CYSTIC ANGIOMATOSIS (HAMARTOUS HAEMOLYMPHANGIOMATOSIS) OF BONE

A CLINICOPATHOLOGICAL STUDY OF THREE CASES

FRITZ SCHAJOWICZ, C. L. AIELLO, M. V. FRANCONI, R. E. GIANNINI

From the Latin-American Registry of Bone Pathology and the Hospital Alvarez, Buenos Aires

The clinical and radiological features in three cases of cystic angiomas of bone are reported. Although these features are generally diagnostic except from histiocytosis X, the definitive diagnosis must be established by a pathological study, preferably of a segment of an involved rib or fibula. The prognosis varies according to the type of clinical presentation—in particular upon whether the lesions are solely skeletal or whether there is extraskelatal visceral involvement. Whereas these last cases may often prove fatal, those with only skeletal involvement have a favourable prognosis: indeed, the cystic bone lesions may regress without any treatment, as occurred in some cases reported in the literature and in two of our three cases.

The name "cystic angiomas" is applied to a rare multicentric, most probably congenital (hamartous) lesion, scattered diffusely throughout the skeleton and often accompanied by angiomatic lesions in other tissues especially the spleen. "Cystic angiomas" is preferable to "diffuse haemangiomas" or lymphangiomas, because the pathological changes may be caused by proliferation of blood vessels, lymphatics, or both. Although the clinical and radiological features are generally characteristic, the process is often mistaken for other cystic lesions of the skeleton, especially histiocytosis X (multiple histiocytic granuloma with or without Hand-Schüller-Christian syndrome) as happened in our cases. Only a wide open biopsy, preferably the partial excision of an affected rib (performed in two of our cases) or fibula (in the third case) establishes the correct diagnosis.

It is important to emphasise that a wide range of affections exists, varying from a relatively mild form in which the changes are limited to the skeleton, with the possibility of a spontaneous regression, to a very severe form with extensive involvement of extraskelatal tissues, leading at times to early death.

Only a small number of well-documented cases have been reported, and in even fewer has the long-term evolution been described or spontaneous regression reported (Spjut and Lindbom 1962; Boyle 1972).

We have had the opportunity to study three cases of this rare entity. There was spontaneous regression of

the lytic skeletal lesions in two, which have been followed for seven and two years.

CASE REPORTS

Case 1. A girl aged fifteen years was admitted in June 1967 for a slowly growing soft tissue swelling in the neck. She was in good general health, and there was no evident abnormality other than the swelling, about two centimetres in diameter, at the right side of the neck. The swelling was soft and not painful.

A skeletal survey revealed widespread cystic lesions in the skull, ribs, pelvis, femur, tibia, fibula, radius, ulna and humerus (Figs. 1, 3, 5 and 7). Blood tests were normal. A diagnosis of histiocytosis X was considered, but a needle biopsy of the upper end of the femur was inconclusive. The cervical tumour was excised, and histological examination suggested that it was a cystic lymphangioma.

A further open biopsy of a tibial lesion was carried out; histologically the medullary cavity was occupied in part by fibrous marrow, showing an evident increase of blood vessels—predominantly veins—with thickened walls, but a definite diagnosis was not made (Fig. 8). For this reason a segmental resection of a seventh rib, including an osteolytic lesion, was performed.

The gross specimen was a rib segment 23 millimetres long, with a slightly expanded cortex, partly destroyed at its inner surface; a longitudinal section showed several cystic cavities filled with blood (Figs. 9 to 11). Histologically many dilated vascular spaces lined by a flattened endothelial layer were observed, separated by thin bone trabeculae. To a large extent these cavernous vessels were filled with red blood cells, but parts were empty and the possibility of their being lymph vessels could not be excluded.

The patient was observed for more than seven years, no treatment being given. Radiographs from November 1974 onwards showed evident regression of the lytic bone lesions (Figs. 2, 4 and 6). Her general health was excellent, and no enlargement of the liver or spleen was observed.

Professor Dr Fritz Schajowicz, Rush-Presbyterian—St Lukes Medical Center, 1753 West Congress Parkway, Chicago 60612, United States of America.

C. L. Aiello, M.D., Hospital Durand, Buenos Aires, Argentina.

M. V. Franconi, M.D. } Hospital Alvarez, Buenos Aires, Argentina.
R. E. Giannini, M.D. }

Requests for reprints should be sent to Professor F. Schajowicz.

Fig. 1

Fig. 2

Case 1. Figure 1—Radiograph of the skull showing multiple cystic lesions of various sizes. Figure 2—Seven years later, the cystic areas have almost completely disappeared without any treatment.

Fig. 3

Fig. 4

Case 1. Figure 3—Radiograph showing multiple cystic lesions in several ribs, some of them slightly expanded. Figure 4—Seven years later there has been spontaneous regression of the lesions.

Fig. 5

Fig. 6

Case 1. Figure 5—Initial radiograph showing numerous cystic lesions in the pelvis, femoral head and uppermost third of the femur. Figure 6—Seven years later there has been considerable spontaneous regression with reduction or disappearance of almost all the cysts.

Fig. 7

Case 1. Initial radiograph showing the osteolytic lesions in both tibiae. Aspiration biopsy and later open biopsy failed to permit a conclusive diagnosis.

Fig. 8

Case 1. Photomicrograph of a tibial biopsy specimen showing fibrous marrow containing several large venous vessels (↑); a, bone trabecula. With this pattern no definite diagnosis was made. (Haematoxylin and eosin, $\times 70$.)

Fig. 9

Case 1. Topographic photomicrograph of the rib specimen showing multiple cystic spaces, partly empty or containing red blood cells, separated by cancellous bone trabeculae. (Haematoxylin and eosin, $\times 14$.)

Fig. 9

Fig. 10

Case 1. Photograph and radiographs of a longitudinal section of the resected rib segment, showing multiple confluent cystic lesions, in great part filled with blood.

Fig. 11

Case 1. Photomicrographs at higher magnification showing cancellous bone trabeculae (*a, a'*) separated by large vascular lacunae with a flattened endothelial layer, partly empty (*b*) or packed with red blood cells (*c*). (Haematoxylin and eosin, $\times 75$.)

Case 2. A girl aged eight years was admitted with intermittent claudication for three years, and diffuse pain in the right lower limb for the last three months. Examination and blood tests were negative. No splenomegaly or hepatomegaly was observed. A radiographic survey showed multiple, well-defined cystic lesions in skull, ribs, femur, tibia and fibula (Figs. 12 to 14). A piece of the right fibula including an osteolytic lesion was excised for examination. The cortex was slightly distended and thinned, the medullary cavity being occupied by multiple cystic spaces, in part containing blood, in part empty, and separated by thin fibrous septae (Figs. 15 to 17). A histological diagnosis of "cystic angiomatosis" was made, possibly of a mixed type: haemolymphangiomatosis. No other treatment was indicated. This patient was lost to follow-up.

Fig. 12

Case 2. Radiograph of the skull showing multiple cystic lesions.

Fig. 13

Case 2.

Figure 13—Radiograph of the thorax showing cystic lesions in several ribs.

Figure 14—Anteroposterior radiographs showing scattered cystic lesions in both tibiae and fibulae. The affected uppermost third of the right fibula was resected for histological study.

Fig. 14

Fig. 15

Fig. 16

Fig. 17

Case 2. Photomicrographs of the fibular biopsy specimen. Figure 15—Low magnification shows the thinned bone cortex (a) with dilated Haversian spaces, occupied by capillary blood vessels, and a large cavernous space (b) only partially occupied by red blood cells. (Haematoxylin and eosin, $\times 70$.) Figure 16—A large vascular lacuna and several congestive capillary vessels. (Haematoxylin and eosin, $\times 100$.) Figure 17—An intracortical cavernous blood vessel surrounded by a flattened layer of endothelium. (Haematoxylin and eosin, $\times 100$.)

Fig. 18

Fig. 19

Case 3. Figure 18—Radiograph taken during an acute abdominal process, showing widespread cystic lesions in the uppermost thirds of both femora, in the pelvis and in several ribs. Two aspiration biopsies of the upper femur and pelvis were negative. Figure 19—Two years later, there has been evident regression of the lesions, without any treatment.

Case 3. A boy aged seven years was admitted for appendectomy. Radiographs showed multiple cystic lesions in the pelvis, both femora and several ribs (Fig. 18); the skull was not affected. A diagnosis of histiocytosis X (Hand-Schüller-Christian syndrome) or polyostotic fibrous dysplasia was made.

A needle biopsy of the right upper femur was negative. A segment of an affected rib was therefore resected for histological examination, showing on longitudinal section several cystic cavities separated by thin fibrous or bony septae.

Fig. 20

Photomicrographs showing, at lower ($\times 100$) and higher ($\times 180$) magnification, large vascular lacunae (a, a') occupying the medullary cavity, surrounded by mature bone trabeculae (b, b'): the lacunae are partly filled with an amorphous material and covered by a thin endothelial wall. (Haematoxylin and eosin.)

The histological study showed cystic spaces of different size, in part empty or containing serofibrinous material, covered by a thin endothelial wall and separated by fibrous septa or bone trabeculae. The microscopic features were compatible with the diagnosis of lymphangioma of bone (Fig. 20).

The patient remained under observation without any treatment. Two years later he showed an evident radiographic regression of the lesions, and was free of symptoms (Fig. 19).

CLINICAL FEATURES

The age of our patients ranged from seven to eleven years, with an average of eight and a half. Two were girls and one was a boy. Boyle (1972) found a male to female preponderance of two to one among cases reported in the English literature.

None of the patients had splenomegaly or hepatomegaly, and only one patient presented with a cystic lymphangioma of the cervical region. The skeletal lesions were widespread, with involvement of both femora, the pelvis and the ribs in all cases and of the skull in two cases. Other cystic lesions occurred in the humerus, scapula, tibia and fibula, but no bone lesions were found in the hands or the feet. The two patients who were seen over periods of two years and more than seven years showed evident spontaneous regression of the bone lesions and were free of symptoms.

RADIOLOGICAL FEATURES

The radiographic appearance of the bone lesions was characteristic, with multiple roundish or ovoid cystic areas of different sizes and with sharply defined margins, often with slightly sclerotic borders or else confluent,

giving a honeycomb aspect, especially in the pelvis. The cortex of a rib or fibula was expanded or thinned, but there was no periosteal reaction.

PATHOLOGICAL FEATURES

Macroscopic appearance. In our three cases the definitive pathological diagnosis was made from segments of a resected rib lesion in two cases and from a resected fibular lesion in the third case. The bone cortex was slightly expanded and thinned, giving the surface a reddish blue colour. In the longitudinal sections small cavities of different size and shape, separated by thin fibrous or bony septa, were observed. Most of the cavities were filled with blood in the two rib sections, but the cavity was almost empty in the fibular segment.

Microscopic appearance. In our three cases the cystic cavities corresponded to dilated, cavernous capillaries, surrounded by a single layer of flattened endothelial cells. In the rib sections most of the capillaries were filled with red blood cells and what seemed to be blood vessels; but others were empty or filled with a serous material—these could have been lymphatics. Most of the cavernous capillaries in the fibular biopsy were empty and were probably lymph vessels. On the other hand, in Case 1 the histological study of a tumour of the cervical region showed it to be a cystic lymphangioma. In this same case a biopsy of a tibial lesion which on first examination was not conclusive, showed in a second study an evident proliferation of enlarged venous vessels (Fig. 8).

DISCUSSION

Cystic angiomatosis of bone is a rare but pathologically distinct entity, characterised by disseminated osteolytic lesions, often with involvement of soft tissues, especially the spleen. The process is more frequent in infants or young children during the first decade of life, and tends to involve ribs, pelvis, femora and skull, but only exceptionally the hands and feet. The characteristic radiological features, together with the clinical appearance, makes it possible to separate this entity from fibrous dysplasia and from hyperparathyroidism. Distinction from histiocytosis X (multiple or disseminated histiocytic granuloma with or without Hand-Schüller-Christian or Letterer-Siwe syndrome) is difficult. In fact in all of our three cases the presumptive diagnosis was histiocytosis X. In spite of some radiographic differences, such as the lack of periosteal reaction in the long limb bone lesions (a frequent finding in histiocytosis X), the diagnosis must always be confirmed by histological examination of a segment of affected bone, a rib or fibula being the most convenient for this purpose. With a puncture or a simple surgical biopsy a definite diagnosis could not be made in the great majority of the reported cases. It is important to establish whether the

lesions involve only the skeleton, as in two of our cases, or if there also exists involvement of soft tissues, especially viscera; in the reported cases the spleen has been most often affected. Contrary to the often fatal evolution of these lesions, the prognosis is more favourable when the skeleton alone is affected or when there is only an associated subcutaneous soft tissue tumour (lymphangioma or haemangioma). In these cases spontaneous regression of the cystic bone lesion may occur, as happened in some reported cases and in two of our patients. For this reason it is important to be familiar with the clinical, radiological and pathological features of "cystic angiomatosis" in order to avoid any unnecessary treatment. Splenectomy is, however, of value if the spleen alone among the viscera is affected.

The term "cystic angiomatosis of bone" is preferred by most authors because in some cases a lymphangioma of the subcutaneous tissue and a haemangioma of the rib and tibia may coexist (Case 1), or because blood and lymphatics may be seen in the same lesion (Case 2). The pathogenesis of this entity is still under discussion; we believe that the hypothesis of a multicentric congenital malformation—that is a vascular hamartoma—is the most acceptable.

We wish to express our appreciation to Dr G. Cohen, Dr A. Martinez and Dr F. Silberman, who have allowed us to use their cases.

REFERENCES

- Boyle, W. J. (1972) Cystic angiomatosis of bone. *Journal of Bone and Joint Surgery*, **54-B**, 626–636.
Spjut, H. J., and Lindbom, Å. (1962) Skeletal angiomatosis. *Acta Pathologica et Microbiologica Scandinavica*, **55**, 49–58.