Case report

Unicentric Castleman’s disease

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Abstract

Castleman’s disease (CD) is a rare benign lympho-proliferative disorder characterized by non-neoplastic lymphnode hypertrophy. Its etiology is unknown. It has been found in association with Kaposi’s sarcoma, necessitating investigation for HIV. CD can be unicentric (localized), multicentric or mixed. We present a case of 13 years old male who presented with cervical lymphadenopathy, intermittent fever and weight loss in whom histopathological examination of a lymph node led to diagnosis of this rare condition hyaline vascular type of unicentric Castleman’s disease.

Key words: angiofollicular lymphoid hyperplasia, Castleman’s disease, hyaline vascular, lymphadenopathy

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Castleman’s disease (CD) is a benign lymphoproliferative disorder with unknown aetiology. It was first described in 1956 as a mediastinal mass by Benjamin Castleman. There are two types of presentations localized or unicentric, and systemic or multicentric. CD most often presents as a solitary soft tissue mass in the mediastinum and may be located extra-thoracically in the neck, abdomen and peripheral lymph node zones. Histologically there are three types: the hyaline vascular type (80%-90%), the plasma cell type (10%-20%) and mixed type (<5%). Surgery is the therapeutic method of choice when the disease is localized. For disseminated CD partial surgical resection along with steroids, chemotherapy, and radiotherapy is recommended.

Case report

We present a case of 13 years male patient who presented with right cervical lymphadenopathy, fever and loss of weight. Routine investigations like complete blood picture, complete urine examination and ESR were within normal limits. A chest X-ray and computerized tomographic (CT) scan of chest and abdomen revealed no organomegaly. A fine needle aspiration cytology of the relevant lymph node showed findings suspicious of granulomatous inflammation and cervical lymph node excision biopsy was advised.

Gross examination

We received a single lymph node measuring 3x1.5x1cm with capsule and peri-nodal adipose tissue. The cut section showed homogenous grey-white areas with no foci of caseous necrosis.

Microscopic examination

Sections from the lymph node showed peri-nodal adipose tissue and capsule. The lymph node architecture was partially effaced, with the cortex showing follicular hyperplasia. A few follicles showed involuting germinal centres with expanded mantle zones. The para-cortical areas showed marked vascular proliferation with areas of hyalinization.
Focal areas showed burnt out germinal centers. Onion skin appearance was also noted by regular layering of lymphocytes around germinal centers. A few hyalinized follicles were present with dense fibro-collagenous areas. The pattern suggested the diagnosis of Castleman’s disease of the hyaline vascular type.

**Discussion**

Castleman’s disease (CD) was first described by Benjamin Castleman in 1956. The other names for CD are angiofollicular lymph node hyperplasia, giant lymph node hyperplasia, lymphoid hamartoma, benign lymphoma/ follicular lymphoreticuloma and angiofollicular lymphoid hyperplasia. Two types are present: the localized form (most common) and the multicentric or systemic forms (relatively uncommon).

Three histological patterns are described:

1. Hyaline vascular type (the most common type)
2. Plasma cell type
3. Mixed type CD presents at any age

The mean age at time of diagnosis is 45 years, with a range of 10 to 85 years. Hyaline vascular type mostly affects younger individuals whereas the plasma cell type affects older individuals. The size of lesion varies, with a mean diameter of 6 cm (1-12 cm). In the case of our patient it was 3 cms. Sites involved in the order of their frequency - mediastinum, head and neck, abdomen and peripheral lymph node zones. The localized form is usually asymptomatic but patients may present with symptoms like asthenia (20%), fever (20%) and weight loss (11%). CD can also be associated with other diseases like autoimmune disorders, Kaposi’s sarcoma, late phases of HIV lymphadenitis and primary immune deficiencies. The multicentric form is almost always symptomatic presenting with symptoms like asthenia (65%) weight loss (67%), fever (69%), peripheral polyadenopathy (very common 84%) with a mean of four sites involved and can be associated with hepatosplenomegaly. However our case showed no such signs.

CD has also been described in association with POEMS syndrome (polyneuropathy, organomegaly, endocrinopathy, monoclonal gammopathy and skin changes) and malignant neoplasms, most often lymphomas, follicular dendritic cell sarcoma and kaposi’s sarcoma in HIV positive patients.

Pathogenesis is usually unknown but IL-6 may be involved in the pathogenesis. Role of IL-6 in the pathogenesis of the disease is thought to be due to its effect of B-cell proliferation resulting in hyperplastic follicles and hence enlarged lymph nodes. Increased VEGF result in angiogenesis and capillary proliferation with hyperplasia. Polarization of T lymphocytes to Type 2 cytokine proliferation may be seen leading to autoimmune phenomena like autoimmune hemolytic anemia, antinuclear
antibody positivity and elevation of IgE levels. This may also induce an acute phase reaction leading to increase in ESR, CRP, IgG, serum fibrinogen, serum amyloid protein (which can result in amyloidosis), hyperfibrinogenemia (can result in venous thrombosis). Treatment of localized forms requires surgical lymph node excision/biopsy.

The hyaline vascular type may represent advanced stage of disease. The nodal architecture is altered by increased number of lymphoid follicles throughout the lymph nodal parenchyma. These follicles are small and their germinal centres are transfixed by radially penetrating capillaries so that characteristic “Lollipop” structure forms. Germinal centres are involuted, poorly cellular and partly or totally replaced by hyaline.

Surrounding small germinal centres, multiple concentric layers of lymphocytes are seen. Regular layering of lymphocytes in “Onion skin” fashion results in another characteristic feature: the so-called “target” appearance of lymphoid follicles. Between follicles are numerous blood vessels, mostly post capillary venules, lined by hyperplastic endothelial cells and surrounded by fibrocollagen. Marked hyperplastic follicular dendritic cells may form concentric rings with lymphocytes trapped between them-hence onion skin pattern. Lymphocytes are small and uniform. Plasma cell type represents earlier stage of disease. Follicular hyperplasia may predominate with large germinal centres surrounded by narrow peripheral cuffs of mature lymphocytes. These germinal centres are active with frequent cells in mitosis and macrophages contain nuclear debris. Sometimes co-existence with hyperplastic follicles/entirely replacing them are numerous involuted, atrophic/hyalinized follicles seen, with hyperplastic blood vessels with collagenized walls. Interfollicular areas and medullary are occupied by large sheets of plasma cells, some mature and immature with occasional binucleate and atypical forms. Intermingled with plasma cells are immunoblasts, plasmacytoid, monocytes, lymphocytes and occasional histiocytes.

Russell bodies may also be present. A complete clinical evaluation and a detailed patient history (along with laboratory and imaging studies including IL-6, ESR, CRP, CT and MRI scans) is helpful, but the diagnosis rests on the histopathological examination of affected lymph nodes. In particular, PET gives important information regarding the metabolic status of lymph nodes (the uptake in affected lymph nodes is relatively less compared to active lymph nodes) and it also helps in assessing response to treatment.

Complete surgical excision is the treatment of choice in the localized form. Complete recovery without relapse is seen in almost all cases. A combination of treatments (surgery, chemotherapy, radiotherapy, anti-IL6 therapy, intravenous immunoglobulin, anti-herpes drugs, etc.) is used in multicentric forms.

Conclusion

Castleman’s disease is a rare benign self-limiting lymphoproliferative disorder with an excellent prognosis. It is important to consider CD in the differential diagnosis for patients presenting with localized or generalized lymphadenopathy especially those with acquired immune-deficiencies. These patients are also at high risk for the development of Non-Hodgkins lymphoma and Kaposi’s sarcoma, and hence regular medical follow up is necessary.

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References


