Case Report

Unicentric Castleman's disease involving central nervous system - plasma cell type: A rare entity

Kandukuri Mahesh Kumar[1*], Krishna Reddy[1], Medak Harika[2]

[1]Assistant Professor, [2]Tutor
Malla Reddy Institute of Medical Sciences (MRIMS), Hyderabad, Telangana State, India
[*]Corresponding author email: **doctormaheshgoud@gmail.com**

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Abstract

Castleman's disease (CD) is a rare disease primarily involving lymph nodes and lymphatic system. Other synonyms used for the Castleman's disease are giant lymph node hyperplasia, and angio-follicular lymph node hyperplasia (AFH). CD is not a true cancer and is a lympho-proliferative disorder which means there is an abnormal overgrowth of cells of the lymphatic system that is similar in many ways to lymphomas (cancers of lymph nodes). Even though CD is not officially a true cancer, one form of this disease (known as multi-centric Castleman's disease) acts very much like lymphoma. In fact we can call it as premalignant condition as many people with this disease eventually develop lymphomas. Multi-centric CD is more common in people infected with HIV. In recent years, it's become clear that another virus, known as human herpesvirus-8 (HHV-8) or Kaposi sarcoma herpes virus (KSHV), is often found in the lymph node cells of people with multi-centric CD. In fact, HHV-8 is found in the lymph nodes of nearly all CD patients who are HIV positive. We present a case of unicentric plasma cell type of Castleman's disease involving central nervous system (CNS) or brain parenchyma in a young male patient which is a rare occurrence.

Key words

Castleman's disease, Plasma cell type, Central nervous system, Giant lymph node hyperplasia, GFAP, CD 79 Alpha.

Introduction

Castleman's disease (CD) is a rare disease primarily involving lymph nodes and lymphatic system. It is also known as giant lymph node hyperplasia, and angiofollicular lymph node hyperplasia (AFH). The 2 main types of CD are called localized or unicentric and multi-centric. Localized (unicentric) Castleman's disease - this

is the more common type of CD. In localized CD, a single group of lymph nodes are affected and it is not widespread. Excision of the affected lymph node or group of lymph nodes will completely eliminate the disease. Multi-centric Castleman's disease (MCD) affects more than one group of lymph nodes or organs containing lymphoid tissue. This form mostly involves people infected with human immunodeficiency virus (HIV). Multi-centric CD is more serious than the localized type, particularly in people with HIV infection. MCD also increases the risk of developing lymphoma, a cancer of lymphoid tissue, which can often hard to treat, unlike unicentric form.

Case report

A male patient aged about 36 years came with the complaints of seizures, numbness over the left side of the face since few months. Patient also complaints of headache, nausea and vomiting since last one week. On examination, there was paresthesia on the left side of the face and dysphasia. Patient was HIV negative and all the laboratory investigations were normal. CT scan brain showed a large well defined heterogenous space occupying lesion predominantly hyperdense measuring 7 x 5 cm causing effacement of fronto-parietal horns of the brain parenchyma and encroaching onto the right lateral ventricle. Surrounding brain parenchyma showed edema with mpression of possibility of hemorrhagic or neoplastic lesion **(Figure - 1)**. Patient was operated and a small tissue along with the duramater was sent for the Intra operative squash cytology for rapid diagnosis. Squash cytology suggested features of meningioma **(Figure - 2)**. Some of the leftover intra-operative tissue was taken for histopathological examination (HPE). Grossly, on cut section the tissue showed few tiny gray white nodules and specks of calcifications noted. Sections studied showed sheets of plasma cells, lymphoid aggregates in the background of reactive glial tissue. Focal areas show lymphoid follicles with germinal centre formation, there are perivascular aggregations of plasma cells, some cells are binucleate, and focally lesion is surrounded by normal meninges **(Figure - 3, 4 and 5)**. Diagnosis on histopathological Castleman's Disease (CD) involving the Central Nervous System (CNS) which was confirmed by using Glial Fibrillary Acidic Protien (GFAP) and B-cell marker CD 79 alpha, which showed strong positivity and Pan-Cytokeratin which was negative which proved cytological diagnosis of meningioma wrong **(Figure - 6, 7 and 8)**. As there were no other swellings in the body, so the final diagnosis was made as Unicentric or Localized Castleman's Disease (CD) – Plasma cell type.

Figure - 1: CT brain showing space occupying lesion in the right fronto-parietal lobe of the brain with peritumoral edematous changes.

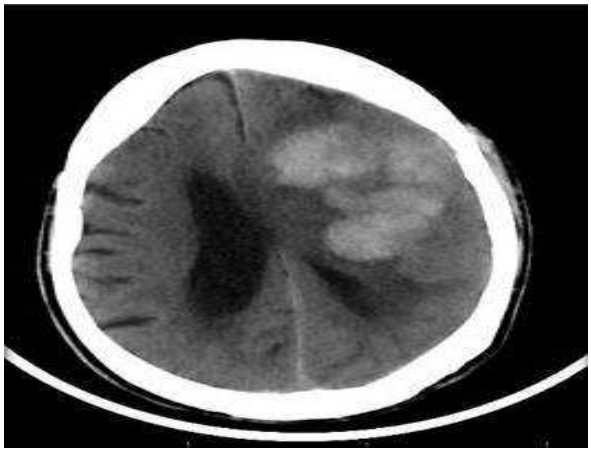


Figure - 2: Intra-operative squash cytology showing elongated plump cells.

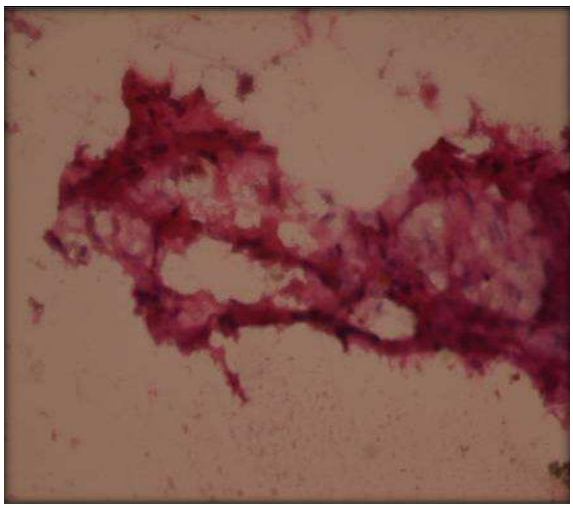


Figure - 3: Low power view of the glial tissue with meningeal lining.

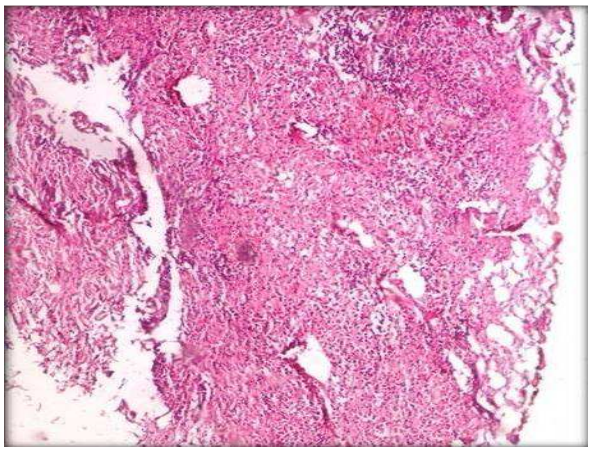


Figure - 4: Medium power view of the glial tissue with focal lymphoplasmacytic collections.

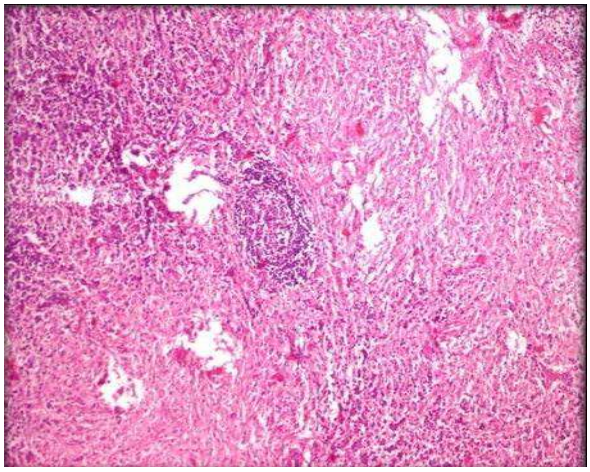


Figure - 5: High power view of the lymphoplasmacytic collections surrounded by glial tissue.

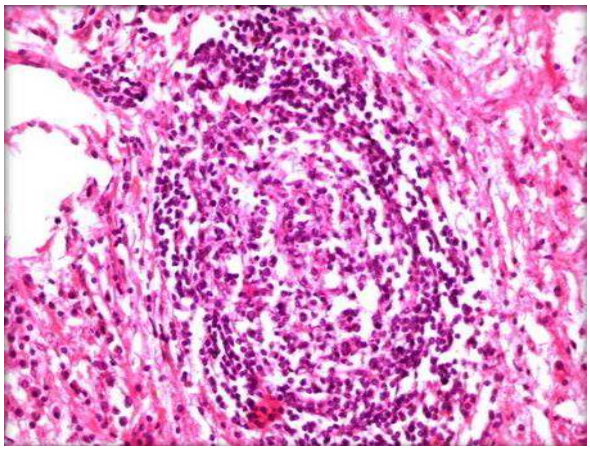


Figure - 6: Immunohistochemistry (IHC) marker Pan-Cytokeratin showing negativity.

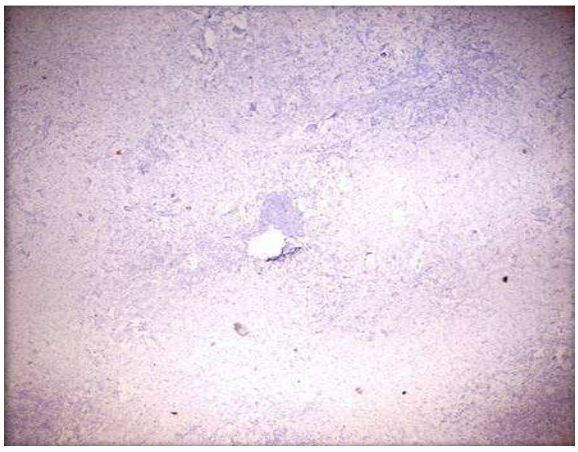


Figure - 7: Immunohistochemistry (IHC) marker Glial Fibrillary Acidic Protein (GFAP) showing positivity for glial tissue.

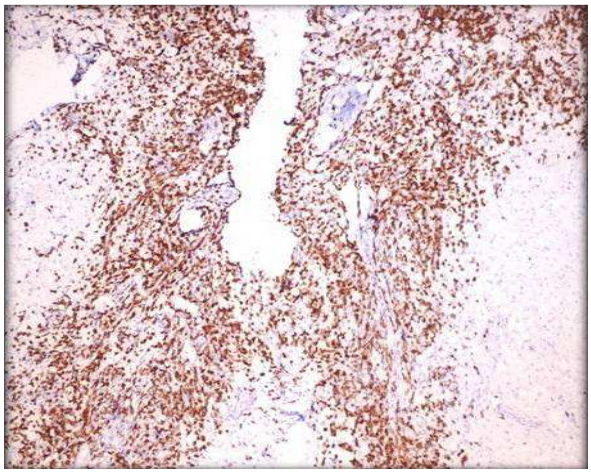
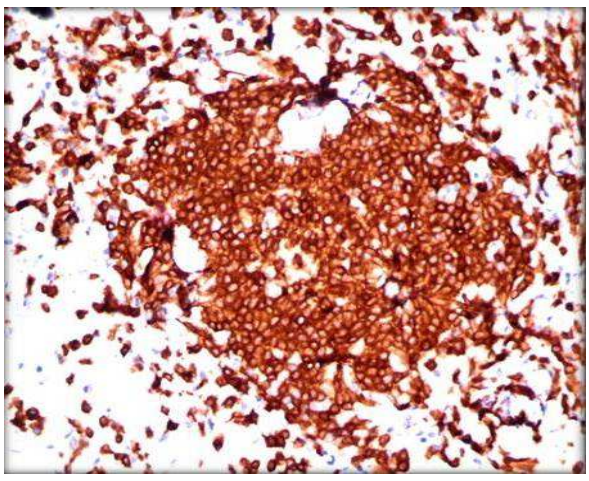


Figure - 8: Immunohistochemistry (IHC) marker CD 79 Alpha showing positivity for Plasma cells.



Discussion

Castleman's disease (CD) is a rare disease of lymph nodes and lymph related tissues. It was first described by Dr. Benjamin Castleman. According to Ken-ichi matsumura, et al. [1] there are only 13 cases of Castleman's disease involving the CNS were reported till 2005. The two main forms of CD are called localized or unicentric and multi-centric. Localized (unicentric) Castleman's disease is the more common type of CD and usually affects a single lymph node or one group of lymph nodes. Lymph nodes in the chest or abdomen are affected most often. People with localized CD are usually cured when the affected lymph nodes are removed with surgery. Multi-centric Castleman's disease (MCD) affects more than one group of lymph nodes and can also affect other organs containing lymphoid tissue such as spleen, thymus, tonsils and adenoids. This form sometimes occurs in people infected with human immunodeficiency virus (HIV). Multi-centric CD is more serious than the localized type, particularly in people with HIV infection. People with MCD often have problems such as serious infections, fevers, weight loss, fatigue, night sweats, and nerve damage that can cause weakness and numbness. Blood tests often show anemia and high levels of antibodies in the blood (hypergammaglobulinemia). Polyneuropathy, organomegaly, endocrinopathy, monoclonal gammopathy, and skin changes (POEMS) syndrome is a rare multi-systemic disease that commonly occur in the setting of MCD. Infections in people with MCD can be very serious, even life threatening. MCD also increases the risk of developing lymphoma, a cancer of lymphoid tissue, which can often hard to treat. There are four microscopic subtypes.

- The **hyaline vascular** type is most common. It tends to be localized, in which case people often have few symptoms and usually have a good outlook, but in rare cases it can be multi-centric.
- The **plasma cell** type is more likely to cause symptoms and to be multi-centric, but it is sometimes localized.
- The **mixed** subtype shows areas of both hyaline vascular and plasma cell types. It occurs less often.
- The **plasmablastic** type was recognized more recently. Like the plasma cell type, it is usually multi-centric, usually causes symptoms, and has a less favorable outlook.

The main pathogenesis of Castleman's disease (CD) is an overgrowth of immune B lymphocytes. Many people with CD have abnormally high blood levels of certain substances made by immune system cells. For example, in the multi-centric form of CD (MCD), the body often makes too much of a protein called interleukin-6 (IL-6). IL-6 normally helps regulate immune function. Increased secretion of IL-6 can cause lymphocytes to grow and divide too quickly. One cause seems to be infection with human herpesvirus-8 (HHV-8), also known as Kaposi sarcoma herpes virus (KSHV). HHV-8 is often found in the lymph node cells in people who have MCD, especially those who are HIV positive. People infected with HIV, however, often have weakened immune system, which allows HHV-8 to grow and cause disease. A large number of dendritic cells participate in inducing and regulating immune responses against pathogens and/or autoantigens in the duramater, leptomeninges and choroid plexus in the rat [2]. In addition, both myeloid and plasmacytoid dendritic cells were detected in the brain tissue of mice with infection and autoimmune encephalitis [3] and also in the cerebrospinal fluid of the humans with inflammatory disorders of the central nervous system [4]. The pathogenesis of peritumoral brain edema may involve impaired microcirculation and/or venous drainage of the surrounding brain due to mechanical compression, hydromechanical concepts of vasogenic edema based on the hydraulic pressure between the tumor and the underlying brain, and

secretion of fluid or chemical factor inducing brain edema from the tumor [5, 6]. Localized intracranial Castleman's Disease (CD) manifests as seizure or focal signs attributable to the involved area and appears as solid extra-axial mass with significant enhancement by contrast medium. These findings are similar to those of meningioma which can lead to misdiagnosis clinically and on squash cytology. In our case, the squash diagnosis was given as meningioma.

Treatment

For treating Castleman's disease (CD), treatment options available are as below.

- Surgery
- Radiation therapy
- Corticosteroid drugs
- Chemotherapy
- Immunotherapy
- Anti-viral drugs

Treatment depends on the whether the CD is localized (unicentric) or multi-centric, as well as other factors. No two patients are exactly alike, so treatment is tailored to each person's situation.

Conclusion

Castleman's disease is a rare entity in the central nervous system, but should be considered in the differential diagnoses of intracranial tumors and intracranial meningiomas. Prognosis of CD is better in unicentric Non-HIV cases and worse in multi-centric HIV positive patients.

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