EXTRA-OSSEOUS OSTEOSARCOMA

A CLINICAL AND HISTOPATHOLOGICAL STUDY OF FOUR CASES

R. LORENTZON, S.-E. LARSSON, L. BOQUIST

From the Departments of Orthopaedic Surgery and Pathology, University of Umeå

Four cases of extra-osseous osteosarcoma were found among 242 cases recorded as osteosarcoma in the Swedish Cancer Registry during the years 1958 to 1968. The tumours occurred in middle-aged and elderly patients. Three of the tumours were situated in the proximal part of the thigh and one in the scapular region. Histopathologically, all tumours were subclassified as osteoblastic osteosarcomas. The patients were treated by primary local excision which in one case was followed by a radical en bloc excision of the entire tumour bed. All cases subjected to simple excision died of metastatic disease five to twenty-four months after diagnosis. The patient treated by en bloc excision is alive and apparently free from disease fourteen years after diagnosis.

True osteosarcomata arising primarily in extraskeletal soft tissues are rare. In a review of the English literature before 1969, Allan and Soule (1971) found sixty-nine cases and added twenty-five of their own collected from 2100 soft-tissue sarcomata recorded at the Mayo Clinic. Since then we have found another fourteen cases reported in the world literature (Nishimura, Ishikawa and Ishiko 1972; Wurlitzer, Ayala and Romsdahl 1972; Patil et al. 1973; Lewis, Lotz and Beazley 1974; Miller, Wirman and McKinney 1974; Shahin, Chaimott and Dintsman 1974). Osteosarcomata arising primarily in the breast, the kidney, the liver, or other organs, are not included in this tumour category because some of them, if not all, represent the malignant growth of a single component in a teratoma (Fine and Stout 1956). In view of the serious prognosis of extra-osseous osteosarcoma (Fine and Stout 1956; Das Gupta, Hajdu and Foote 1968; Allan and Soule 1971; Wurlitzer et al. 1972) and the rarity of the lesion, additional cases still warrant recording.

The present study represents a review of four cases of extra-osseous osteosarcoma recorded in the Swedish Cancer Registry during the eleven-year period from 1958 to 1968 inclusive.

CASE REPORTS

Case 1. An eighty-four-year-old woman was admitted in May 1965 with a two months' history of a slowly growing swelling in the right groin. Four years earlier she had been treated for multiple contusions of the soft tissues caused by a fall. At that time there had been a large haematoma in the left, not in the right, inguinal region. Otherwise, there was no history of trauma.

Physical examination revealed nothing abnormal except for a hard, non-tender swelling in the right inguinal region. The skin overlying the tumour was bluish-red but there was no ulceration. The lump could be moved freely over the underlying soft tissues. Radiographs of the pelvis, hips, proximal femora, knees and upper arms disclosed no destructive lesions. No radiograph was taken of the lungs. The results of routine laboratory analyses of blood and urine were normal.

A tumour measuring 6.5x8.0x8.0 centimetres was excised. It was situated entirely within the subcutaneous tissues and could easily be dissected free from the underlying femoral vessels and nerves. There was no connection between the tumour and any bone. On histopathological examination, the diagnosis of osteosarcoma primarily arising in soft tissues was made. There were no complications and the patient was discharged two weeks after operation.

During the following months, the patient's general condition steadily deteriorated and she died in October, approximately four months after diagnosis. On the death certificate extra-osseous osteosarcoma was given as the cause of death, but no necropsy was performed.

Case 2. A seventy-year-old man was admitted in June 1961 with a progressively growing swelling of two months' duration in the proximal part of the right thigh. He had had no pain and had no history of trauma. Physical examination revealed nothing abnormal except for a hard mass, measuring 2x2 centimetres, located medially within the right thigh, 7 centimetres below the inguinal ligament. The mass could be freely moved in relation to the skin and underlying tissues. Radiographs of the right proximal femur disclosed a calcified mass in the subcutaneous tissues but no skeletal lesion. Angiographic examination showed no tumour vessels, nor was there any displacement of the femoral vessels by the tumour. The lungs were radiographically normal. Routine laboratory examinations gave normal results.

The tumour, which was excised, was situated entirely within the subcutaneous tissues. There was no extension into the underlying muscle fascia, nor into the femur. On histopathological examination, the diagnosis of osteosarcoma in the subcutaneous tissues was made. There were no complications, and the patient was discharged four days after operation.

Eight months later a painful soft-tissue mass was noticed in the region of the left scapula. Physical examination revealed a hard mass situated just below the lower border of the left scapula, measuring approximately 10x15x1.5 centimetres. The tumour was fixed to the underlying tissues but not to the skin. A recurrence measuring approximately 1x2 centimetres was found in the proximal part of the scar in the right thigh. A radiographic survey showed a normal skeleton but aroused suspicion of metastases in the right lung. The two
subcutaneous tumours were excised in March 1962. Histopathologically, both lesions had the same features as the original osteosarcoma. Despite treatment with cytostatic drugs, large pulmonary metastases appeared and the patient died of pulmonary insufficiency in July 1962. No necropsy was performed.

Case 3. A forty-three-year-old woman was admitted in August 1959 with a slowly growing swelling of two months' duration in the lateral part of the right thigh. There was no history of trauma. Physical examination revealed nothing abnormal except for a slightly tender, firm mass situated in the soft tissues outside the greater trochanter of the right femur. The mass measured approximately 1 x 2 centimetres and was fixed to the surrounding tissues. Radiographs of the right hip, the right femur and lungs were normal. Routine laboratory analyses gave normal results.

The tumour, which was excised, was situated beneath the subcutaneous fat tissue and infiltrated diffusely into the surrounding muscle tissue. There was no connection between the tumour and the femur. On histopathological examination the diagnosis of osteosarcoma, evidently arising in the soft tissues, was made. Because of the histopathological finding a second, more radical procedure was performed later with excision of parts of the fascia lata and underlying gluteus maximus and vastus lateralis muscles. Histopathologically, small remnants of osteosarcoma tissue were found within the removed specimen, but the excision now seemed radical. There were no complications after the operation.

In October 1959, physical examination aroused suspicion of local recurrence of the tumour. A large excision was therefore performed, comprising a skin area measuring 6 x 15 centimetres and including all the underlying soft tissues except the gluteus minimus muscle. The greater trochanter of the femur was also removed. Histopathological examination disclosed no recurrent tumour tissue. There were no complications, and in January 1960 the patient resumed work.

Clinical and radiographic examinations performed at regular intervals, the last one being fourteen years after the diagnosis was first made, did not disclose any recurrence nor any metastases. The patient is still alive (March 1978).

Case 4. A thirty-one-year-old woman was admitted in January 1959 with a slowly growing mass of eight months' duration in the left scapular region. She had had no pain or tenderness and had no history of trauma. Physical examination revealed nothing abnormal except for a firm and non-tender mass, measuring approximately 5 x 5 centimetres, over the proximal part of the left scapula. The mass was fixed to the underlying tissues but not to the skin. Radiographs of the lungs and routine laboratory studies gave normal results.

The tumour and parts of the underlying muscles were excised. The supraspinatus and infraspinatus muscles were apparently infiltrated by tumour tissue. There was no connection between the tumour and the scapula. On histopathological examination, the tumour was shown to have been radically excised and the diagnosis of osteosarcoma was made. There was no complication, and the patient was discharged one week after operation. However, in January 1961, she died from pulmonary metastases.

All tumours showed a sarcomatous stroma and areas of osteoid and chondromatous tissue (Fig. 1). The stroma was in all cases highly cellular and pleomorphic. Typical and atypical mitotic figures were found at a varying frequency among the stromal cells. The stroma occasionally exhibited a fibrosarcomatous appearance with occurrence of spindle-shaped, hyperchromatic cells, often in parallel arrangement. Necrodes and bleedings were occasionally encountered. A concentration of endothelial-lined spaces of varying width containing blood was found in one tumour (Case 4; Fig. 2). Multinucleated giant cells and a few so-called tumour giant cells were seen in some portions of the tumours.

The osteoid was atypical and irregularly distributed. The chondromatous tissue was cellular, anaplastic (Fig. 3), and exhibited tumour cells with one, two or many nuclei. The nuclei were either small and hyperchromatic, without visible nuclear details, or large and vesicular with distinct nucleoli. Mitotic figures were encountered both in osteoid and chondromatous tumour tissue. Small areas of focal bone formation could be observed in the chondromatous tissue.

All tumours were subclassified as osteoblastic osteosarcoma. No chondroblastic or fibroblastic osteosarcoma was thus present in our series, but as reported above, the tumours were partly chondromatous and fibrosarcomatous.

At the periphery (Fig. 4) the tumours were highly cellular and pleomorphic, and mitotic figures like those in the central portions occurred. No so-called zone phenomenon was observed. The peripheral portions of the tumours were seen to infiltrate into the surrounding soft tissues but no contact with normal bone was observed.

The metastases showed a microscopical appearance identical to that of the primary tumours (Fig. 5).

**DISCUSSION**

Before making a diagnosis of extra-osseous osteosarcoma the possibility of other benign and malignant conditions must be considered. Primarily it is important to clarify that the tumour is clearly extra-osseous. In our cases there was no indication of a connection between normal bone and the tumour tissue; the tumours were completely surrounded by soft tissues, the adjacent bone being uninvolved. Thus, the tumours in our cases were definitely extra-osseous. However, they were microscopically similar to the osteosarcoma in the skeleton.

The classification of the tumours in our cases as extra-osseous osteosarcomata and the differentiation from other bone-forming conditions are based mainly upon the occurrence of malignant stroma and osteoid and chondromatous tissue. The anaplasia and mitotic activity suggested malignancy, which was verified by the occurrence of metastases. This excludes other diagnoses, such as myositis ossificans and so-called...
pseudosarcomatous lesions of the soft tissues (Jeffreys and Stiles 1966; Angervall et al. 1969; Lagier and Cox 1975; Dahl and Angervall 1977).

Extra-osseous osteosarcoma is rare. These four cases constituted only 2.6 per cent of all unequivocally genuine osteosarcomata recorded in the Swedish Cancer Registry from 1958 to 1968 (Larsson et al. 1979). The yearly incidence in Sweden, as calculated from the findings in the present study, corresponds to one case per twenty-two million inhabitants. In comparison, twenty-six extra-osseous osteosarcomata were found at the Mayo Clinic during a period when 650 osteosarcomata arising primarily in bone were diagnosed (Dahlin 1967; Allan and Soule 1971). Including our four cases, a total of 111 cases of extra-osseous osteosarcoma have been recorded in the world literature (Fine and Stout 1956; Das Gupta et al. 1968; Allan and Soule 1971; Nishimura et al. 1972; Wurlitzer et al. 1972; Patil et al. 1973; Lewis et al. 1974; Miller et al. 1974; Shahin et al. 1974). The average age for all recorded
cases is fifty-one years, and for the present cases fifty-seven years. This is in sharp contrast to the early age of the majority of patients with intra-osseous osteosarcoma (Larsson et al. 1979). In three of our four cases, the tumour involved the thigh which has been the most common single site of all recorded tumours (forty-three out of 111 cases).

The significance of trauma as the cause of these tumours is not quite clear. Fine and Stout (1956) stated that seven out of their forty-six extra-osseous osteosarcomata (15 per cent) had developed in myositis ossificans. On the other hand, the patients studied by Allan and Soule (1971) and by Wurlitzer et al. (1972) had no history of antecedent trauma. One of the cases in the present report (Case 1) had sustained multiple contusions four years before the onset of extra-osseous osteosarcoma. However, there was no haematoma in the region of the later tumour, nor any subsequent development of myositis ossificans.

The malignant potential of extra-osseous osteosarcoma is high. From a total of thirty-five cases suitable for five-year analysis, Fine and Stout (1956) accepted only one of their own cases and two from the literature as five-year cures. In the series of Allan and Soule (1971), the corresponding five-year survival rate was five out of eighteen patients; however, three of these patients died from recurrent or metastatic disease after respectively seven, nine and fourteen years, indicating an even worse long-term prognosis. Local excision of the tumour has invariably resulted in a high rate of local recurrences: in five out of twelve patients (42 per cent) reported by Fine and Stout (1956), in five of nine patients (56 per cent) reported by Das Gupta et al. (1968), in sixteen of twenty-one patients (76 per cent) reported by Allan and Soule (1971) and in all seven of the patients so treated in the series of Wurlitzer et al. (1972). Only one out of five long-term survivors in the series of Allan and Soule (1971) had been treated by simple excision and radiotherapy; the remaining four patients had all undergone more aggressive surgical treatment. In the present study, the only long-term survivor (Case 3) had received radical local excision of the entire tumour bed. Therefore, radical en bloc excision of the tumour including all the surrounding soft tissues and the underlying muscles without disturbing the tumour mass, is strongly recommended. Because of the risk of spreading the existing tumour along the muscle and in the fascial compartments, en bloc resection including whole muscles or entire muscle groups from origin to insertion, should be performed in certain cases (Lewis et al. 1974). In patients with advanced tumours, primary amputation is probably the best treatment. Patients treated with radiotherapy have had no benefit or, in a few cases, only a temporary palliative response (Allan and Soule 1971; Wurlitzer et al. 1972). A few patients have also received various chemotherapeutic agents, but no curative effect has been observed (Allan and Soule 1971; Wurlitzer et al. 1972).

REFERENCES