

# Case Report

## Castleman's disease or angiofollicular hyperplasia as a solitary pulmonary nodule: case report\*

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### Abstract

Castleman's disease is a rare disorder generally characterized by a mediastinal nodule, with a great variety of alternative presentations regarding age, clinical manifestations and evolution. This case report describes a 40-year-old female patient presenting with uncharacteristic chest pain for a few years. A chest X-ray revealed a hypotransparency on the right side. Computed tomography and pulmonary arteriography did not elucidate the diagnosis, which was made through surgical resection and anatomopathological examination of the nodule, which presented characteristics of angiofollicular hyperplasia, or Castleman's disease. This article emphasizes the importance of adding this disease to the list of morbidities in the differential diagnosis of pulmonary solitary nodules.

**Keywords:** Giant lymph node hyperplasia; Angiography; Coin lesion, Pulmonary; Case reports [publication type].

### Introduction

Castleman's disease, also referred to as angiofollicular hyperplasia, giant follicular hyperplasia, hamartoma lymph node or benign lymphoma, was first described in 1956.<sup>(1)</sup> It is a rare disease, characterized by mediastinal lymph node enlargement, and can also appear in other locations, such as the neck, armpit, pelvis, retroperitoneum, and pericardium.<sup>(2)</sup> The clinical presentation and evolution vary. The localized form is generally asymptomatic and is typically an incidental finding. The systemic form is typically characterized by chest pain, dyspnea, and hemoptysis, although it can also present as pneumonia or pleural effusion.<sup>(2)</sup> Histologically, 90% of cases are of the hyaline-vascular type. However, there is also the plasmacytic type,<sup>(1)</sup> which typically includes an increase in the erythrocyte sedimentation rate, hyperimmunoglobulinemia and elevated levels of interleukin 6.<sup>(2-4)</sup> Radiologically, these tumors generally

present as well-defined mediastinal masses.<sup>(5)</sup> Affected patients tend to be young (mean age, 23 years; range, 8-66 years), of either gender, and asymptomatic; the evolution is typically benign.<sup>(2,3)</sup> The differential diagnosis should include diseases that present large mediastinal masses, such as Hodgkin's lymphoma and the thymomas, as well as certain rheumatologic diseases that cause lymph node enlargement.

### Case report

A 40-year-old female patient was oligosymptomatic with uncharacteristic chest pain for 20 years. The patient reported that the pain appeared about once a month, with pressure in the right hemithorax, lasting for a few hours, and that it was sometimes accompanied by dyspnea. A chest X-ray revealed a hypotransparency on the right side.

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A computed tomography scan revealed a nodule of approximately 3 cm in diameter. The nodule was quite near the pulmonary artery, and vascular origin therefore could not be ruled out (Figure 1).

We performed pulmonary arteriography, which did not reveal a relationship between the nodule and the pulmonary artery (Figure 2). The bronchoscopy findings were normal. The thoracotomy was performed, and an extrapulmonary nodule was found between the superior and middle lobes. The nodule was easily resected.

A peri-operative frozen section biopsy of the resected nodule suggested malignancy. Paraffin sections, stained with hematoxylin and eosin, revealed a histological pattern of angiofollicular

hyperplasia, which is characteristic of Castleman's disease (Figure 3).

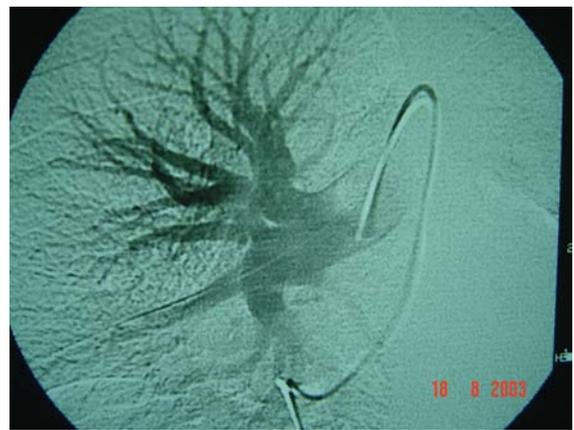
The patient presented a favorable post-operative evolution. The staging did not reveal any other disease foci, and the patient was referred to an outpatient hematology clinic for follow-up evaluation.

### Discussion

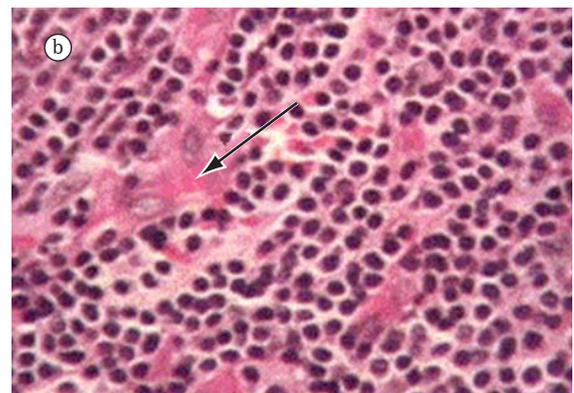
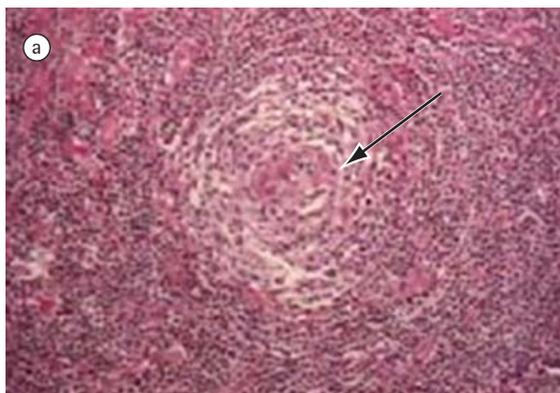
Castleman's disease was first described in 1956 in a review of thymic tumors. It is characterized as a lymphoproliferative, isolated, benign disease of young adults. It is typically associated with HIV and human herpesvirus 8, generally presenting favo-



**Figure 1** - Computed tomography scan of the chest: nodule in the right hemithorax.



**Figure 2** - Arteriography of the right pulmonary artery showing a normal aspect.



**Figure 3** - Histopathologic examination showing angiofollicular hyperplasia. a) The characteristic histological pattern is produced by the great number of lymphoid follicles regularly distributed on a background of lymphocytes; and b) A detail of the enlarged lymphoid follicle shows that the central vessels present thick walls, and that endothelial cells are prominent.

rable evolution after surgical resection. Most of the patients are asymptomatic, and the diagnosis is most often made through incidental radiological findings. It is the result of chronic stimulation by an antigen of viral origin. There are no gender-related differences, and the average age of individuals with Castleman's disease is 35 years. The most common location is in the mediastinum (in 70%), and it is rarely seen in the abdomen. Abnormal laboratory test results are rare, anemia, high erythrocyte sedimentation rate, and hypergammaglobulinemia accounting for less than 25% of all cases.<sup>(1,2,6-8)</sup> The patient described herein presented only uncharacteristic chest pain, and all laboratory test results were normal.

In 1978, one group of authors described the multicentric form of the disease, which presents nonspecific symptoms suggestive of inflammatory disease: fever, night sweats, weight loss, weakness, and enlarged peripheral lymph nodes.<sup>(9)</sup>

Currently, three histological variables are recognized: hyaline-vascular, which are the most common (seen in 90% of cases); plasmacytic (8-9% of cases); and mixed (1-2% of cases). The present case was of the hyaline-vascular type, characterized by the presence of numerous lymphoid follicles, regularly distributed on a background of lymphocytes. The lymphoid follicles present a periphery of mature lymphocytes and a center composed of cells with large vesicular nuclei, surrounding one or more blood vessels, with thick walls and tumescent endothelial cells. Eosinophilic material similar to hyalinized collagen also surrounds the vessels, in a concentric manner.<sup>(2)</sup>

Patients with systemic Castleman's disease present more intense clinical manifestations and more aggressive clinical evolution, as well as often presenting concomitant HIV positivity. Such patients are generally elderly males that present peripheral lymph node enlargement, together with enlargement of the spleen and liver. The histological examination typically reveals the plasmacytic or mixed variant and rarely the hyaline-vascular variant.<sup>(2)</sup>

One group of authors reviewed the clinical, radiological, and histopathologic characteristics of 30 patients with the disease. The majority of the patients (80%) presented a nodule or well-delimited

mediastinal mass (hyaline-vascular histological variant), and 50% of those patients were asymptomatic. Few patients presented accompanying lymphadenopathy.<sup>(10)</sup>

In the cases in which the surgical resection was incomplete, although there might be a favorable evolution for years, radiotherapy can be used. The systemic treatment is debatable. There is no single treatment. Rather, there are a variety of possibilities, including surgery and radiotherapy, as well as the use of steroids, antiviral agents, specific antibodies, monochemotherapy and polychemotherapy.<sup>(2,3,8,11)</sup>

Castleman's disease, despite its rarity, should be included in the differential diagnosis of asymptomatic or oligosymptomatic nodules and mediastinal masses.

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