Castleman’s disease

Alejandra Billagra1, Daniel Weil1, Santiago Vivante1, Jose Croxatto2, Davi Ferrerer1.

1. Hospital de Clinicas “José de San Martín”, Buenos Aires, Argentina.
2. FOA, Fundación Oftalmológica Argentina, Buenos Aires, Argentina.
3. Hospital de Enfermedades Infecciosas Francisco Muñiz, Buenos Aires, Argentina.

Abstract:
Castleman’s disease is a rare lymphoproliferative disorder, comprising hyaline vascular elements, and plasma cells, which can be present in unicentric or multicentric forms. This disease rarely involves the orbit/eye globe.

We report the case of a 55-year old patient who was found to have a focal lesion in the orbit. Histopathology studies revealed features consistent with Castleman’s disease. The patient was treated with surgical resection and radiotherapy and was free of disease recurrence at 16-months follow up.

Keywords: Castleman disease, orbit, interleukinas, lymphoproliferative, unicentric.

Introduction
Castleman’s disease (CD) is an atypical lymphoproliferative disorder, rare and non-neoplastic, which cause is unknown.

In 1956, Benjamin Castleman presented a series of 13 cases involving a node-like lesion featuring lymphoproliferative B-cells surrounding a capillary in the mediastinum.1

Based on clinical presentation, this disease may be classified as unicentric or multicentric. From the histopathological point of view, it may be classified into 3 types: hyaline-vascular, plasma and mixed cell types (the latter being the most common type). The hyaline-vascular type is characterized by a germinal center giving the lymph node the appearance of a “lollipop on a stick” with a zone of lymphocytes in a concentric or “onionskin arrangement” surrounding a lymph vessel.2 The plasma cell type is characterized by hyperplastic germinal centers and the presence, in the interfollicular areas, of sheets of plasma cells and hypervascularity. The mixed type presents hyaline degeneration in the same lymphatic follicles with sheets of plasma cells arranged in the same patterns as both types described above.3,4

The hyaline-vascular type was originally described by Castleman and is most commonly found as a solitary mass in the mediastinum (70%), abdomen, neck and axilla.1 It is extremely rare in the orbit; actually, only a few cases of CD with orbital involvement have been reported so far.5-12

Case Report
A 55-year old woman was referred to us with a three-year history of proptosis of the left eye which had increased over the last month. There was no history of an overall condition. Examination showed corrected visual acuity of 20/20 OD and 7/20 OS. There was complete ipsilateral ptosis and proptosis and downward displacement of the eye globe. Hertel exophthalmometer measurements were 16mm OD and 22mm OS. Ocular motility evaluation showed pain and some restriciton. Under slit lamp
examination, there was conjunctival injection and chemosis (Figure 1). MRI showed a T1 hyperintense lesion and a T2 isointense lesion with irregular margins displacing the eye globe (Figure 2).

An excisional biopsy was performed through an anterior orbitotomy via upper eyelid crease. A highly vascularized friable mass was found (Figure 3). Histopathology studies revealed a lymphoproliferative lesion consistent with CD of a mixed type (Figure 4 and 5).

Clinical and hematological evaluation showed absence of systemic complications. The patient was diagnosed with unicentric CD, confined to the orbit. The patient underwent radiotherapy as an ancillary treatment. She was later referred to the hematology service and was free of disease recurrence at 16-months’ follow up.

Discussion

Since the disease was first described in 1950, only a few cases of ocular and orbital involvement have been reported.5-12

The latest hypothesis explaining the cause of CD is related to the overproduction of interleukin-6 (IL-6), estimulated by HHV-8 or an unidentified endogenous infection (Clonal proliferation) or exogenous factor (cytokines). IL-6 promotes the proliferation of plasma cells, increases resistance to apoptotic signals, induces differentiation of precursors of regional B-cells, and has a paracrine role in the production of vascular endothelial growth factor—production by plasma cells. An extensive analysis of immunophenotyping using flow cytometry and/or immunohistochemistry and molecular analysis are important to distinguish CD from pseudo tumors, lymphomas, HIV related lesions, Kaposi’s sarcoma and other reactive disorders12.

The unicentric variant is more favorable and is treated with surgical resection. The multicentric form is associated with fever, chills, night sweats with widespread lymphadenopathy, organomegaly and polyneuropathy; in addition to anemia, thrombocytopenia, hypoalbuminemia, hypocholesterolemia, hypergammaglobulinemia, an elevated erythrocyte sedimentation rate (ESR), increased lactate dehydrogenase and high levels of interleukin-6 (IL-6), and bone marrow plasmacytosis. The prognosis for localized intraorbital CD is good12,13.

There are reports that surgical resection of the lesion could be curative in the unicentric CD of any histopathological type. However, there is no standard treatment for multicentric CD and it usually requires more aggressive systemic treatments. Both the choice of therapy and their results are varied, including surgical resection combined with chemotherapy, radiotherapy, immunomodulators (corticoids, interlephon, retinoic acid, and thalidomide), antiviral therapy, and monoclonal antibodies (monoclonal antibody anti-IL-6 and anti-CD20).14,15,16

Conclusion

Castleman’s disease is an infrequent pathology and orbital involvement is extremely rare. The prognosis for unicentric CD is fairly good and surgical resection is curative in most cases. In any case, it’s important to perform a complete screening to rule out systemic complications.

REFERENCES