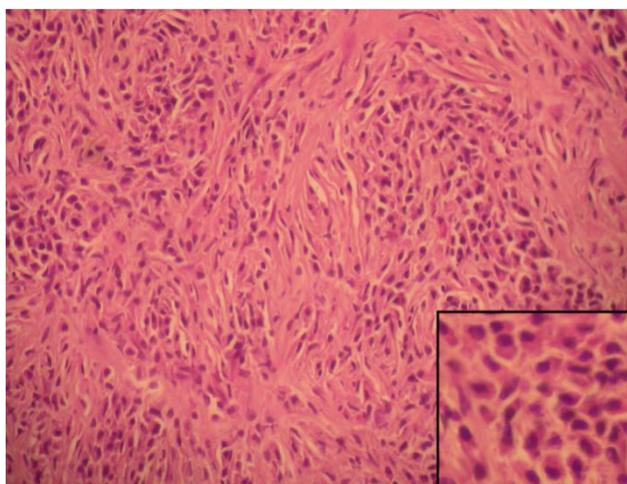
Thoraco-abdomino-pelvic CT scan showed a right large mass of tissular density measuring 43x58x60 mm in the anterior mediastinum in contact with the aortic arch and trachea, compressing the right brachiocephalic vein resulting in its thrombosis which was extended to the subclavian and the right axillary vein (Figure 1). The mass presented an intense contrast enhancement associated with small hypodensities and macrocalcifications. A second mass measuring 22x30 mm with the same description was identified in the subcarinal region. CT scan didn't show other abnormalities especially no abnormally enlarged lymph nodes and no pulmonary or hepatic lesions. There was no evidence of a congenital thrombophilic state. Antinuclear and antiphospholipid antibodies were negative. Hyperhomocysteinaemia was ruled out. Regarding these findings, a lymphoma was suspected.



**Figure 1.** CT axial section in mediastinal window. One arrow: large mass of tissular density. Two arrows macrocalcifications. Three arrows brachiocephalic vein thrombosis



**Figure 2.** lymphocytes in onion bulb appearance (H & E X200)

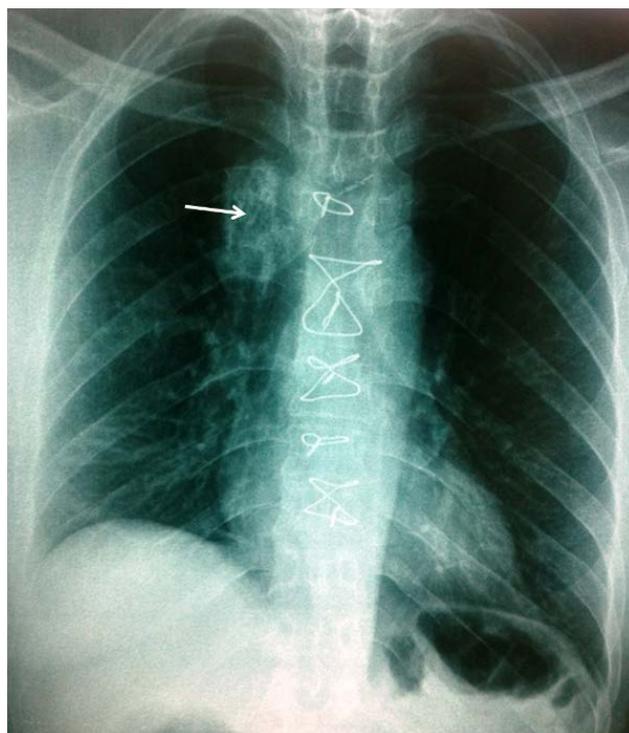


**Figure 3.** Interfollicular Plasmacytosis (H & E X200). Cartridge (H & E X400)

Histopathological examination of ganglionnar biopsy performed with thoracotomy showed atrophic germinal centers, containing thickened wall vessels with a small size lymphocytes disposed in concentric circles giving an

onion bulb appearance (Figure 2). Interfollicular tissue was rich, fibrous, hyalinized with focal plasmacytosis (Figure 3). Immunohistochemistry revealed the absence of epithelial cells (cytokeratin negative). Lymphocytic population was CD20 + and CD3+ with a mild predominance of lymphocytes CD3+. Bone marrow biopsy was normal. The diagnosis of unicentric mixed variant of CD with deep venous thrombosis due to local compression was retained.

Anticoagulation was prescribed. It is currently five years of decline. Chest X ray and CT scan showed a stable aspect with the same lymphadenopathies (Figure 4). During the follow up, the patient didn't present any risk factor of venous thrombosis mainly any signs of malignancies or Behcet disease.



**Figure 4.** Chest x-ray, right mediastinal opacity

### 3. Discussion

First described by Benjamin Castleman in 1954, Castleman disease (CD) is a rare benign disorder characterized by lymphocyte proliferation [7,8]. It may occur anywhere along the lymphatic chain but is frequently found in the mediastinum [9]. It can be divided into different subtypes according to clinical appearance and histopathological features. Regarding the clinical presentation, unicentric (localized) and multicentric (systemic) form can be identified. The unicentric type usually presents as a benign, asymptomatic disease affecting one single or localized group of lymph nodes most often observed in the mediastinal region [10]. Multicentric CD frequently associated with HIV infection and Kaposi's sarcoma, is more aggressive presenting often with systemic symptoms and abnormal laboratory findings. Three different histological forms of CD are identified: the hyaline-vascular form, accounting for the vast majority of the cases (90%), plasma-cell form, which usually is found with multisystemic clinical symptoms as well as

multicentric organic involvement, and finally the less common type, the mixed form which is a combination of both [11]. The latter is in the most of cases multicentric [12]. The unicentric mixed variant of CD, as presented by our case, is rare [10,13]. Unicentric CD is localized and largely asymptomatic, and the disease is diagnosed incidentally on imaging studies. Symptoms may be seen in a subset of patients as a result of the pressure effects of the mass. In our patient, thoracic pain due to vascular compression and thrombosis was the presenting manifestation. Thrombosis in CD was described in few cases [2,3,4]. An increased risk of thrombosis in CD may be caused by a combination of many factors. As currently understood, CD is considered to be an heterogeneous entity related to conditions of immune deregulation [14]. So, many autoimmune thrombogenic states may be associated with CD. We mention Behcet disease [5,6], positivity of antiphospholipid antibodies [15,16,17] and nephrotic syndrome [14,18,19,20]. But, the most incriminated mechanisms of thrombosis in CD are local vascular compression by masses and lymphadenopathies [2] and an excessively elevated interleukin-6 plasma level. In fact, overexpression of this cytokine in germinal center cells of the lymph nodes was shown in the plasma cell type of CD [10]. IL-6 is a proinflammatory cytokine responsible for the variety of clinical symptoms in CD. There was a correlation between serum IL-6 level, lymph node hyperplasia, hypergammaglobulinemia, increased level of acute phase proteins, and clinical abnormalities in CD [21]. This inflammatory state is a procoagulant factor favouring thrombosis in CD.

Diagnosis of CD is based on histology. It can be helped by radiologic findings. The Classic thoracic CD is usually seen as a single, non-invasive dominant mass with involvement of contiguous structures [22]. The CT findings consist of a homogeneously intense contrast enhancement lesion, as a result of the high degree of vascularization that this tumor usually shows [22]. The definitive diagnosis of CD is based on histology. Many other lymphoproliferative disorders may resemble to CD regarding the histopathologic features. So, results should be carefully evaluated and immunochemistry can be so helpful in the differentiation.

The optimal treatment for patients with unicentric disease is surgical excision, which is usually curative. More aggressive therapeutic options are available for patients with multicentric disease parting from corticosteroids to chemotherapy and even bone marrow transplantation. Treatment of complications of CD is also a large part of the management of this disease.

In our case, surgical excision was refused by the patient. Adjuvant measures included anticoagulation for deep venous thrombosis and corticosteroids therapy with a favorable outcome.

#### 4. Conclusion

Unicentric mixed CD with concomitant deep venous thrombosis is a rare condition. Despite the presumed benignity of the localized form of CD, the risk of deep venous thrombosis should be borne in mind especially in mixed histological variant.

#### Conflicts of Interest

The authors report no conflicts of interest.

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