 CASTLEMAN’S DISEASE AS CERVICAL MASS: A REPORT OF THREE CASES AND REVIEW OF THE LITERATURE

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Summary: Castleman’s disease as cervical mass: a report of three cases and review of the literature.

Castleman’s disease is a rare disorder characterized by benign lymph node hyperplasia involving lymphatic tissue in the neck, mediastinum, abdomen and other areas. Disease was described for the first time in 1956 by Castleman. The etiopathogenesis of the disease is unknown. The disorder can be classified into three histopathological types: hyaline-vascular, plasma-cell and mixed.

We report three cases of the Castleman’s disease (hyaline-vascular type) in three female patients with unilateral swelling of the neck. None of the patients developed any local or distant recurrence in postoperative follow-up.

Key Words: Castleman’s disease - Neck - Hyaline-vascular type.

Introduction

A number of terms were used to describe Castleman’s disease, including angiofollicular or giant lymph node hyperplasia, since Castleman and colleagues described this entity in 1956 (1). Castleman et al. described this disease as ‘hyaline vascular’ type but, in contrast, in 1969 Flendrig et al. and later in 1972 Keller et al. recognised a different histological type, which is now referred to as the ‘plasma cell’ type. But these two types were manifestations of the same disease because there were cases with overlapping histological features (2, 3).

This entity is currently classified into two major subgroups: localized Castleman’s disease and multicentric (disseminated) Castleman’s disease. There are also three histologic variants: hyaline-vascular, plasma cell and transitional (mixed type) in English literature (4, 5).

The localized form, identified by Benjamin Castleman, usually presents in young adults with localized masses in the mediastinum (60-75%), neck (20%) or less commonly intra-abdominal masses (10%). However multicentric Castleman’s disease presents with polylymphadenopathy and frequently multi-organ involvement and is associated with systemic features. Multicentric Castleman’s diseases are less common than the localized variant and while multicentric form follows a more aggressive natural course, systemic symptoms are rare in the localized form (6).
pically the hyaline-vascular type and most multicentric cases subsequently described have been of the plasma-cell type (7).

We report three patients with Castleman’s disease arising in lymphoid tissue of the cervical region and underwent total excision.

**Patients and methods**

We present 3 cases of Castleman’s disease localized in cervical region that were treated in Diyarbakir Education and Research Hospital between 2006-2009. Diagnosis were made by histopathological examination. HIV, HHV-8, EBV and HBV viral loads were studied by PCR method. Also IL-6 levels were measured by immunoassay method. The characteristics of three patients were showed in Table 1.

**Case 1**

A 17-year-old female was admitted to our hospital. She had suffered from neck swelling in the last one year. General physical examination revealed a mass, 3 cm of diameter, at posterior of the left sterno-cleido-mastoid muscle (SCM). Laboratory studies and chest radiography found no abnormalities. Computed tomography (CT) showed a mass, 41x20x25 mm in size, at posterolateral left SCM with irregular borders (Fig. 1). The tumor was resected completely. In the postoperative follow-up no local progression or recurrence or other problems were observed.

**Case 2**

A 27-year-old female patient presented with a 7-month history of supraclavicular mass. Physical examination revealed no significant abnormality except a firm, movable and non-tender mass measuring 3x4 cm in size, at posterior of the right SCM muscle. CT revealed a well-defined mass (3.2x4.3x5.2 cm) at the posterior of the right SCM muscle. Laboratory data and tumor markers were within the normal limits. Chest X-ray was normal. Extensive resection was performed. The mass was well capsulated and easily removed. There has been no evidence of progression or recurrence after 18 months of follow-up.

**Case 3**

A 23-year-old female patient was admitted to emergency unit with complaint of painful right cervical mass for last 7-8 months. Examination revealed a mass on the left SCM. CT imaging of the neck showed a mass measuring 3.5x4.2x4 cm in diameter, which was located behind left SCM. There were no specific deviations in the biochemical results. Resection was performed. There was no local recurrence in postoperative follow-up.

**Pathology**

Histopathological examination of the surgical specimens revealed lymphoid mantles with germinal centers of varying sizes. These germinal centers were penetrated by hyalised venules. Also the follicles were separated by hypervascular interfollicular tissue. High power demonstrated that the single follicle was composed entirely of concentrically arranged small lymphocytes penetrated by a number of small vessels. These histological findings are consistent with a diagnosis of Castleman’s disease hyaline-vascular type (Fig. 2).

| TABLE 1 - CHARACTERISTICS OF PATIENTS WITH CASTLEMAN’S DISEASE. |
|-----------------|-----------------|-----------------|
| **Case 1**      | **Case 2**      | **Case 3**      |
| Age, yrs        | 17              | 27              | 23              |
| Sex (M/F)       | F               | F               | F               |
| Onset           | 12 months       | 7 months        | 8 months        |
| IL-6 level (pg/ml) | 19.4               | 10.3             | 4.1             |
| EBV viral load  | Neg             | Neg             | Neg             |
| HHV-8 viral load| Neg             | Neg             | Neg             |
| HBV viral load  | Neg             | Neg             | Neg             |
| HIV viral load  | Neg             | Neg             | Neg             |
| Pathological type | Hyaline-vascular | Hyaline-vascular | Hyaline-vascular |

Fig. 1 - The follicle consist of large, concentrically arranged mantle zone lymphocytes surrounding atrophic germinal centers. The interfollicular areas contain a network of small vessels (hematoxylin and eosin, 200x magnification).
Castleman’s disease can be classified into three histopathological groups: hyaline-vascular type, with a good prognosis, plasma-cellular and mixed types; the latter two are both more aggressive than the hyaline-vascular type (8). All of our cases were of hyalin-vascular type and revealed very good prognosis.

Males and females are affected equally and the age is ranged from 8 to 66 years. Several immunological mechanisms have been proposed for the etiology including overproduction of interleukin-6 and human herpes virus type 8 infection (3, 9). The HHV-8, EBV, HBV and HIV viral loads were evaluated by PCR method. There were no abnormality in the results. In patients quantitative analysis were made by using IL-6 kit in Immulite-DPS® device by immunoassay method. Two of them showed elevated IL–6 levels (normal range <5 pg/ml) (10).

However there is no consensus on the underlying etiology of this entity but two main theories have been proposed. One theory submits that the disorder represents a reactive lymphoid hyperplasia initiated by chronic antigenic stimulation associated with a viral trigger (which remains undefined), most likely mediated through the respiratory or gastrointestinal tract, the most common affected sites. The other theory proposes that the masses are due to a developmental growth disturbance of the lymphoid tissue, i.e. a vascular lymphoid hamartoma (11).

Two clinical types of this disease have already been described, i.e. the localized or unifocal type and the multicentric or multifocal type. Traditionally the majority of cases can be categorized as localized hyaline-vascular, localized plasma cell or multicentric plasma cell. The patients presented here were diagnosed as localized Castleman’s disease of the hyaline-vascular type.

The localized hyaline-vascular type is often asymptomatic or, as in our patients, there are symptoms caused by the mass effect of the lesion. This type is seen in 90% of the cases of localized disease (12). This form may represent reactive lymphoid hyperplasia due to chronic antigenic stimulation from viral infection (13). The other 10% of the cases of localized disease is defined as the localized plasma cell type. These patients present with symptoms such as fever, fatigue, weight loss and laboratory abnormalities.

The multicentric type is a systemic disease with disseminated lymphadenopathy, hepatosplenomegaly and other symptoms (14). This type is a more aggressive form with a potentially malignant profile in association, for example, with polyneuropathy, organomegaly, endocrinopathy, monoclonal proteinemia and skin lesions, Hodgkin’s disease, Kaposi’s sarcoma and acquired immunodeficiency syndrome (15).

The diagnosis of Castleman’s disease is ultimately made by histology, thereby requiring either removal or biopsy of the lesion. Histological examination of the lymph node in the localized hyaline-vascular type shows small hyaline vascular follicles with interfollicular capillary proliferation. Histology of the affected lymph-nodes in the localized plasma cell type shows large follicles with intervening sheets of plasma cells. The multicentric type is histologically similar to the localized plasma cell type (14).

There are some benign and malignant conditions, including lymphoma and thymoma, which may appear histologically similar to Castleman’s disease. Therefore, immunohistologic and immunologic gene rearrangement studies of the specimens can be useful in solidifying the diagnosis. Identifying an immunophenotypically varied population of B lymphocytes with polyclonal surface and cytoplasmic immunoglobulin markers helps to confirm the diagnosis of Castleman’s disease and to differentiate it from lymphoma (11).

The most prominent sites are mediastinum (60-75%), neck (20%) or less commonly abdomen (10%) and axilla (4%). Reviewing the literature, we found only a few case reports of cervical Castleman’s disease and most of them presented with a solitary neck mass (16-18). Only Song et al. reported a series of Castleman’s disease that includes 12 patients (19).

The preoperative imaging of Castleman’s disease is non-specific. At CT scan, the lesions may present as a homogenous or heterogenous soft tissue mass, and contrast enhancement depends on the injection rate and volume of contrast media. The differential diagnosis must include infectious and inflammatory lesions such as...
lymphadenitis, tuberculosis, sarcoidosis, toxoplasmosis, cytomegalovirus, mononucleosis, HIV and cat scratch disease (20).

The only diagnosis and curative treatment is the complete surgical excision of the mass and the surrounding nodes. All symptoms disappear after removal of the tumour. No recurrences have been reported in the literature after complete resection of the hyaline-vascular type. For patients who have incomplete or unresectable lesions, radiotherapy has been used with limited effectiveness. The unfortunate few case of the more aggressive plasma cell variant often require treatment with steroids and systemic chemotherapy.

References