

Multiple capillary hemangiomas: A distinctive lesion of multicentric Castleman's disease and POEMS syndrome

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ABSTRACT

A diagnosed case of Castleman's disease, proven by biopsy from enlarged inguinal lymph nodes, presented with multiple, asymptomatic, erythematous papules and nodules prevalent since nine years over the trunk and extremities. The lesions had been gradually increasing in number and size. The patient had had plasmacytoma of the lower thoracic vertebra 12 years ago, for which he was adequately treated with chemotherapy and local radiotherapy. Dermatological examination revealed erythematous papules and nodules on the face, trunk, and extremities that were diagnostic of capillary hemangiomas. Histopathology of the erythematous, soft papule was suggestive of capillary hemangioma. Contrast-enhanced computerized tomography of the abdomen and pelvis showed multiple retroperitoneal nodes suggestive of Castleman's disease along with multiple osteolytic lesions in the pelvic girdle and vertebrae. The patient was treated with injection rituximab and is currently under follow-up. We report this case to highlight a rare association between Castleman's disease and POEMS syndrome.

Key Words: Capillary hemangiomas, Castleman's disease, POEMS syndrome, Vascular endothelial growth factor

INTRODUCTION

Castleman's disease is a benign, atypical, lymphoproliferative disorder that is often associated with POEMS (polyneuropathy, organomegaly, endocrinopathy, M-protein/monoclonal gammopathy and skin changes) syndrome. Recent data suggest a common etiopathogenesis of human herpes virus-8 infection, interleukin-6 (IL-6), and vascular endothelial growth factor (VEGF) linking Castleman's disease and POEMS syndrome.^[1,2] We report here a distinctive case of multiple capillary hemangiomas in a case of Castleman's disease associated with some features of POEMS syndrome.

CASE REPORT

A 55-year-old male patient diagnosed with Castleman's disease in 2006 at a cancer institute, was referred for multiple, asymptomatic, red, raised, polypoid lesions

prevalent since nine years, all over the body. The onset of complaints started with an increase in the size of a similar lesion present since childhood on the forehead. This was followed by appearance of new lesions all over the body which gradually increased in number and size.

The patient noticed an asymptomatic swelling over the left inguinal region five years ago, which gradually increased in size along with distension of the abdomen, but the patient did not seek any medical advice for this. He was recently diagnosed with Castleman's disease based on a biopsy of the inguinal swelling. On inquiry, the patient revealed that he had plasmacytoma of the lower thoracic vertebra 12 years ago for which he was adequately treated with chemotherapy and local radiotherapy.

General examination was normal but the per abdomen examination detected an ill defined mass occupying the left

How to cite this article: Misri R, Kharkar V, Dandale A, Patel V, Mahajan S, Khopkar U. Multiple capillary hemangiomas: A Distinctive lesion of Multicentric Castleman's Disease and POEMS Syndrome. *Indian J Dermatol Venereol Leprol* 2008;74:364-6.

Received: July, 2007. **Accepted:** November, 2007. **Source of Support:** Nil. **Conflict of Interest:** None Declared.

iliac fossa and infraumbilical area along with left inguinal lymphadenopathy. Dermatological examination revealed erythematous and skin colored papules and nodules on the face, trunk, and extremities, 0.2 - 4 cm in size, round to oval in shape with a lobulated surface [Figures 1 and 2]. Lesions were nontender, soft, non compressible, with a smooth surface and a few lesions showed a very interesting pattern of fine, arborizing, erythematous flare in the surrounding area [Figure 3]. There was no associated bruit.

Based on the above findings, a diagnosis of multiple capillary hemangiomas in a case of Castleman's disease was made. Investigations revealed anemia (hemoglobin 9.3 mg%) but leukocyte counts were normal. Blood urea nitrogen (54 mg%) and serum creatinine levels (1.5 mg%) were raised but blood sugar levels were normal. Liver function tests showed raised serum proteins (8.8 gm%) with normal albumin and raised globulin (5 gm%). Alkaline phosphatase was raised (135 IU) with transaminases and bilirubin being within normal limits. A normal bone marrow aspiration ruled out



Figure 1: Erythematous papules and nodules on the trunk



Figure 2: Erythematous papules and nodules on the face

the possibility of recurrence of the plasmacytoma.

X-ray of the chest was within normal limits but contrast enhanced computerized tomography of the abdomen and pelvis showed multiple retroperitoneal nodes suggestive of Castleman's disease along with multiple osteolytic lesions in the pelvic girdle and vertebrae. However, there was no organomegaly or free fluid in abdomen. Histopathology of two erythematous, soft papulo-nodular lesions was suggestive of capillary hemangiomas.

The patient was started on an eight-dose course of injection rituximab (375 mg/m²) intravenously weekly for Castleman's disease. He tolerated the medication well and the follow up CT scans demonstrated decrease in size of lymph nodes and no new lesion appeared during the follow up. Due to the patient's discomfort and to enhance the cosmetic appearance, radiofrequency ablation was done for the cutaneous capillary hemangiomas affecting the face and other exposed areas. Three months later, the hemangiomas were found to be persistent with no decrease in the size of the lesions. There was however, no recurrence of lesions at the site of the ablated lesions.

DISCUSSION

Castleman's disease [CD] also known as giant lymph node hyperplasia or angiofollicular lymphoid hyperplasia, was first described by Benjamin Castleman in 1956.^[3] There are two forms of CD: the solitary type and the multicentric type. The multicentric type presents with fever, anemia, weight loss, night sweats, generalized lymphadenopathy, organomegaly, CNS dysfunction, renal disease, raised ESR, thrombocytopenia, raised globulins and decreased



Figure 3: Fine arborizing erythematous flare surrounding few lesions

albumin. Of these symptoms, our case had anemia, lymphadenopathy, raised globulins and renal disease. Prognosis of CD is poor with a five year mortality of 18%. Histologically, there are two variants of CD: i) the hyaline vascular type which is the most common (90%) and is often associated with the solitary type, and ii) the plasma cell variant (10%) nearly always associated with the multicentric type, as was the case in our patient. Treatment of CD consists of chemotherapy with intravenous immunoglobulin, thalidomide, antiIL-6 therapies, rituximab and autologous stem cell transplantation. CD, especially of the multicentric type, has been associated with POEMS syndrome (11-30%), paraneoplastic pemphigus (16%), nonHodgkin's lymphoma, HIV infection, and follicular sarcoma.

The acronym, "POEMS" syndrome (or Crow Fukase syndrome) stands for Polyneuropathy, Organomegaly, Endocrinopathy, M Protein/Monoclonal gammopathy and Skin changes such as hyperpigmentation, hypertrichosis, thickening of skin, hyperhidrosis, acrocyanosis, and hemangiomas: capillary and glomeruloid. Sometimes glomeruloid hemangiomas are seen on microscopic examination. Glomeruloid hemangiomas, a term coined by Chan *et al*, are superficial dermal dilated vascular spaces filled with aggregates of capillaries. At low power these structures resemble glomeruli and hence the name.^[1] According to some authors,^[4] patients with POEMS syndrome should have ≥ 3 of the above five features, while others such as Angela *et al* have proposed that the presence of two major criteria and one minor criterion is sufficient for its diagnosis.^[5] The criteria for diagnosis are as follows: i) the first major criterion is polyneuropathy, which is usually symmetrical. It involves both motor and sensory nerves, begins distally, and has a progressive proximal spread. Associated cranial or autonomic nerves are not involved. Both demyelination and axonal degeneration are noted. ii) The second major criterion is a monoclonal plasma cell proliferative disorder such as osteosclerotic myeloma, monoclonal gammopathy of unknown significance, and Waldenström macroglobulinemia, but not with classic multiple myeloma. iii) Minor criteria are sclerotic bone lesions (sometimes osteolytic lesions), CD, organomegaly, peripheral edema, endocrinopathy, skin changes, papilledema, ascites, effusions, polycythemia, fatigue and clubbing. However, this approach may be inadequate and atypical presentations of POEMS may be misdiagnosed.^[6] Our patient presented with one major criterion of having a plasma cell proliferative disorder-plasmacytoma^[7] and three minor criteria such as CD, multiple capillary hemangiomas, and osteolytic bone lesions. There is no particular order and duration for the appearance of the lesions; it may take months or years. However, early diagnosis is important to reduce morbidity.^[5]

CD is rarely associated with multiple capillary hemangiomas and POEMS syndrome. Our case presented with CD, multiple capillary hemangiomas, and features suggestive of POEMS syndrome. To date, five cases have been reported of this interesting association supporting the suggestion that hemangiomas develop in response to angiogenic stimuli.^[1,2,8] In one of the cases, the hemangiomas regressed after chemotherapy^[2] whereas the lesions have persisted even after chemotherapy in our case. The hemangiomas in both CD and POEMS syndrome develop in response to angiogenic stimuli such as VEGF^[1,8] which induces a rapid and reversible increase in vascular permeability or due to some role of the M protein via unknown mechanisms. The exact frequency of hemangiomas in patients with POEMS syndrome is difficult to judge from literature as descriptions are meager.^[4,9] Vascular lesions may appear before the full-blown POEMS syndrome develops; hence, careful evaluation and follow-up of all patients presenting with capillary hemangiomas or glomeruloid hemangiomas^[1] is strongly advocated to reduce the associated morbidity.

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