Paraneoplastic pemphigus is a rare dermatologic condition that can occur as a paraneoplastic manifestation of lymphoproliferative disorders, visceral malignancies, Castleman disease and thymomas. In a pediatric age group paraneoplastic pemphigus has a striking association with Castleman disease and has a particularly poor prognosis in this age group. We describe a case of paraneoplastic pemphigus associated with retroperitoneal hyaline vascular variant of Castleman disease with a fatal outcome despite aggressive management.

**CASE REPORT**

A 16-year-old boy presented with one month history of low grade fever, cutaneous rash and painful oral ulcers. Examination revealed an ill-looking boy with lichenoid rash on the upper limbs and genitalia with multiple oral ulcers and hemorrhagic crusts on the lips Figure 1. His lab examination was unremarkable. The patient was thought to have ulcerative lichen planus and was treated with systemic and local steroids, and antibiotics without any definite improvement. The histopathological examination of skin biopsy was suggestive of lichenoid dermatitis with acantholysis. Abdominal ultrasound revealed moderate splenomegaly and a well-circumscribed hypoechoic mass in relation to the right iliac vessels. Color Doppler showed a large vessel entering from the hilum of the lesion with intense vascularity within the mass. CECT of abdomen revealed a well-circumscribed intensely enhancing retroperitoneal mass displacing the iliac vessels (Figures 2 and 3). There was no evidence of lymphadenopathy elsewhere. In view of the clinical picture of ulcerative oral mucosal lesions and lichenoid rash, a diagnosis of Castleman disease with paraneoplastic autoimmune multiorgan syndrome (paraneoplastic pemphigus) was strongly considered. Exploratory laparotomy was performed and the retroperitoneal mass was excised. Histopathological findings were consistent with the diagnosis of hyaline vascular variant of Castleman disease (Figures 4 and 5). The patient developed severe respiratory distress due to tracheobronchial involvement and died on the 4th post operative day.
DISCUSSION

Paraneoplastic autoimmune multiorgan syndrome (or paraneoplastic pemphigus) is an autoimmune disease with mucocutaneous manifestations, and is associated with different tumors (lymphoproliferative disorders such as non-Hodgkin’s lymphoma, chronic lymphocytic leukemia, visceral malignancies, Castleman disease, thymomas, Waldenström’s macroglobulinemia and thymoma, among others). Mucocutaneous manifestations include lichenoid rash on body and genitalia, genital erosions, ulcerative gingivitis/stomatitis, hemorrhagic crusting of lips, scarring conjunctivitis, desquamative esophagitis and ulcerative tracheobronchitis. The cutaneous manifestations may mimic pemphigus vulgaris/vegetans, bullous pemphigoid, Stevens-Johnson syndrome and lichen planus pemphigoides. Paraneoplastic autoimmune multiorgan syndrome is rarely encountered in children and has a particularly adverse prognosis in this age group. In one series of 14 children, paraneoplastic pemphigus was associated with Castleman disease in 12 patients, and had a fatal outcome in 10 children. IgG antibodies against plakins were seen in all cases; antiplectin antibodies were seen in 90% of cases.

Castleman disease is a rare, non neoplastic lymphoproliferative disorder that can occur in neck, mediastinum, abdomen and pelvis. It is classified into three histologic subtypes: hyaline vascular, plasma cell and mixed. Castleman disease is also classified into two clinical types: multifocal (multicentric) or localized (unicentric). The unicentric Castleman disease corresponds to the hyaline vascular variant (>90%), and the multicentric disease corresponds to the plasma cell variant. The radiological hallmark of hyaline vascular type of Castleman disease is an intensely enhancing solitary enlarged lymph node or nodal mass. Three radiological patterns of Castleman disease are seen: solitary non invasive mass (50%), dominant infiltrative mass with associated lymphadenopathy (40%), and matted lymphadenopathy without a dominant mass (10%). Prominent feeding vessels may be observed in the vicinity of the nodal mass. The radiological differential diagnosis to be considered in case of a retroperitoneal intensely enhancing solitary mass is in the present case include paraganglioma, hemangiopericytoma, schwannoma, solitary fibrous tumor and lymphoma. Sarcoma, leiomyoma and gastrointestinal stromal tumor should also be considered. The histologic features include hyaline vascular lymph follicles with expanded mantle zones containing small lymphocytes in concentric rings (onion skin appearance), interfollicular capillary proliferation with perivascular hyalinisation, and a single penetrating vessel in the center of the follicle.

Figure 1. Clinical Photograph of the patient showing an ill-looking boy with evidence of hemorrhagic crusts on lips and rash on face.

Figure 2. Axial CT of Pelvis shows a well circumscribed intensely enhancing retroperitoneal mass posterior to the right iliac vessels.
Castleman disease has also been associated with many autoimmune diseases (peripheral neuropathy, cytopenias, SLE, Sjogren's syndrome and myasthenia gravis), and there are many reports of its association with paraneoplastic pemphigus and ulcerative lichen planus.8–11 The present case is unusual in being a case of hyaline vascular type with aggressive systemic features and, unfortunately, a fatal outcome. The treatment of Castleman disease with paraneoplastic pemphigus and ulcerative lichen planus.

Figure 3. Serial contrast enhanced CT images of pelvis reveal avidly enhancing retroperitoneal mass displacing the right iliac vessels anteromedially.

Figure 4. Microscopic picture of resected retroperitoneal mass shows lymphoid tissue with interspersed vessels having hyalinised walls.

Figure 5. Histopathology of the excised mass shows a central hyalinised vessel with surrounding lymphoid cells.

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pemphigus consists of surgical excision of the mass and immunosuppressive therapy. High doses of steroids, plasmapheresis, intravenous immunoglobulin and radiation have also been used. Other drugs used include anti IL-6 receptor therapy (tocilizumab, siltuximab), and CD-20 antibody (rituximab). The prognosis remains particularly dismal in the pediatric age group, the most common cause of death being airway and pulmonary involvement, as in the present case.\(^1,3,4,7\)

CONFLICT OF INTEREST

None declared.

REFERENCES