■ CASE STUDIES

Castleman's Disease of the Neck

Enrique Coscarón Blanco,[a] Tomás Zamora Martínez,[b] María Cruz Pérez Liedo,[a] María Soledad Suárez Ortega[a] and José Luis Blanco García[a]

[a]Servicio de Otorrinolaringología, Hospital Virgen de la Concha, Zamora, Spain
[b]Servicio de Anatomía Patológica, Hospital Virgen de la Concha, Zamora, Spain

Castleman's disease is an uncommon benign lymphoid disorder usually found in the mediastinum (70%) which is thought to be due to antigenic hyperstimulation of unknown origin. Two histological subtypes may be found in relation to 2 different clinical patterns with clinical and therapeutic implications. Diagnosis is frequently accomplished only by histological analysis after surgery since no specific features have been found in imaging studies. Surgical excision is both diagnostic and curative in localized forms, whereas additional therapies are required in multicentric forms. This report is of Castleman's disease presenting as a neck mass, an infrequent occurrence, with an analysis of management controversies and a review of the literature.

Key words: Castleman's disease. Lymphoproliferative diseases. Lymphoid tumours of the neck. Non-epithelial tumours of the neck.

Enfermedad de Castleman cervical

La enfermedad de Castleman es un trastorno linfoproliferativo benigno muy poco frecuente que generalmente aparece en el mediastino (70%) que se cree debido a una sobrestimulación antigénica de causa desconocida. Se han descrito dos diferentes subtipos histológicos con diferentes comportamientos clínicos e implicaciones terapéuticas. A menudo sólo se diagnostica esta enfermedad mediante el estudio histológico de la pieza tras su exéresis quirúrgica debido a la inexistencia de patrones de imagen específicos en las pruebas de radiodiagnóstico para esta enfermedad. El tratamiento quirúrgico es diagnóstico y a la vez curativo en las formas localizadas, mientras que son necesarios tratamientos complementarios en las formas multicéntricas. Describimos un caso de enfermedad de Castleman de presentación cervical, forma infrecuente de esta enfermedad, y realizamos una revisión de la literatura disponible incidiendo en las controversias que surgen en cuanto a su diagnóstico y tratamiento.

Palabras clave: Enfermedad de Castleman. Trastornos linfoproliferativos. Tumores linfoides del cuello. Tumores no epiteliales del cuello.

CASE STUDIES

Twenty-eight year old male patient with a clinically asymptomatic swelling on the left side of his neck located at the level of the middle third of the sternocleidomastoid muscle for the past 6 months. The patient noted the mass fortuitously while shaving. He did not report systemic symptoms. A deep, hard, painless mass was noted on physical examination, the largest diameter of which measured some 4 cm, inside the sternocleidomastoid muscle that covers it and hides it from examining manoeuvres (Figure 1).

The rest of the ENT examination is within normal limits. The computerized tomography (CT) reveals a solid, homogeneous mass with clear margins, measuring 4.2 cm at its largest and uniformly enhanced when IV contrast was administered. The mass was located on the left side of the neck inside the sternocleidomastoid muscle, which was displaced. The vascular axis was not displaced nor were any radiologically significant adenopathies apparent, although some adenopathies present were just within normal size limits, with none measuring more than a centimetre. Significant vascular pedicles were seen, first above then following an oblique course and inferiorly to form pipe curls (Figures 2 and 3). Magnetic resonance imaging (MRI) did not contribute any data of interest. In the CT angiography, a prominent vascular trunk was seen from which both vascular pedicles originated, as well as a third vessel that was inserted in the middle of the internal aspect of the mass.

The authors have not indicated any conflict of interest.

Correspondence: Dr. E. Coscarón Blanco.
Plaza del Maestro, 10, 2.º A. 49014 Zamora. España.
E-mail: kikekoska@yahoo.es

Received June 20, 2006.
Accepted for publication February 1, 2007.

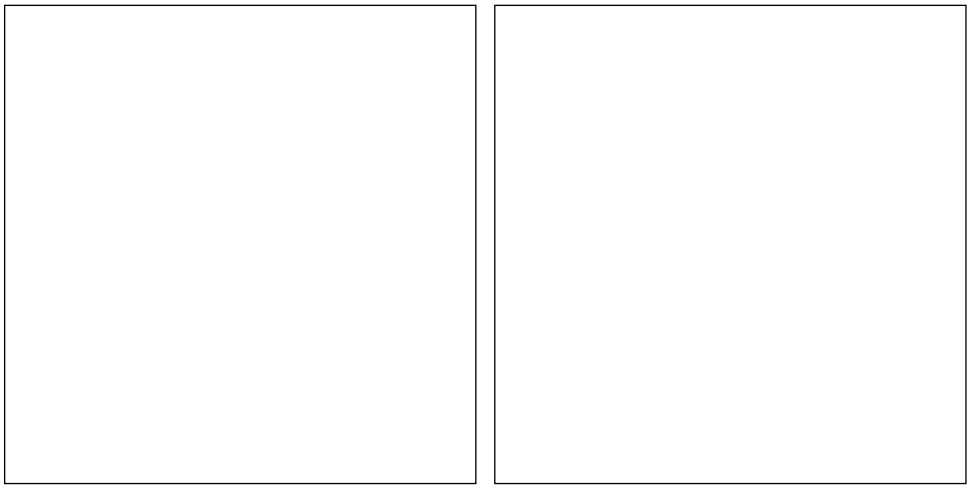

Figure 1. Swelling on the left side of the neck behind and deep in the sternocleidomastoid muscle, which hides it and hinders accurate determination of its extension and relation with other cervical structures.

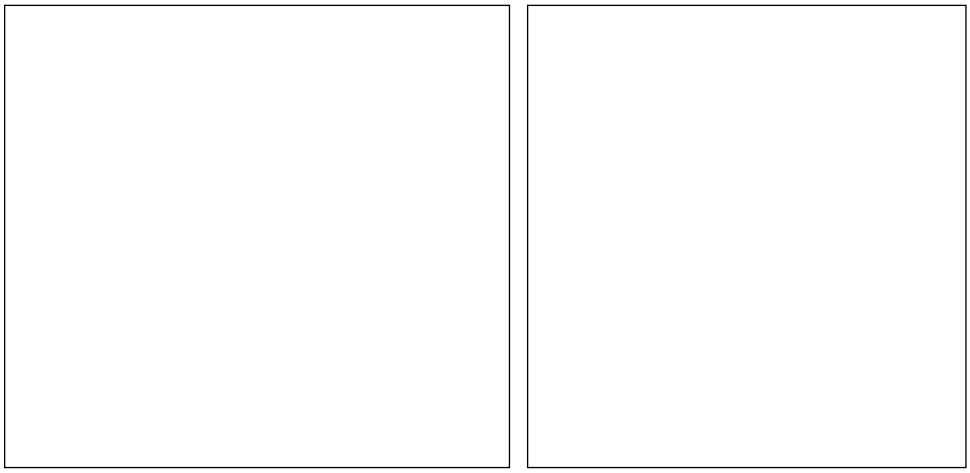

Figure 2. Computerized tomography: oval, homogeneous, hyperintense swelling with well-defined margins, and without signs of intratumoral necrosis, located below the sternocleidomastoid muscle, in close contact with the internal jugular vein.
Note the profuse vascularization surrounding the tumour. There are no signs of infiltration of adjacent structures.

Both studies revealed numerous vessels coursing along the posterolateral aspect of the swelling, although the mass was ruled out as being vascular. An exploratory cervicotomy was performed, identifying the vascular axis and individualizing and ligating the vascular pedicles seen in the CT angiography with subsequent dissection of the swelling. A smooth, whitish, hard, oval swelling was removed, intraoperatively similar to a lymphomatous adenopathy (Figure 4), together with the adenopathies identified on the CT. The post-operative period was uneventful. The pathology study of the specimen revealed adenopathies with overall well-conserved architecture, with an increased number of follicles and hyperplasia of the IgD+ mantle cells, with concentric layers of cells, fusion of bcl2 germ centres and increased vasculature with a hyaline vascular pattern. The interfollicular area presented a vascular pattern with groups of plasmacytoid dendritic cells in the follicles (Figure 5). The study for type 8 Herpes virus (HHV-8) was negative. No hypergammaglobulinaemia or other haematimetric alterations was demonstrated. All these findings are compatible with Castleman's disease with a hyaline vascular pattern. The patient remains asymptomatic and does not present any clinical signs of relapse.

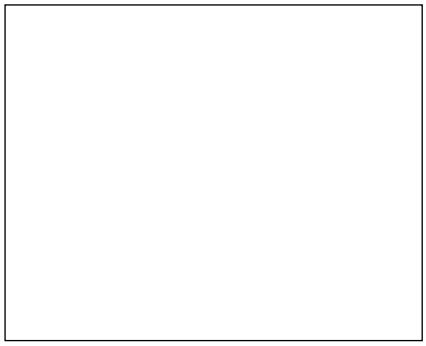

Figure 3. Image of computerized tomographic angiography: note the hypervascularity of the mass, as well as the presence of 2 important feeding pedicles, one cranial and the other caudal.

DISCUSSION

Castleman's disease is a rare, benign, lymphoproliferative disorder described by Castleman as "hyalinizing lymphoid hyperplasia" in 1956.[1] It has also been called angiofollicular hyperplasia, lymphoid hamartoma, benign giant lymphoma, follicular lymphoreticuloma, and lymphoid angiomatosis, which reflects the relative uncertainty surrounding its origin

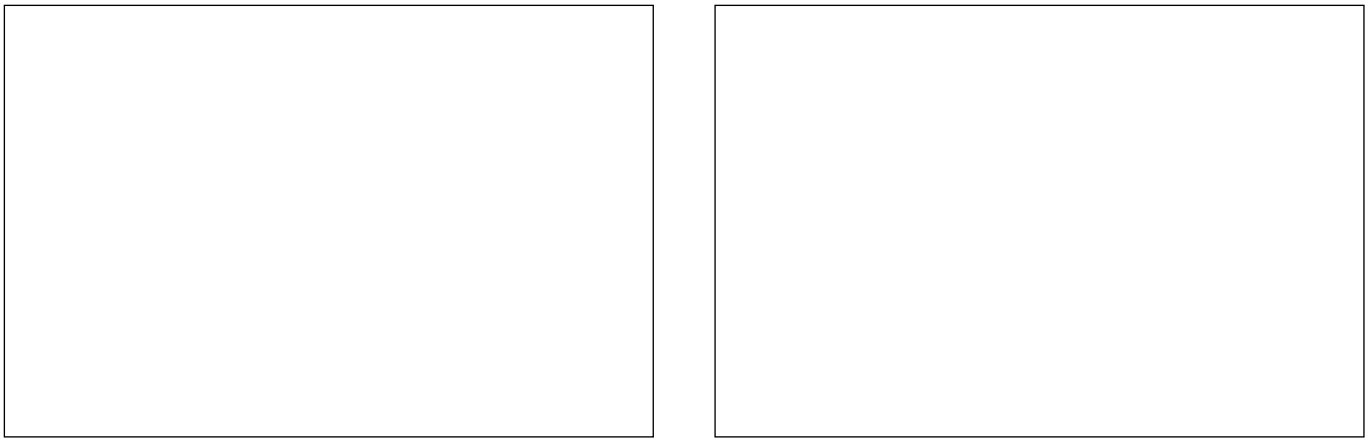

Figure 4. Intraoperative images of the swelling. Vascular pedicles are seen that were identified and ligated.

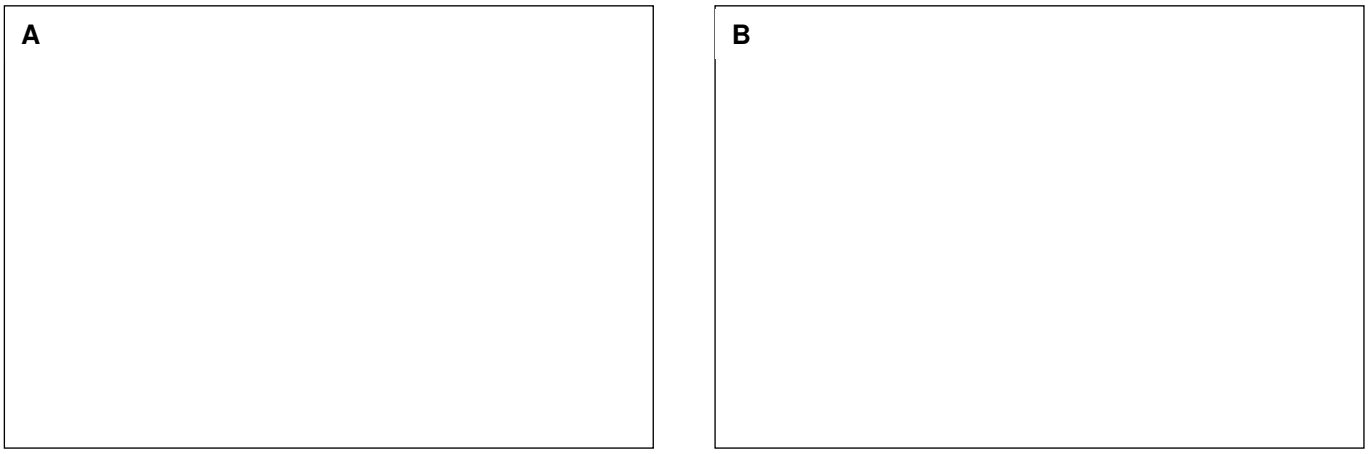

Figure 5. Histological study with haematoxylin-eosin. A: adenopathies with generally well-conserved architecture, with an increased number of follicles and hyperplasia of the mantle in concentric onion-like layers. B: detail of the germ centres, with cell depletion and characteristically occupied by hyalinized vessels (arrow). The demonstration of several such follicles with this architecture constitutes a diagnostic criterion.

and typification as a tumour or infectious inflammatory illness.[2-5]

It has no predominance with respect to gender and appears in the mediastinum (70%) and abdomen in a majority of the cases, although on occasion it may also appear in other parts of the body such as the axillae, pelvis, or neck.[6-8]

Its aetiology and pathogenesis are unknown, though there is thought to be chronic virus-induced and interleukin-6-mediated antigenic hyperstimulation, with some cases linking it to HHV-8 (plasmoblastic histological subtype).[4,9,10]

Two clinical forms have been reported that tend to correspond to 2 well-defined histological patterns.[4,9,10,11]

There is a localized form that evolves as a bulky, asymptomatic swelling mainly located in the mediastinum or in the abdomen in order of frequency, and appearing in children or young adults. Symptoms, when they occur, are usually due to the mass effect or compression of structures and pain is the most common. They evolve without systemic symptomatology. In 90% of the cases, a hyaline vascular pattern is seen characterized by follicles with highly hyperplastic mantles, typically made up of concentric onion-like rings of cells comprising small lymphocytes, arranged around a regressively small germ centre, with lymphoid depletion and arrival of hyalinized vessels and prominent dendritic cells.[10,12,13] If, in addition, multiple germ centres with these characteristics were observed, it would be considered a definitive diagnostic criterion.[12] The existence of dendritic cells would speak in favour of a dysfunction in these antigen-presenting cells as the pathogenic centre. These dendritic cells produce large amounts of interferon alpha-1, mainly in response to viral infections, enabling an increase in the survival of the antigen-activated T lymphocytes.[13,14]

There is also another more widespread or multicentric form of the illness affecting more than one organ or producing swellings at various levels; it generally courses with general symptoms such as asthenia, fever, skin rash, weight loss, multiple adenomegalies, and hepatosplenomegaly. Blood work may reveal anaemia, signs of haemolysis, an increased globular sedimentation rate (ESR), and hypergammaglobulinaemia.

Histologiclly, it is possible to see a pattern with a great proliferation of plasmatic or plasmablastic cells (a particularly aggressive histological subtype).

Castleman's disease has been related, almost always in its systemic or multicentric form, with other conditions such as the POEMS syndrome (acronym for polyneuropathy, organomegaly, endocrinopathy, m-protein, skin changes), build-ups of amyloid, lymphoma (18%), plasmocytoma, Kaposi's sarcoma (13%), thrombotic renal microangiopathy, and a marked tendency towards intercurrent infections.[4,9,15-20]

Castleman's disease in the neck has been described in CT scans as a well-defined and clearly-delimited homogeneous lesion with moderate to intense uptake of contrast and without any other noteworthy characteristics, radiologically indistinguishable from other diseases with hyperuptake in the ganglia and particularly lymphoma.[6,8,21,22] In the pelvis, some authors have described the presence, in more than 50% of the cases, of intraganglionar calcifications which may help in the diagnosis, albeit an apparently exceptional circumstance in the neck, probably because its diagnosis is reached sooner.[7] Some authors[6] have also tried to see the presence of a scar or intraganglionar fibrosis as characteristic of this illness. None of these criteria was present in our patient. The magnetic resonance image obtained is also non-specific, appearing as a swelling with hyposignal in T1 and hypersignal in T2, with occasional areas of hyposignal due to calcifications.[8]

In the cervical manifestation of this illness, we feel that microaspiration biopsy is not very useful because it would only help to confirm, with some reservations, the absence of a malignant process. However, lymphomas, the main clinical entity in the differential diagnosis, may resemble lymphoid hyperplasia, so it is necessary to have a complete specimen to ensure the diagnosis and, subsequently, study the subtype morphology pattern to establish the most appropriate therapeutic and follow-up strategies.

It is worth mentioning the profuse vascularization, which occasionally gives rise to considerable feeding pedicles that we must suspect and seek out when planning the surgical intervention, for which a vascular imaging study using CT angiography may be of great assistance, as happened in our case.[8,23,24] In the localized forms, complete excision is curative, and the relapses described are anecdotal, although some authors have recommended radiotherapy in some cases.[6,25-31] The profuse vascularization of the swelling entails an important risk of intra-operative haemorrhage, so some groups systematically use pre-surgical embolization to minimize it.[26,32] However, in the multicentric forms, various regimes of radiotherapy, chemotherapy, and steroids have been put forward as treatment modes depending on the experience of each department.[10,24,33] In our case, we excise the mass following control of the feeding pedicles to devascularize the mass, without complications. The post-operative period elapsed without incident, and so far we have not detected relapses or other diseases associated with this illness in the subsequent follow-up visits carried out. In our opinion, follow-up visits must be considered necessary as the scant number of cases reported on this illness at the cervical level means the possibility of relapse or the appearance of associated diseases cannot be excluded.

REFERENCES

1. Castleman B, Iverson L, Menendez VP. Localized mediastinal lymphnode hyperplasia resembling thymoma. Cancer. 1956;9:822-30.
2. Schnitzer B. Reactive lymphoid hyperplasias. In: Jaffe ES, editor. Surgical pathology of the lymph nodes and related organs. Philadelphia: WB Saunders; 1995. p. 107-11.
3. Chaloupka JC, Castillo M, Hudgins P. Castleman disease in the neck: Atypical appearance on CT. AJR Am J Roentgenol. 1990;154:1051-2.
4. López García-Asenjo JA, Martín Rodilla C. Patología de las enfermedades no neoplásicas de los ganglios linfáticos. In: Fariña J, editor. Anatomía patológica. Barcelona: Salvat; 1990. p. 699-708.
5. Frizzera G. Castleman's disease: More questions than answers. Hum Pathol. 1985;16:202-5.
6. Tan TY, Pang KP, Goh, HKC, Teo ELH, Abhilash B, et al. Castleman's disease of the neck: A description of four cases on contrast-enhanced CT. Br J Radiol. 2004;77:253-6.
7. Luburich P, Nicolau C, Ayuso MC, Torra R, Clavero JA. Pelvis Castleman disease: CT and MR appearance. J Comput Assist Tomogr. 1992;16:657-9.
8. Glazer M, Rao VM, Reiter D, McCue P. Isolated Castleman disease of the neck: MR findings. AJNR. 1995;16:669-71.
9. Armitage JO, Longo DL. Neoplasias malignas de las células linfoides. In: Kasper DL, Braunwald E, Fauci AS, Hauser SL, Longo DL, Jameson JL, editors. Harrison. Principios de Medicina Interna. 16th ed. México: McGraw-Hill Interamericana; 2006. p. 719-34.
10. McClain KL, Natkunam Y, Swerdlow SH. Atypical cellular disorders. Hematology. 2004;283:96.
11. Montserral Costa E, Díaz-Mediavilla J, Campo Guerri E, Bosch Albareda F, López-Guillermo A, Sans-Sabrafén J, et al. Enfermedades ganglionares. In: Farreras-Rozman. Medicina Interna. 14th ed. Madrid: Harcourt; 2000. p. 1958-91.
12. Warnke RA, Weiss LM, Chan JKC, Path MRC, Cleary ML, Dorfman RF, editors. Atlas of tumor pathology. Tumors of the lymph nodes and spleen. Washington: Armed Forced Institute of Pathology; 1995. p. 104-6.
13. Rosai J. Ackerman's Surgical Pathology. 8th ed. St. Louis: Mosby; 1996. p. 1688-9.
14. Cella M, Jarrossay D, Facchetti F, et al. Plasmacytoid monocytes migrate to inflamed lymph nodes and produce large amounts of type I interferon. Nat Med. 1999;5:919-23.
15. Mandler RN, Kerrigan DP, Smart J, et al. Castleman's disease in POEMS syndrome with elevated interleukin 6. Cancer. 1992;69:2697-703.
16. Ordi J, Grau JM, Junque A, et al. Secondary amyloidosis associated with Castleman's disease. Report of two cases and review of literature. Am J Clin Pathol. 1993;100:394-7.
17. Gould SJ, Diss T, Isaacson PG. Multicentric Castleman's disease in association with a solitary plasmocytoma. A case report. Histopathol. 1990;17:135-40.
18. Vasef M, Katzin WE, Mendelshon G, et al. Report of a case of localized Castleman's disease with progression to malignant lymphoma. Am J Clin Pathol. 1992;98:633-6.
19. Zárate-Osorno A, Medeiros LJ, Danon AD, et al. Hodgkin's disease with coexistent Castleman-like histologic features. A report of three cases. Arch Pathol Lab Med. 1994;270:4.
20. Lajoie G, Kumar S, Min KW, et al. Renal thrombotic microangiopathy associated with multicentric Castleman's disease. Report of two cases. Am J Surg Pathol. 1995;19:1021-8.
21. Davis BT, Bagg A, Milmore GT. CT and MR appearance of Castleman's disease of the neck. AJR Am J Roentgenol. 1999;173:861-2.
22. Yi AY, DeTar M, Becker TS, Rice DH. Giant lymph node hyperplasia of the head and neck (Castleman's disease): A report of five cases. Otolaryngol Head Neck Surg. 1995;113:462-6.
23. McAdams HP, Rosado de Christenson M, Fishback NF, Templeton PA. Castleman disease of the thorax: Radiological features with clinical and histopathologic correlation. Radiology. 1998;209:221-8.
24. Somdas MA, Ketenci I, Bicer S, Senturk M, Guney E. Castleman's disease as an unusual neck mass: Case report. Ann Otol Rhinol Laryngol. 2004;113:459-61.
25. Chronowski GM, Ha CS, Wilder RB, Cabanillas F, Manning J, Cox JD. Treatment of unicentric and multicentric Castleman disease and the role of radiotherapy. Cancer. 2001;92:670-6.
26. Sánchez de Toledo Sancho J, Fàbrega Sabaté J, Marhuenda Irastorza C, Lucaya Layret X, Torán Fuentes N, Gros Subias L, et al. Enfermedad de Castleman. An Pediatr (Barc). 2005;63:68-71.
27. Molino Trinidad C, Marchán Carranza E, Villanaueva Liñán J. Enfermedad de Castleman: Presentación como una masa mediastínica calcificada. Arch Bronconeumol. 1996;32:155-6.

28. Osma U, Cureoglu S, Yaldiz M, Topcu I. Castleman's disease (giant lymph node hyperplasia) of the neck: A case report. Eur Arch Otorhinolaryngol. 2001;258:42-4.
29. Sanz C, Sierra J, Cobarro J, Avellaneda R, Montserrat E, Rozman C. An unusual case of Castleman's disease restricted to the neck. ORL J Otorhinolaringol Relat Spec. 1992;54:331-3.
30. McCarty MJ, Vukelja SJ, Banks PM, Weiss RB. Angiofollicular lymph node hyperplasia (Castleman's disease). Cancer Treat Rev. 1995;21:291-310.
31. Frizzera G. Castleman's disease and related disorders. Semin Diagn Pathol.1988;5:346-64.
32. Safford SD, Lagoo AS, Mahaffey SA. Preoperative embolization as an adjunct to the operative management of mediastinal Castleman disease. J Pediatr Surg. 2003;38:E42.
33. Herrada J, Cabanillas F, Rice L, Manning J, Pugh W. The clinical behavior of located and multicentric Castleman disease. Ann Intern Med. 1998;128: 657-62.