Skeletal angiomatosis in association with gastro-intestinal angiodysplasia and paraproteinemia: A case report

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ABSTRACT

Skeletal-extraskeletal angiomatosis is defined as a benign vascular proliferation involving the medullary cavity of bone and at least one other type of tissue. It has also been known as cystic angiomatosis in which multiple cystic lesions are scattered diffusely throughout the skeleton often with similar angiomatous changes in other tissues, usually the spleen.

A case of skeletal angiomatosis in association with gastro-intestinal angiodysplasia and paraproteinemia is reported.

Keywords: skeletal angiomatosis, paraproteinemia, bone tumour

CASE REPORT

A 67-year-old man presented to the Emergency Department in 1997 with cellulitis affecting his left leg. Examination of the legs demonstrated non-pitting edema of the ankles and legs and erythema consistent with cellulitis. Laboratory investigation at that time confirmed hypoalbuminemia, hyperglobulinemia, anemia, thrombocytopenia and neutropenia. A plain radiograph of the leg demonstrated cystic angiomatosis of the tibia and fibula (Fig. 1a and 1b). Serum protein electrophoresis verified a monoclonal band of IgG and a paraprotein of 20g/l. A bone marrow biopsy demonstrated mild myeloid hypoplasia, consistent with a pre-lymphoma condition. Investigation of the tibial and fibular lesions was undertaken with Technetium 99m MDP whole body bone scan, gallium scan and MRI. The MRI showed involvement of most of the bones of the leg and tarsus with the disease process (Fig. 2). A CT scan of the chest revealed multiple pleural nodules. CT scan of the abdomen revealed multiple, enlarged para-aortic lymph nodes in addition to splenomegaly. An open biopsy of the tibia was subsequently performed and the initial diagnosis of hemangioendothelioma was made (Fig. 3 & 4). The patient was treated with radiation therapy. This consisted of a two phase approach. The first phase involved 40 Gy in 20 fractions at 2 Gy per fraction prescribed to the isocenter using lateral opposed fields and megavoltage photons. The
Figure 1  (a) Anteroposterior radiograph of the tibia and fibula with the characteristic ‘swiss cheese’ appearance of the affected bones. (b) Lateral radiograph of the tibia and fibula with the characteristic ‘swiss cheese’ appearance of the affected bones.

Figure 2  A T2 weighted magnetic resonance image of the leg demonstrating angiomatosis affecting the tibia, fibula, talus and calcaneum.
second phase consisted of a further 20 Gy in 10 fractions to reduced fields. This produced repeated episodes of skin ulceration in the irradiated field. The pathologic specimen was subsequently re-examined and cystic angiomatosis confirmed as the diagnosis.

The neutropenia was treated by repeated infusions of Granulocyte-Colony Stimulating Factor. Investigation of his anemia with endoscopy and colonoscopy identified angiodysplasia in the duodenum which was managed with argon beam coagulation.

At the most recent review in December 2000, the bone disease was unchanged and the marrow disease had developed into low grade B cell non-Hodgkin’s lymphoma.

Figure 3  Low power view of the biopsy was taken from the tibial lesion. Multiple vascular channels are seen of varying sizes, lined by a thin layer of endothelium.

Figure 4  High power view of the tibial lesion demonstrates vascular channels varying in size from large to capillary size. The lining endothelium is one layer thick and shows little cytologic atypia. The background is of a loose fibrillary nature.

DISCUSSION

Cystic angiomatosis is frequently associated with similar angiomatous changes in the viscera and soft tissues, although there have been recommendations to separate those cases of bone with co-existent soft tissue lesions into a separate category of skeletal-extraskeletal angiomatosis. This is the first case of the triad of cystic angiomatosis of bone, angiomatosis of the viscera and paraproteinemia reported. Cutaneous angiomatosis, however, in association with monoclonal gammopathy has been previously reported.

Cystic angiomatosis of the skeleton is usually manifested by the age of puberty and the usual range
extends to the third decade in the reported series.\textsuperscript{1,2,5} In contrast, Devaney et al.\textsuperscript{3} reported 3 of their 14 cases in patients over the age of 50. The patient in this case report increases the series of patients who develop this condition outside the usual range. This suggests that the condition of cystic angiomatosis has two age peaks. This may indicate that this condition has two etiologies, a congenital and an acquired.

Devaney et al.\textsuperscript{3} reported three cases of angiomatosis in patients above the age of 60 years. In one of these, malignant lymphoma developed. Unfortunately, laboratory investigations were not reported for this or any of the older patients. It is conceivable that immunoglobulin deposits may have an etiologic role in the development of the bony changes in this older age group, therefore an acquired condition.

Boyle\textsuperscript{1} hypothesized that cystic angiomatosis developed either as a metastasising angioma or a vascular hamartoma, a congenital malformation of multicentric origin. Angiomatosis of skin has been reported in association with intravascular immunoglobulin deposits from a monoclonal gammopathy and it has been suggested that the immunoglobulin deposits produced vascular injury leading to the angiomatosis.\textsuperscript{6} The mechanism of this injury is presumed to be by activation of the complement cascade by the immune complex. Complement activation results in chemotaxis of polymorphs producing cell death through the extracellular release of lysosomal enzymes. In addition, complement complexes bind to cellular membranes to produce loss of membrane integrity resulting in osmotic lysis. It also recruits macrophages to phagocytose the debris. In addition, histamine and leukotriene B4 are released which are potent vasodilators and also enhance vascular permeability.\textsuperscript{7} The combination of cell death, macrophage invasion and enhanced vascular flow may be pathogenic in this condition. IgG and IgM are the only immunoglobulins that are capable of activating complement. This patient’s gammopathy was IgG class.

Treatment of the skeletal disease has been conservative, involving radiation treatment, and has been unsuccessful as has been previously reported.\textsuperscript{1,8} Angiomatosis shows no tendency toward malignant degeneration\textsuperscript{1} but it has been reported that malignant de-differentiation may occur following radiation treatment for this condition.\textsuperscript{4} There have been no signs of malignant degeneration of the bone disease in the four years of review of this patient.

The differential for this condition includes Gorham’s disease (disappearing bone disease) and lymphangiomatosis. Gorham’s disease produces resorption of most or all of a bone associated with a proliferation of vascular channels. Histologically it may be identical to cystic angiomatosis and differentiation is made on the basis that Gorham’s disease produces significantly more destruction with osteolysis and tends to involve one bone only. Lymphangiomatosis is usually found in association with polyostotic angiomatosis and must be differentiated on the basis of histological confirmation of thin walled, widely dilated irregular spaces lined by flattened endothelium, lumina containing proteinaceous fluid and lymphoid aggregates in the stroma.

REFERENCES