Castleman’s Disease with Paraneoplastic Pemphigus

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Abstract
Castleman’s disease is a rare autoimmune disorder with varied clinical presentations. Castleman’s commonly involves mediastinum and hence it is thoracic in most of the reported cases. Paraneoplastic pemphigus (PNP) and myasthenia gravis can be associated with multicentric Castleman’s disease. Its association with HIV, Kaposi sarcoma, and lymphoma is also well known. We report a rare combination of unicentric, extrathoracic Castleman’s disease with PNP and myasthenia gravis.

Key Words: Autoimmune, Castleman’s disease, myasthenia gravis, pemphigus

Introduction
Castleman’s disease is a rare disorder which can mimic lymphoma. Its association with various autoimmune diseases is well known and hence presentation can vary. This case report is an attempt to create awareness among us not to neglect a common symptom like oral ulcers which are resistant to treatment.

Case Report
A 25-year-old lady with no significant medical history including allergic diseases such as bronchial asthma was admitted to a tertiary care hospital of South India because of recalcitrant erosive lesions on her oral mucosa and lip that had begun 3 months earlier. The patient was treated for Steven Johnson syndrome in a private hospital with steroids prior to the admission. On admission, there were extensive erosions in the oral mucosa and tongue with thick hemorrhagic crusts on the lip [Figure 1] and erosive lesions over labia majora. Cutaneous and conjunctival lesions were not evident at that point of time. Histological examination of a biopsy taken from a violaceous, indurated lesion of the lower lip showed a band-like infiltrate of lymphocytes and histiocytes throughout the papillary dermis, hydropic degeneration of basal keratinocytes, and necrotic keratinocytes within the hypertrophic epidermis. Skin biopsy was suggestive of interface dermatitis suggestive of pemphigus vulgaris [Figure 2]. Anti Nuclear Antibody was negative. HIV was non-reactive by ELISA. Biopsy from un-involved buccal mucosa for direct immunofluorescence was negative for antibodies. During hospital stay, she developed respiratory paralysis and thus need ventilator support. Electrolytes and thyroid profile were normal. Workup for respiratory weakness with limb weakness with preserved deep tendon reflexes was done with neostigmine test. Positive response to the test was suggestive of myasthenia gravis; hence, pyridostigmine and steroids were started with which she was off ventilator in next 48 hours. Ultrasound abdomen and subsequently computed tomography (CT) imaging of the abdomen done revealed a solid tumor of 8.5 × 4 × 5.5 cm of size in right paraspinal area near the hilum of right kidney [Figure 3]. Workup for pheochromocytoma prior to surgery was done which showed normal urinary metanephrins. Physical examination revealed slightly decreased breath sounds in both lungs with no crackles. Mild hyperinflation without infiltrates was visible on chest radiographs, but conventional CT of the chest showed no remarkable abnormalities. She underwent surgery for the retroperitoneal tumor and highly vascular tumor of 8 × 6 × 5 cm was removed without any intraoperative and post-operative complications. Histopathology revealed Castleman’s disease of hyaline vascular variety [Figures 4-6]. Skin lesions improved at the end of 2 weeks post-operatively [Figure 7] and she was discharged with an advise to taper her steroids and to continue pyridostigmine for myasthenia gravis.

Discussion
Castleman’s disease is a rare lymphoproliferative disorder. Three histopathological variants are Hyaline vascular variant, plasma cell variant, and mixed variants. Clinically, the disease can be localized or multicentric. Thoracic site is most common constituting 70% cases; among them around 80% is in mediastinum. Retroperitoneal, base of urinary bladder are the other sites which can be involved.[1,2]

Localized variant of Castleman’s disease does not usually present with systemic symptoms. The enlarged lymph node

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mass may be the only incidental finding in some cases. Myasthenia gravis is a rare but well-known association with Castleman’s disease. Other common associations are HIV, Kaposi sarcoma, Non-Hodgkin lymphoma, and polyneuropathy, organomegaly, endocrinopathy, monoclonal gammopathy, and skin changes syndrome.
paraneoplastic Pemphigus (PNP), an autoimmune syndrome that was first described by Anhalt et al. in 1990, are mostly associated with lymphoproliferative neoplasms, i.e., non-Hodgkin’s lymphoma, chronic lymphocytic leukemia, Castleman’s disease and, less commonly, thymoma and retroperitoneal sarcomas. Presence of intractable stomatitis and anti-plakin protein autoantibodies is a constant feature; however, there have been reports of antibody negative PNP in literature.[2‑4,5]

Progression of disease and death occurs frequently despite treatment of the associated neoplasm and regardless of therapeutic intervention for the autoimmune disease. Even after complete resection of Castleman’s disease, the autoimmunity remains active for up to 2 years. Any recurrence of oral lesions or rise in antibody levels would signal recurrence or new lesions of Castleman’s disease.[6] A study of 28 patients presenting with stomatitis with Lichenoid skin lesions who later on were found to have Castleman’s disease on follow-up showed fatality among 22 patients over a period of 2 years secondary to respiratory failure. Post-mortem revealed evidence of progressive bronchiolitis obliterans in those cases indicating progressive autoimmune damage to the lung. Autoimmunity has been attributed to the production of interleukin-6 (IL-6).[2] Treatment with anti-IL-6 has been shown to improve platelet counts among patients with autoimmune thrombocytopenia with Castleman’s disease;[6] however, there has been no study among patients with PNP.[7]

In our patient, diagnosis of myasthenia was made on the basis of neostigmine test where 0.04 mg/Kg is given intramuscularly or 0.02 mg/Kg intravenously (one time only) observing for clinical improvement of weakness. This test is an alternative for “Tensilon (Edrophonium) test.”[9] Our patient had a rare combination of PNP with extrathoracic Castleman’s disease with myasthenia gravis. Castleman’s disease being hyaline vascular variety presenting with systemic manifestation is also a rare presentation. On follow-up, patient had progressive breathlessness with severe obstructive lung disease on pulmonary function test. She developed progressive hypoxia and succumbed to ventricular arrhythmia at the end of 1 year.

**Conclusion**

Castleman’s disease, though described as benign entity, its varied presentation with myasthenia, PNP, and progressive lung damage resulting in bronchiolitis obliterans secondary to autoimmune injury makes it lethal. Unicentric hyaline vascular variety with systemic manifestations behaves similar to multicentric and hence is associated with bad prognosis as in our case. Any non-healing oral ulcers with or without skin lesions should alert the treating physician for extensive workup and to intervene at the right time.

**What is new?**

Presence of extrathoracic Castleman’s disease is rare. Presentation of unicentric hyaline vascular variant Castleman’s disease with systemic manifestations like paraneoplastic pemphigus (PNP) and myasthenia is uncommon.

**References**

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