Unicentric castleman disease in the differential diagnosis of a Paravesical Mass: A case report

Luyanne Azevedo Cabral Ferreira¹, Rafaela de Lacerda Trajano Pinel¹, Rodrigo Neves Ferreira², Antônio Chambô Filho¹

¹Department of Obstetrics and Gynaecology, Santa Casa de Misericórdia Hospital, Vitória, Espírito Santo, Brazil
²Department of Pathology, Santa Casa de Misericórdia Hospital, Vitória, Espírito Santo, Brazil

Summary

Castleman disease is a rare condition with variable forms of clinical presentation. Diagnosis is therefore difficult and the ideal management of the disease has yet to be defined. Prognosis varies as a function of histologic type. Treatment can range from curative surgery for the unicentric form of the disease to a combination of treatments for the multicentric form. This paper describes an unusual case of unicentric Castleman disease in which the differential diagnosis included several gynaecological malignancies. The lesion was resected, with histopathology and immunohistochemistry confirming the diagnosis. The surgical procedure was completed without complications and follow-up of the patient over one year has shown no signs of recurrence. A literature review was performed, and the possible conditions to be included within the differential diagnoses are discussed.

Key words: Castleman disease; Unicentric Castleman disease; Paravesical mass; Pelvic tumors.

Introduction

Castleman disease is a morphologically distinct lymph node hyperplasia. The differential diagnoses includes certain malignant lymphoid neoplasms [1]. The disease is rare and its clinical presentation varies, hampering diagnosis. The ideal management remains to be established [2]. A chronic inflammatory response appears to be present; however, the etiology of the disease remains to be fully clarified. Castleman disease is more common in young adults and is rarely found in children [3, 4]. The condition is also referred to as giant lymph node hyperplasia or angiofollicular lymph node hyperplasia.

The objective of this paper is to describe Castleman disease within the differential diagnosis of gynaecological neoplasms. The authors report a 20-year old female patient presenting with a paravesical mass. Castleman disease was investigated and confirmed by histopathology and immunohistochemistry. The clinical features of the disease, as found here, and the treatments used are described.

Case Report

The institution’s internal review board approved the publication of this report under approval letter number 3.280.542 (CAAE: 10605619.0.0000.5065). The patient agreed to the publication and gave her written consent.

A 20-year old asymptomatic, nulliparous woman was found to have a paravesical mass identified incidentally at transvaginal ultrasound (Figure 1). The sonographic image revealed a predominantly hypoechoic nodule measuring 33 cubic centimeters in volume with posterior enhancement in the right adnexal region and intense vascularization at Doppler, with no adherence to the planes. The mass in the pelvic region was not palpable. The patient reported no weight loss. The presence of the pelvic mass measuring approximately 4 cm at ultrasound could possibly correspond to a uterine fibroid, pedunculated neoplasm or an ovarian tumour. The patient then underwent a laparotomy. The resected lesion consisted of a dark red, mobile retroperitoneal tumour with a regular, smooth surface (Figure 2). Histopathology revealed a lymph node with preserved general architecture, atrophic germinal centres, and prominent mantle zone that appeared concentrically positioned around the germinal centres in an “onionskin” pattern. Arterial hyalinosis occasionally penetrated the lymph node follicles (Figure 3). Immunohistochemistry confirmed the presence and normal distribution of B and T lymphocytes in the lymph node and negativity for Bcl-2 in the follicular centre cells. These findings are consistent with Castleman disease of the hyaline-vascular type. No association was found with the human herpesvirus 8 (HHV-8). The immunohistochemical panel employed included CD20, CD3, CD10, Bcl-2, Ki-67 and HHV-8 (Table 1).

Following resection of the lesion, the patient progressed without complications and to date there has been no sign of recurrence.

Discussion

Although Symmers first described this condition in 1921, it was not until 1954 that Castleman recognized it
Table 1. — Immunohistochemical panel.

| Antibodies                          | Clone | Result          |
|------------------------------------|-------|-----------------|
| B lymphocyte antigen CD20          | L26   | Positive B Lymphocytes |
| T-lymphocyte receptor CD3 (epsilon chain) | SP7   | Positive T Lymphocytes |
| Common acute lymphoblastic leukaemia antigen CD10 | 56C6  | Positive Follicular centre cells |
| Antiapoptotic protein Bcl-2        | 124   | Negative Follicular centre cells |
| Cell proliferation antigen Ki-67   | MIB-1 | Positive 10%    |
| Human herpes virus 8 (HHV-8)       | LN-53 | Negative        |

Figure 1. — Ultrasound image of the lesion revealing a predominantly hypoechoic nodule measuring 33 cubic centimetres in volume.

Figure 2. — Macroscopic appearance of the surgical specimen: a retroperitoneal tumour with a dark red, regular, and smooth surface.

as an independent disease entity with its own manifestations and characteristics. Castleman disease most commonly presents as hyperplasia of the mediastinal lymph nodes, mimicking thymoma. It is more often of the hyaline-vascular type and generally leads to symptoms resulting from a mass effect [3, 5]. In 1956, Castleman completed his description of the systemic form of the disease, the plasma cell variant. In 1972, Keller et al. showed that the histological characteristics of the unicentric disease could also include plasmacytosis and, in such cases, there would be a greater number of associated systemic symptoms [6]. An intermediate form with histologic abnormalities of both types has also been reported [3]. The etiology of the disease has yet to be fully explained [2]. A primary disorder could be present in the plasma cells, leading to the production of elevated levels of IL-6 or even an initial deregulation in their synthesis. This would result in the maturation of plasma cells with their consequent proliferation and acute-phase protein synthesis [3]. Another hypothesis is that this condition could be a reactive lymphoid hyperplasia induced by chronic antigen stimulation associated with a viral infection such as HHV-8 or Epstein-Barr [2, 4, 7, 8]. In the present case, immunohistochemistry was negative for HHV-8, as typically found in cases of the unicentric form of the disease. Castleman disease may also be linked to autoimmune diseases, lymphomas, and acquired immunodeficiency syndrome (AIDS) [5]. The incidence of Castleman disease is 15 cases per million person-years for the unicentric form and 5 cases per million person-years for the multicentric form, although regional variations exist [9]. There are various histologic classifications for the disease; however, the most commonly used were established by Schillin (1969) and Keller (1972) [3]. Schillin divided Castleman disease into types I and II, the former corresponding to the plasma cell variant of the disease and the latter to the hyaline-vascular form, while Keller divided the disease into the hyaline-vascular type and the plasma cell type. From a clinical point of view, Castleman disease is classified as localized (unicentric), systemic (multicentric) or the mixed cell subtype. In its unicentric form, as in the present case, it generally consists of a localized tumour, usually in the mediastinum and less commonly in the neck, lung, axillae, mesentery, broad ligament, retroperitoneal space, the soft tissues of the limbs, and the nasopharynx. It is generally discovered serendipitously with imaging exams, as occurred in the present case [5, 10, 11]. The pelvic cavity is an unusual site [11]. Histopathology confirms the hyaline-vascular form in 70% of cases, the plasma cell form in 10-20% of cases, and rarely, the mixed cell form [5, 12]. The clinical presentation depends on the site affected by the disease; however, in many cases there are few symptoms, or symptoms related only to direct pressure from the presence
of the local mass [5]. Surgery can be curative, although there is the possibility that the unicentric form may coexist with or progress to Hodgkin lymphoma [1]. The differential diagnoses of the unicentric form includes lymphoma, solid tumours, follicular hyperplasia, and toxoplasmic lymphadenitis [5]. In the present report, since the tumour was paravesical and consisted of a right adnexal mass the differential diagnosis included a local gynaecological neoplasm.

Unlike the present case, the clinical condition in the systemic form includes the presence of inflammatory signs and immunological alterations such as fever, asthenia, sweating, weight loss, anaemia, thrombocytopenia, altered liver function, increased erythrocyte sedimentation rate, pergamaglobulinemia and hypoalbuminemia [4, 5, 7, 8]. In the mixed cell form, lymphocytes and the spleen can be affected, generating polyserositis [3]. According to some studies, if left untreated the unicentric form of the disease can progress to the multicentric form.

A microscopic point of view, there are currently three morphological variants of Castleman disease [5]. The hyaline-vascular type is associated, in around 90% of cases, with the unicentric clinical form. Lymphoid follicles with prominent germinal centres containing intense vascular proliferation and hyalinized vessels (vessels in an “onionskin” pattern) are seen, as in the case reported here [1, 3-6]. However, a broad mantle zone in a concentric pattern (lollipop pattern) may also be found. If stromal cell atypia and nodules from a proliferation of follicular dendritic cell-type cells are encountered, these findings could be interpreted as precursors of a malignant lymphoidneoplasm [1]. Sometimes a variable cell infiltrate containing plasma cells, eosinophils, immunoblasts, and plasmacytoid monocytes (KP1-positive) is found. There is inter-follicular vascular proliferation, and these vessels are strongly positive for factor VIII at immunohistochemistry in contrast with the vessels of the germinal centres, which are weakly positive for this vascular marker [1]. In contrast, in the plasma cell variant, a diffuse plasma cell proliferation is generated in interfollicular tissues, with possible additional findings being Russell bodies, large hyperplastic follicles, dense lymphoplasmacytic infiltrate of the stroma, a small number of lymphocytes, and poorly developed or absent central-follicular capillary network [1]. The mixed type has an appearance that is mid-way between the other two [4].

From a clinical and radiological point of view, Castleman disease is indistinguishable from lymphoma [4]. In most cases, including the present one, ultrasonography reveals a homogenous, hypoechoic and clearly outlined mass [10]. Chest X-ray, tomography or magnetic resonance imaging are useful tools for detecting the site of the disease. Tomography has the advantage of enabling guided biopsy to be performed [8]. In turn, biopsy enables the definitive diagnosis of Castleman disease to be reached [5, 8].

Treatment of the unicentric form of the disease consists of surgical resection of the lesion [1], as performed in the present case. Long-term follow-up is necessary, since there is a risk of non-Hodgkin lymphoma [4, 8] or of disease recurrence. The present patient has been followed-up for one year since the surgical procedure with no changes in her clinical status.

If surgery is contraindicated, radiotherapy may result in complete radiographic and clinical resolution of the unicentric form of the disease [13]. There is no current consensus regarding the optimal treatment regimen for the systemic form; however, multimodal treatment is recommended [8], including chemotherapy, high-dose corticosteroid therapy, plasmapheresis, bone marrow transplantation, and human anti interleukin-6 monoclonal antibody [8].

Figure 3. — Histological section (haematoxylin-eosin and Bcl-2 staining) revealing the characteristics of a lymph node with preserved general architecture, atrophic germinal centres and prominent mantle zone in an “onionskin” pattern. Arterial hyalinosis occasionally penetrated the lymph node follicles (magnification ×400).
Conclusion

Clinical, laboratory and imaging findings in Castleman disease may vary substantially, hampering the ability to confirm the diagnosis. In view of the rarity of the disease, additional studies are required to clarify its pathophysiology and consequently optimize its diagnosis and treatment. As shown in the present case, the unicentric form of Castleman disease should be included in the differential diagnosis of pelvic tumours, particularly in asymptomatic patients. Surgical removal is curative in cases of the localized hyaline-vascular type; however, when untreated, it may progress to the multicentric form of the disease.

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Conflict of interest

The authors declare no conflict of interest. The founding sponsors had no role in the design of the study; in the collection, analyses, or interpretation of data; in the writing of the manuscript, and in the decision to publish the results.

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Corresponding Author:
L.A. CABRAL FERREIRA, M.D.
Av Nicolau Von Schilgen 200, Apt 802 Mata da Praia, 29065130 Vitória, Espírito Santo (Brazil)
e-mail: lazcabral@gmail.com