Castleman’s disease: An unusual presentation*

Doença de Castleman: Uma apresentação pouco frequente*

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Abstract

Castleman’s disease is a rare lymphoproliferative disorder, with focal or systemic lymph node involvement, which rarely affects the lung parenchyma. We report the case of an asymptomatic immunocompetent male patient who had the rarest histological variant of the disease, a nodular parenchymal presentation. The patient underwent lobectomy, and the postoperative evolution was favorable. In the last 10 years, there have been only five reports of Castleman’s disease presenting as a solitary pulmonary nodule. This case underscores the fact that Castleman’s disease, albeit rare, should be included in the differential diagnosis of pulmonary nodules.

Keywords: Giant lymph node hyperplasia; Lymphoproliferative disorders; Solitary pulmonary nodule.

Resumo

A doença de Castleman é uma doença linfoproliferativa rara, com envolvimento ganglionar localizado ou sistêmico, raramente atingindo o parênquima pulmonar. Relatamos o caso de um paciente imunocompetente, assintomático, com a variante histológica mais rara da doença, com apresentação nodular parenquimatosa. O paciente foi submetido a lobectomia, com evolução benigna. Nos últimos 10 anos, somente cinco casos de doença de Castleman com apresentação na forma de nódulo pulmonar único foram descritos na literatura. Este caso reforça a necessidade de inclusão da doença de Castleman no diagnóstico diferencial dos nódulos do pulmão, embora ela seja rara.

Descritores: Hiperplasia do linfonodo gigante; Transtornos linfoproliferativos; Nódulo pulmonar solitário.

Introduction

Castleman’s disease is a rare lymphoproliferative disorder of unknown cause, with unifocal or systemic lymph node involvement, in which extranodal involvement is rare (5%). Only a few cases of lung parenchyma involvement have been described in the literature.

Here, we report the case of a patient presenting with the plasma cell variant of the disease—presenting as a solitary pulmonary nodule—and treated by lobectomy.

Case report

We report the case of a 60-year-old White male wine technician. The patient was a former smoker (60 pack-years) who had quit smoking 1 year before the appointment. He had no history of exposure to air pollutants.

The patient had metabolic syndrome but no personal or family history of lung disease.

The patient had been asymptomatic until March of 2008, when he underwent a routine chest X-ray. The chest X-ray revealed hypodensity consistent with a pulmonary nodule located in the right lower lobe. This finding was subsequently confirmed by a CT scan taken in April of the same year (Figure 1). The nodule was 2 cm in diameter, had no calcifications, and had ill-defined borders. There was no evidence of adenopathy or pleural involvement.

Physical examination revealed good general health, and the vital parameters were within the normal range. The mucous membranes were hydrated and their coloration was normal. The patient had no palpable lymph node enlargement in any of the various lymph node sites. Heart
therapy, and there was no evidence of disease recurrence in the ninth month after the resection.

**Discussion**

Castleman’s disease is a rare lymphoproliferative disorder of unknown cause, originally described by Castleman in 1956.[1-3] In the literature, the disease has been described using other terms, such as angiofollicular lymph node hyperplasia, benign giant lymphoma, lymph node hamartoma, and giant lymph node hyperplasia.[1,2,4]

Castleman’s disease affects individuals of different ages, having been described in adolescents and in individuals up to the seventh decade of life,[1] although it is more common in young adults (mean age, 35 years).[2] There is no gender predominance.[1,2,4]

Although Castleman’s disease typically affects mediastinal lymph nodes,[4] it can also affect intra-abdominal lymph nodes, as well as lymph nodes located in the axillary region, the cervical region, the shoulders, the pelvis, and the pancreas.[1,2,5,6] It should be highlighted that extranodal involvement occurs in only 5% of cases.[1]

Regarding the form of presentation of Castleman’s disease, there are two clinical types: the localized or unicentric form; and the systemic or multicentric form.[1]

Current evidence indicates that Castleman’s disease is not a distinct entity but rather a diverse set of rare lymphoproliferative disorders,
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Kaposi's sarcoma (13%), and non-Hodgkin's lymphoma (18%). It occurs in individuals of a more advanced age. It presents with multiple lymph node involvement in more than one mediastinal compartment or bilaterally, and it rarely translates to parenchymal opacities, sometimes affecting other organs. It is associated with systemic symptoms of asthenia and malaise (81%), fever (71%), and weight loss (58%). It is also associated with cases of glomeruloid hemangioma, mixed connective tissue disease, organomegaly, neurological findings, endocrinopathy, monoclonal gammopathy, and skin changes, as well as with carcinomas of the colon, kidney, and thyroid.

From a morphological standpoint, the hyaline-vascular variant is characterized by the presence of atrophic lymphoid follicles with hyalinized blood vessel walls and concentric rings of lymphocytes. The plasma cell variant is distinguished from the hyaline-vascular variant by the lack of lymphoid follicles and hyalinized vessels, as well as by the accumulation of plasma cells.

The localized form is associated with the hyaline-vascular variant in 90% of the cases. This variant is generally asymptomatic and can be diagnosed incidentally, typically manifesting as a well-defined mediastinal nodule or mass. It can be associated with iron-deficiency anemia and thrombocytopenia.

The plasma cell variant, which is usually associated with the disseminated form, is common in the contexts of HIV infection, differing in terms of their histopathological patterns and biological behavior.

There are three histopathological subtypes, the prognoses and clinical manifestations of which differ: the hyaline-vascular variant, which accounts for most of the cases; the plasma cell variant (8-9% of the cases); and the mixed variant (1-2% of the cases).

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The plasma cell variant, which is usually associated with the disseminated form, is common in the contexts of HIV infection, Kaposi's sarcoma, and non-Hodgkin's lymphoma. It occurs in individuals of a more advanced age. It presents with multiple lymph node involvement in more than one mediastinal compartment or bilaterally, and it rarely translates to parenchymal opacities, sometimes affecting other organs. It is associated with systemic symptoms of asthenia and malaise, fever, and weight loss. It is also associated with cases of glomeruloid hemangioma, mixed connective tissue disease, organomegaly, neurological findings, endocrinopathy, monoclonal gammopathy, and skin changes, as well as with carcinomas of the colon, kidney, and thyroid.

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In a case series of 30 patients with a histopathological diagnosis of Castleman's disease, one group of authors identified 24 cases (80%) of localized disease (previously defined as disease that affected only one mediastinal compartment) and 6 cases (20%) of disseminated disease (defined as disease that affected more than one mediastinal compartment or with extrathoracic involvement). In that case series, females predominated, regardless of the form of the disease. The mean age of the patients with localized disease was 34 years, whereas that of those with disseminated disease was 42 years. Of the patients with localized disease, 58% were asymptomatic. In addition, 96% of the patients with the localized form were reported to have presented with the hyaline-vascular histological variant. Only 1 patient presented with the plasma cell variant. Most of the patients with disseminated disease were symptomatic (only 1 patient was asymptomatic), and the plasma cell variant was found in 4 (66.6%) of the patients.

The diagnosis can be difficult in asymptomatic patients.

Figure 2 - Photomicrograph of a fragment of the resected nodule demonstrating lymphoid follicular hyperplasia (LFH), with a predominance of plasma cells (PC) and non-hyalinized blood vessels, which confirmed the pulmonary involvement in the plasma cell variant of Castleman’s disease (H&E; magnification, ×100). GC: germinal center; and Br: bronchus.

Figure 3 - Photomicrograph of a fragment of the resected nodule demonstrating a predominance of plasma cells (PC). (H&E; magnification, ×100). Br: bronchus.
Aspiration biopsy cannot always be performed and is habitually nondiagnostic, a mediastinoscopy or thoracotomy being therefore required in order to perform the biopsy. A CT scan generally reveals a well-delimited, localized mass, with areas of intense contrast uptake (unlike what occurs in lymphomas or thymomas). Although scintigraphy might not be able to distinguish between Castleman’s disease and other tumors, it is useful in the evaluation of the multifocal nature of the disease, of the response to treatment, and of the evolution of the disease.

Localized disease is habitually treated by surgical resection of the lesion; incomplete resection or radiotherapy can be used as adjuvant therapy in patients at risk of recurrence or in inoperable cases. Systemic therapy, namely chemotherapy, systemic corticosteroid therapy, and, more recently, monoclonal antibody treatment, should be reserved for use in patients with disseminated disease.

As previously reported, the prognosis varies according to the histological type. In patients with the hyaline-vascular variant, surgical treatment is considered curative and the prognosis is excellent, whereas in patients with disseminated disease, the mean survival is 6–36 months, infection being the most common cause of death.

The use of lobectomy for the surgical treatment of Castleman’s disease is a questionable choice, because an intraoperative examination that would have definitively ruled out malignancy might have allowed us to perform a less extensive resection. This analysis underscores the need to perform intraoperative examination systematically in the surgical approach to pulmonary nodules.

We also highlight the fact that the histological variant reported here presented clinically as a nodule in the lung parenchyma and progressed favorably, contrary to what was expected to occur in the plasma cell subtype.

References