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TELANGIECTATIC OSTEOSARCOMA

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Of the 242 cases of osteosarcoma recorded in the Swedish Cancer Registry for the years 1958 through 1968 only one was found to represent telangiectatic osteosarcoma. Another case was recently diagnosed in our department. The characteristic morphologic features of these neoplasms were anaplastic stroma, high mitotic activity, osteoid-formation, widely anastomosing blood spaces, and alkaline phosphatase activity. The experience gathered indicates that telangiectatic osteosarcoma constitutes a histopathologic variant of genuine osteosarcoma with a serious prognosis, necessitating the same kind of treatment as for the genuine tumour.

Key words: bone neoplasms; diagnosis; telangiectatic; histopathology

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Opinions differ in the literature as to the existence of a special type of osteosarcoma which merits the designation telangiectatic osteosarcoma, and the clinical significance of this kind of tumour is also disputed. It is well known that differentiation between telangiectatic osteosarcoma and other bone lesions with rich vascularization often is difficult, and this is particularly true for the differentiation between telangiectatic osteosarcoma and aneurysmal bone cysts. Because of these difficulties in differential diagnosis, Ruiter et al. (1977) used computerized discriminant analysis for the study of nuclear size, mitotic index, cellularity, and nuclear DNA-content and thus facilitated differentiation between these tumours.

The prognosis of telangiectatic osteosarcoma has been reported not to differ from that of other kinds of osteosarcoma (Jaffe 1956, Marcove et al. 1970, Farr et al. 1974, Matsuno et al. 1976). Spjut et al. (1970) found no need for subclassification of osteosarcoma into sclerosing, osteolytic, telangiectatic or medullary types because of a lack of prognostic significance of such a differentiation.

Because of the existence of these differing opinions and diagnostic difficulties we found it worthwhile, in our studies of malignant primary bone tumours, to pay attention to tumours which might represent telangiectatic osteosarcomas. Among all the tumours which we have studied, there have only been two which are of interest in this context. These cases are reviewed in the present study.

PATIENTS AND METHODS

Case 1 was recently treated at our clinic, and Case 2 was found during our review of all osteosarcomas recorded in the Swedish Cancer Registry from 1958 through 1968 (Larsson et al. 1978).

Case reports

Patient 1. A 14-year-old boy was admitted on January 9, 1976, because of pain in the medial

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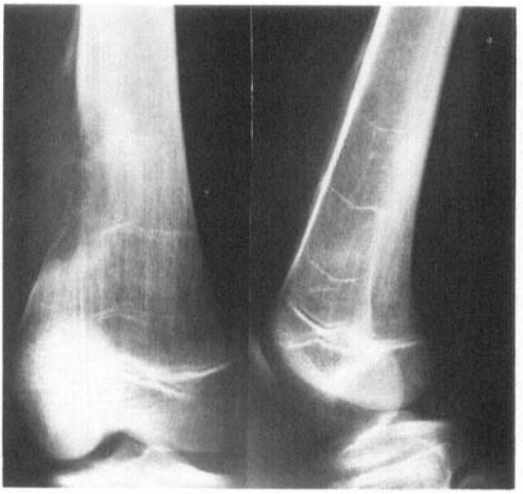

Figure 1. Radiographs revealing a destructive lesion involving the medial portion of the distal femur and causing subperiosteal new bone formation (patient 1).

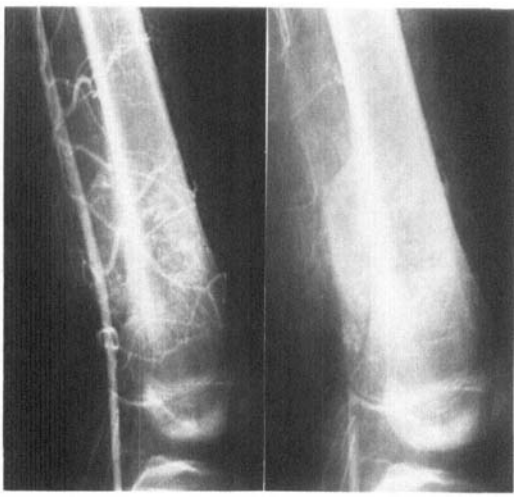

Figure 2. Angiographs showing hypervascularity with non-homogenous accumulation of contrast medium and a large number of pathologic vessels (patient 1).

part of the left knee of 2 months duration. There was no history of antecedent trauma. Physical examination revealed a firm swelling that was fixed to the medial femoral condyle. The regional lymph nodes were not involved. The erythrocyte sedimentation rate was 55 mm per hour. Other routine laboratory analyses were normal.

Roentgenograms showed a 6 cm long destructive lesion in the distal and medial part of the left femur (Figure 1). A soft tissue tumour could be seen outside the area of bone destruction. Angiography revealed a highly vascularized tumour with an abundance of tortuous vessels in the destroyed part of the femur, and also in the surrounding soft tissues (Figure 2). A pulmonary roentgenogram and a scintigram of the liver were normal.

Fine needle aspiration biopsy disclosed polymorphous, partly spindle-shaped mesenchymal cells and a few multinucleated giant-cells (see below). Cytologically, a diagnosis of giant-cell tumour of bone or osteosarcoma was considered.

On January 21, 1976, an open biopsy was performed on the lesion in the distal femur. The tumour was so highly vascularized that it was very difficult to achieve haemostasis, and there was a total blood loss of 1,800 ml. The histopathological diagnosis was telangiectatic osteosarcoma (see below).

On January 30, 1976, an amputation of the left femur was carried out, 15 cm below the greater trochanter. Three weeks postoperatively, chemotherapy with Adriamycin® was instituted at a dose of 105 mg as single injections given every week over a 6-week period. He was fitted with a prosthesis and could return home.

Despite the treatment, roentgenograms revealed the occurrence of pulmonary metastases in November 1976. He died in pulmonary insufficiency on December 27, 1976.

Patient 2. A 16-year-old boy was admitted on February 20, 1965, because of successively increasing pain of 14 days duration localized in the left knee region around the proximal part of the fibula. Physical examination showed a 10×7 cm large, tender swelling over the head of the left fibula. There was no involvement of the regional lymph nodes. Routine laboratory investigations were normal including the sedimentation rate. Roentgenograms revealed a destructive lesion involving the whole proximal part of the fibula. A pulmonary roentgenogram was normal.

On March 4, 1965, a cystic chocolate-brown, easily bleeding, soft tumour was excised. The bone was completely destroyed by the tumour, but there was no major extension into the surrounding soft tissues. The operation was performed in a bloodless field. There was no excessive bleeding when the tourniquet was released.

The histopathological appearance of the removed specimen was difficult to interpret. Aneurysmal bone cyst or giant-cell tumour of bone were considered, but the final diagnosis was telangiectatic osteosarcoma (see below).

Postoperative high-energy radiotherapy was

given. However on April 3, 1965, pulmonary roentgenograms revealed the occurrence of metastases. Despite palliative chemotherapy with cyclophosphamide, there was progression of the metastatic lesions and the patient died on July 9, 1965, in pulmonary insufficiency.

Fine needle aspiration biopsy

Material obtained at fine needle aspiration biopsy (Figure 3) from patient 1 disclosed sheets of highly polymorphous cells. Some of these were of the spindle-shaped, fibroblastic type, whereas others were rounded, oval or irregular (Figure 3A). The chromatin density of the nuclei varied. One or more nuclei of varying size could be observed. The nucleoli were medium-sized and moderately distinct. Mitotic figures were seen among the polymorphous cells (Figure 3B). The amount of cytoplasm varied; in most cells there was a moderate amount of cytoplasm which showed light staining. Cytoplasmic granulation and vacuolation were seen in some cells.

Some multinucleated giant-cells were encountered (Figure 3C). The nuclei were usually rounded or oval and varied slightly in size and staining affinity. Rather small and moderately distinct nucleoli were observed in these cells. A moderately dense cytoplasm with fine granulation was seen. The outline of the giant-cells was usually irregular.

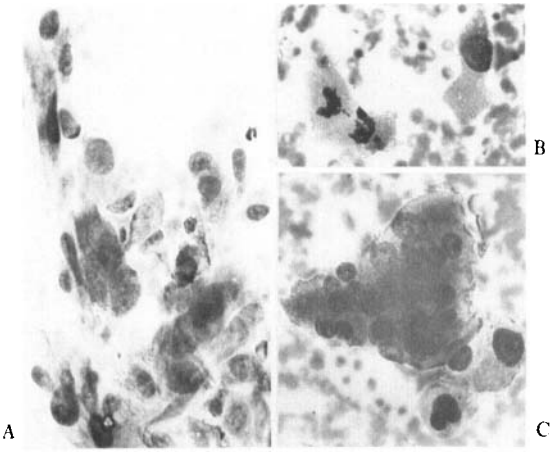

Figure 3A. Fine needle aspiration biopsy showing polymorphous and polychromatic tumour cells, some of which are spindle-shaped. May-Grünwald-Giemsa stain × 520 (patient 1).

Figure 3B. Mitotic figure in one tumour cell. May-Grünwald-Giemsa stain × 560 (patient 1).

Figure 3C. Multinucleated giant-cell with rounded or oval nuclei and a moderate amount of cytoplasm. May-Grünwald-Giemsa stain × 520 (patient 1).

Light microscopy

The tumours from both patients were fixed in 10 per cent neutral formalin. The following stains were applied: haematoxylin-eosin, van Gieson's stain, periodic acid-Schiff (PAS) and Laidlaw's silver impregnation. In addition, alkaline phosphatase activity was studied using the method of Barka & Andersson (1963).

At re-examination, essentially similar findings were made in both cases. Low power field examination disclosed polymorphous tumours with a rich number of widely anastomosing blood spaces of varying size and shape. The solid areas exhibited osteoid formation (Figure 4). The amount of osteoid varied considerably in different parts of the same tumour. Tumour bone or cartilage were not seen.

The solid areas were mainly composed of polygonal cells with a moderate or high polymorphism. In addition, some areas exhibited spindle-shaped cells. Most tumour cells were large and possessed oval or slightly irregular nuclei with one, two or more distinct nucleoli (Figure 5). The chromatin was finely or coarsely dispersed and the nuclear membranes distinct. Mitotic figures were frequently encountered. Many of these were atypical.

A few multinucleated giant-cells were observed (Figure 6). They possessed medium-sized, rounded or oval nuclei with moderately distinct chromatin and medium-sized nucleoli. The cytoplasm exhibited a moderate density and occasionally small vacuoles. The outline was usually irregular.

The blood spaces varied considerably in size

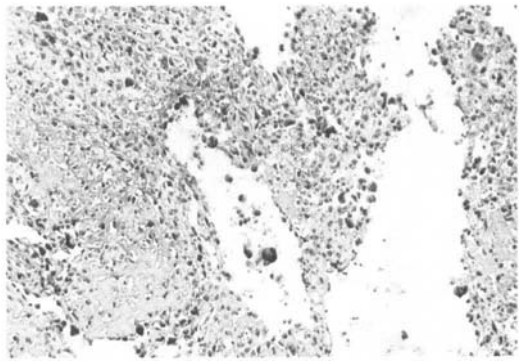

Figure 4. Blood spaces containing some seemingly desquamated tumour cells. Osteoid is seen in the solid areas. Haematoxylin-eosin × 80 (patient 2).

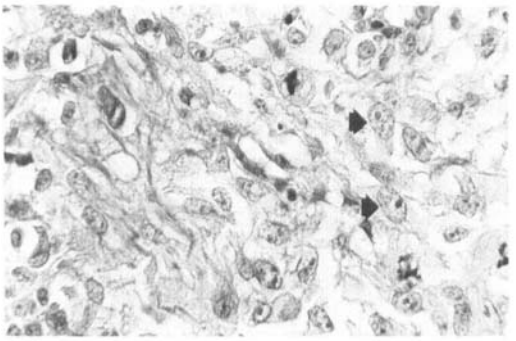

Figure 5. Solid tumour area showing oval or slightly irregular nuclei with one or more distinct nucleoli (arrows). Mitotic figures are seen. Haematoxylin-eosin × 500 (patient 1).

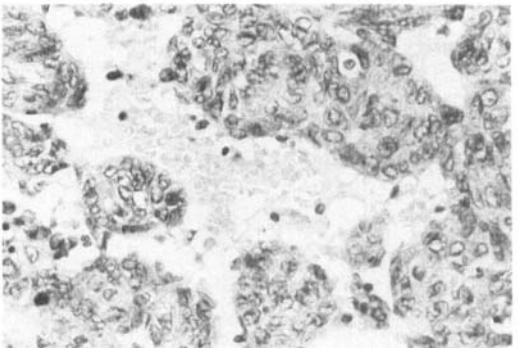

Figure 7. Irregular blood spaces without endothelial lining. Erythrocytes are seen in the lumina. The solid areas are moderately polymorphous. Van-Gieson's stain × 500 (patient 2).

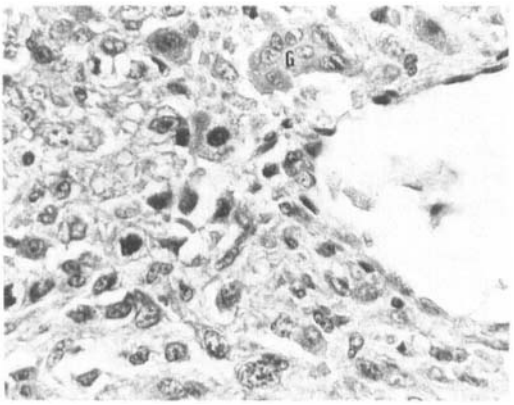

Figure 6. Blood space lined by endothelial-like cells. The solid area exhibits polymorphism, polychromasia, one multinucleated giant-cell (G) and mitotic figures. Haematoxylin-eosin × 500 (patient 1).

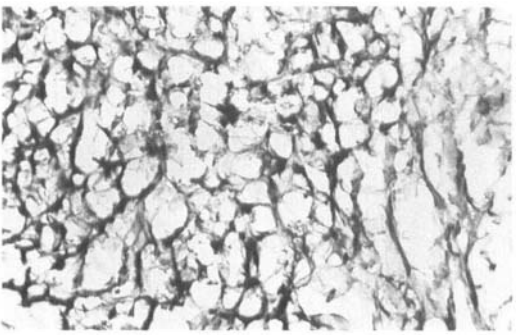

Figure 8. Alkaline phosphatase activity in solid tumour area. × 500 (patient 1).

and shape. Erythrocytes were found in the lumina (Figure 7). Most blood spaces were lined by flattened cells of endothelial type (Figure 6), whereas no such lining was found in other blood spaces (Figure 7). Still other spaces were surrounded by rounded or cuboidal cells. Evident alkaline phosphatase activity was found in the tumours (Figure 8).

DISCUSSION

Telangiectatic osteosarcoma was considered by Ewing (1922, 1939) to be a distinct clinical and pathological entity. However, recent reviews (Dahlin 1967, Jaffe 1956, Marcove et al. 1970, Price & Sumner-Smith 1966) designate telangiectatic osteosarcoma as a histopathological variant of osteosarcoma with no special clinical significance. This opinion was also supported in the review of Farr and co-workers (1974). The frequency of telangiectatic osteosarcoma has not been dealt with in previously published large series on osteosarcoma. In the recent study by Farr and co-workers (1974) only 29 patients with telangiectatic osteosarcoma could be found among a total of 1,480 cases of osteosarcoma, i.e. 2 per cent. In our review (Larsson et al. 1978) of all 242 cases of osteosarcoma recorded in the Swedish Cancer Registry during the years 1958 through 1968, we found only one case which warranted subclassification as telangiectatic osteosarcoma.

The other case was recently diagnosed in our department. Telangiectatic osteosarcoma thus constitutes, at the most, no more than 2 per cent of all types of osteosarcoma. With a mean yearly incidence of 2.8 cases of osteosarcoma per million people in Sweden (Larsson & Lorentzon 1974a) telangiectatic osteosarcoma is very rare, the yearly incidence being about 5.6 cases per 100 million people.

There was a male predominance with a ratio of 1.9:1 in the series of Farr et al. (1974), while for all types of osteosarcoma we found a sex ratio of 1.4:1 (Larsson & Lorentzon 1974b). Except for a less common involvement of the tibia the data published by Farr et al. (1974) indicated no difference as regards the clinical course between telangiectatic osteosarcoma and genuine osteosarcoma as a group. The cure rate was approximately 18 per cent. The clinical symptoms in our cases were characteristic of osteosarcoma, including local pain around a swelling in the knee region, and either increased or normal sedimentation rate. Roentgenograms showed a destructive lesion similar to that of genuine osteosarcoma. Angiography, carried out in Case 1, showed a highly vascularized tumour. The rich vascularization was further demonstrated by the presence of profuse bleeding at biopsy, almost like bleeding directly from the femoral artery. Case 2 did not exhibit such profuse bleeding at operation, although, at light microscopy, the tumour was as vascularized as that of Case 1. The use of a tourniquet in Case 2 and the more peripheral location of the lesion in the proximal fibula might explain the observed difference in bleeding from the tumours.

Characteristic light microscopic features of the tumours in our cases were anaplastic stroma, high mitotic activity, osteoid formation, widely anastomosing blood spaces and alkaline phosphatase activity. Multinucleated giant-cells were rather sparsely represented. The morphological findings and the clinical course indicate malignancy. Because of the light microscopic characteristics the histopathological diagnoses which primarily should be considered are osteogenic sarcoma on the one hand and aneurysmal bone cyst on the other hand. Although genuine giant-cell tumours may produce osteoid (Murphy & Ackerman 1956, Shuffstall & Gregory 1953, Williams et al. 1954) and also may be rich in blood vessels, there was no evidence in our cases of giant-cell tumour. The anaplasia in our tumours was characteristic of a sarcomatous tumour such as osteosarcoma, and reduced the possibility of it being an aneurysmal bone cyst. This opinion is also held by Clough & Price (1968) and Tillman et al. (1968). The latter authors have also suggested that the presence of irregular tumour osteoid indicates telangiectatic osteosarcoma rather than aneurysmal bone cyst. Based upon these findings we maintain that telangiectatic osteosarcoma can be differentiated from other bone lesions. The alkaline phosphatase activity found in our tumours also suggests osteosarcoma. Fine needle aspiration biopsy suggested malignant bone tumour in our cases but did not help in the differentiation of the lesion.

Reed & Rothenberg (1964) have proposed that the vascularity pattern of aneurysmal bone cysts is a non-specific reaction representing a primary lesion, whereas vascularity of other bone tumours represents a late secondary change. The finding in our cases of seemingly desquamated tumour cells in the lumina, and the absence in many blood spaces of an endothelial lining, might indicate a secondary nature of the blood spaces. It is of interest that we have observed a similar rich vascularization in experimentally produced mouse osteosarcoma (Larsson et al. unpublished). Osteosarcoma containing a rich amount of blood-filled cysts has also been described in a dog (Price & Sumner-Smith 1966).

Angiographically, telangiectatic osteosarcoma is hypervascularized as most of the osteosarcomas. Genuine giant-cell tumour of bone and some of the aneurysmal bone cysts are also hypervascularized (Lundström et al. 1977) which in some cases could make differential diagnosis difficult. As in all cases

of malignant bone tumour, the final diagnosis should always be based upon a thorough evaluation of all clinical, roentgenographical and histopathological data. In view of the differences with regard to treatment and prognosis, the differentiation of telangiectatic osteosarcoma from other bone lesions, particularly benign lesions such as aneurysmal bone cyst, is very important. From our experience we agree with Farr et al. (1974) that telangiectatic osteosarcoma constitutes a histologic variant of genuine osteosarcoma, with a similar serious prognosis, necessitating the same kind of treatment.

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