MALIGNANT OSTEOLASTOMA

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The clinical, radiographic and pathological features are described of eight cases of a bone tumour which we propose to classify as "malignant osteoblastoma". It presents the characteristics of genuine osteoblastoma but of an aggressive pattern, with more abundant and often plump hyperchromatic nuclei, greater nuclear atypia, and numerous giant cells of osteoclastic type. This rare tumour is regarded as the malignant counterpart of osteoblastoma and appears to be only locally aggressive. It should be separated from conventional osteosarcoma not only because of its peculiar histological pattern, but also because of its different clinical and radiological features and better prognosis. Thus seven of the eight patients were alive and free of disease from one and a half to eleven years after the initial surgical treatment, which in only two cases included amputation. Excision or block resection is the preferred method of treatment.

In a previous paper (Schajowicz and Lemos 1970) we reported in detail a study of 142 cases of conventional osteoid osteoma and forty-two cases of so-called benign osteoblastoma filed at the Latin-American Registry of Bone Pathology, and advocated that they should be considered as closely related variants of a bone tumour of osteoblastic origin. We proposed the term "osteoblastoma" for both processes, calling the smaller sclerosing lesion of cortical bone "circumscribed osteoblastoma" (which corresponds to the conventional osteoid osteoma), and "genuine osteoblastoma" for the lesion of cancellous bone with little or no reactive sclerosis and with a certain preference for short and flat bones. Similar criteria had previously been adopted by Byers (1968) and later by da Souza Dias and Frost (1974), who classified these entities as "cortical osteoblastoma" and "spongioid osteoblastoma" respectively.

In our paper we emphasised that the adjective "benign" should be avoided because several instances of recurrence had been reported (Lichtenstein and Sawyer 1964; Canepa and Defabiana 1965; Spjut, Dorfman, Fechner and Ackerman 1971). The possibility of malignant transformation had also to be considered, Mayer (1967) having reported the case of a man of forty-three who, thirteen years after curettage of a lesion of the roof of the acetabulum diagnosed by Jaffe as benign osteoblastoma, developed an osteosarcoma at the same site.

At this time we mentioned three tumours with peculiar features suggesting a primary bone-forming tumour of low-grade malignancy, which we tentatively classified as "malignant osteoblastoma". We believed that a longer follow-up of similar cases would be necessary to determine the course and prognosis. Since that time two of the cases have been followed for nine and eleven years.

Five more cases have been studied in our laboratory, three of the patients being well and free from disease between three and four and a half years after the initial surgical treatment. On the basis of this experience we think that it is now appropriate to consider the problems of nomenclature, differential diagnosis and treatment. We believe that "malignant osteoblastoma" is the most appropriate term for this lesion.

CASE REPORTS

Case 1—An Italian man aged forty-seven had pain in the left groin radiating to the knee for four months before admission to hospital. There was no history of injury. The pain became more severe with active and passive movement of the hip. Clinically there was pain in the left thigh on palpation. Radiographs showed an osteolytic lesion of the femoral neck which was not well limited (Fig. 1). The cortex was preserved and there was no bone sclerosis. In November 1955 curettage of the cavity and filling with bone chips was performed. Two weeks later internal fixation with a stainless steel nail was done. Subsequent radiographs showed partial filling of the cavity with bone. The patient was discharged wearing a plaster cast. In April 1956 he returned with pain in the same hip and in poor general condition. Radiographs showed a recurrence with destruction of the whole neck and head of the femur and invasion of the soft tissue (Fig. 2). Needle biopsy was performed (Figs. 3 and 4) and radiotherapy started. After twenty applications the patient's general condition was worse with marked swelling and oedema of the limb. Radiographs now showed extensive calcification of the tumour. By July 1956 the size of the upper thigh had increased and a large mass was palpable. The patient was discharged in poor general condition and died eight months later from peritonitis, perhaps due to local spread of the tumour.

Case 2—A woman aged nineteen was admitted to hospital in February 1964 complaining of pain and stiffness of the left shoulder for about a year. The region was painful on palpation. The radiographs showed an osteolytic lesion of the upper end of the humerus extending to the metaphysis, with

FIG. 1

FIG. 2

Case 1. Figure 1—A radiograph of the femoral neck showing the osteolytic lesion. Figure 2—The radiograph five months later showing rapid extension with destruction of the cortex, pathological fracture, and some spotted areas of calcification.

FIG. 3

FIG. 4

Case 1. Figure 3—A photomicrograph showing the typical pattern of osteoblastoma with osteoid trabeculae (a) and numerous osteoclasts (b). ($\times 220$.) Figure 4—Another photomicrograph showing partly calcified bone trabeculae (a) surrounded by abundant hypertrophic osteoblasts, and a multinucleated osteoclastic giant cell (b). The pleomorphism and hyperchromatism of the osteoblasts are clearly seen. ($\times 650$.)

slight expansion and thinning of the cortex, and crossed by several septa forming a number of cavities of different size. Biopsy was performed (Figs. 5 to 7) but the several pathologists consulted found it impossible to make a definite diagnosis, the most probable being malignant giant-cell tumour and atypical osteosarcoma of low-grade malignancy. By March

1964 the lesion had extended and resection of the upper third of the humerus followed by a fibular graft was performed (Figs. 8 and 9). The graft was not well tolerated and was replaced by another in 1964. The patient was in good general health in February 1975, twelve years after the first complaint and eleven years after the first operation.

FIG. 5

FIG. 6

FIG. 7

Case 2. Figure 5—A photomicrograph showing cellular tissue with formation of osteoid (a) and scanty immature woven bone trabeculae (b) by the tumour cells, which in general are spindle-shaped and not very atypical. ($\times 220$.) Figure 6—Another area of the tumour with the appearance of an osteoclastoma. The stromal cells, however, look more like osteoblasts and have produced osteoid in some areas. ($\times 220$.) Figure 7—Another area showing predominant dark blue immature bone spicules (c) and reactive more mature bone (d). ($\times 100$.)

FIG. 8

FIG. 9

Case 2. Figure 8—A radiograph of the resected specimen. Figure 9—A photograph showing the tumour, greyish-white in colour with some haemorrhagic zones.

Case 3—A woman aged forty-six was admitted to hospital in August 1965 complaining of pain in the right leg for three months. On examination there was a tender swelling of the lower third of the fibula. Radiographs showed a large osteolytic lesion of the metaphysis limited by a thinned and

expanded cortex, with small spots of central calcification (Fig. 10). Needle biopsy was performed in September 1965, and resection of the tumour being indicated, this was carried out in October (Fig. 11). The microscopic sections showed a peculiar picture that was classified as "malignant osteoblas-

toma" (Figs. 12 and 13). A local recurrence appeared in November 1967. After a further biopsy 20 centimetres of the fibula were resected (Figs. 14 and 15). The patient was in good health in February 1975, nine and a half years after the first resection.

thirds of the leg there was a hyperaemic area 2 centimetres in diameter. There was no deformity of the leg or oedema of the ankle. Movement of the limb was normal. The laboratory findings were unremarkable. Radiographs showed an area of osteolysis with spotted calcification in the upper third of the

FIG. 10

FIG. 11

Case 3. Figure 10—A lateral radiograph through the tibia showing the osteolytic lesion of the fibula. There are some spotted areas of calcification in the centre of the lesion and areas of sclerosis in the lower and middle part. Figure 11—Cut surface of the specimen. The tumour was greyish-white in colour with an area of haemorrhage in the centre.

FIG. 12

FIG. 13

Case 3. Figure 12—A photomicrograph showing a highly cellular area forming compact groups of tumour cells of osteoblastic type with scanty osteoid formation (a), and an irregular network of fine densely calcified bone spicules (b). Some osteoclastic giant cells are also seen (c). ($\times 220$.) Figure 13—Showing an area of abundant dark blue spicules of very immature bone, without evidence of pleomorphism or atypical mitosis. ($\times 360$.)

FIG. 14

FIG. 15

Case 3. Figure 14—Cut surface of specimen. Figure 15—Radiograph showing dense calcification of the recurrence.

Case 4—A woman aged forty-four was admitted to hospital in August 1957 complaining of pain in the left leg for six months. Periodic exacerbations of pain were relieved by aspirin. Clinically the patient was in good general health but had a painful limp. At the junction of middle and upper

tibial diaphysis, about 11 centimetres across (Fig. 16). The boundaries were not well defined; the cortex was expanded but not invaded. Curettage was carried out in August 1957. The histological appearance was that of typical osteoblastoma though with features simulating a fibrosarcoma. The

FIG. 16

FIG. 17

Case 4. Figure 16—A lateral radiograph taken in August 1957. Figure 17—A radiograph taken seven months after curettage.

FIG. 18

FIG. 19

FIG. 20

Case 4. Figure 18—A photograph of the amputation specimen, showing many haemorrhagic and some irregularly calcified areas. Figure 19—A photomicrograph of a representative area showing osteoid and calcified trabeculae formation by spindle-shaped cells of fibroblastic type. ($\times 100$.) Figure 20—The cells do not show atypical mitosis or pleomorphism. ($\times 220$.)

postoperative course was uneventful and the patient was discharged. By October 1957 radiographs showed reconstruction of the cortex and more uniform calcification of the tumour. The patient returned in November 1957 with severe pain. Radiographs now showed a recurrence with an aggressive

appearance and destruction of the cortex. The patient did not return to hospital until March 1958, complaining of acute pain and a visible tumour. Radiographs showed complete disappearance of the metaphysis and diaphysis over a distance of 15 centimetres without periosteal reaction (Fig. 17). The

tumour (Fig. 18) had invaded the soft parts and the surgical wound on the surface of the leg. It was purple in colour and bled at a touch. Mid-thigh amputation was performed in March 1958. Histological examination showed the same microscopic pattern as before (Figs. 19 and 20), and a diagnosis was made of "malignant osteoblastoma with areas of

expanding well-defined lesion with spotty calcification, apparently arising from the spinous process and lamina of the first lumbar vertebra (Fig. 21). After both an aspiration and a surgical biopsy in September 1971 a complete extirpation of the tumour, which invaded the spinal canal but not the meninges, was performed. The tumour was mostly of soft

FIG. 21

Case 5—Antero-posterior and lateral radiographs showing the lesion of the spinous process and lamina of L.1.

FIG. 22

FIG. 23

FIG. 24

Case 5. Figure 22—A photomicrograph of an area rich in giant cells of osteoclastic type and hypertrophic osteoblasts, showing very active osteoid (a) and formation of immature bone (b). ($\times 220$.) Figure 23—Compact fields of hypertrophic osteoblasts are forming osteoid (a) and calcified bone trabeculae (b). ($\times 360$.) The appearances in Figures 22 and 23 are those of an actively growing osteoblastoma, but in other areas there were many giant cells. Figure 24—Showing an area of immature bone formation ("spiculated blue bone") similar to that seen in osteosarcoma. ($\times 160$.)

fibrosarcomatous appearance". This patient was last seen in 1961, three years after the amputation, when her general condition was good.

Case 5—A girl aged six was admitted in September 1971 complaining of pain and swelling in the lower costal region posteriorly for three months. The radiographs showed an

consistency and surrounded by a shell of new bone. The histological picture is shown in Figures 22 to 24. The patient was well and without recurrence in February 1975, over three years from excision of the lesion.

Case 6—A girl aged fourteen was admitted in October 1971 complaining of pain and swelling of the outer side of the right

knee for six months. Radiographs showed an osteolytic lesion of the upper end of the fibula, expanding and thinning the cortex like a giant-cell tumour (Fig. 25). With that diagnosis a segmental resection was performed. The gross and microscopic aspects were also very similar to those of giant-cell tumour but with abundant bone formation by hypertrophic, plump osteoblasts and no pleomorphism or atypical mitoses (Figs. 26 and 27). Late in 1973 an extensive

and 30). The patient was well with and no sign of disease one year after the amputation and four and a half years from the first treatment.

Case 7—A woman aged thirty-three attended in March 1973, complaining of pain in the inguinal region for several months. Radiographs showed an expanding trabeculated lesion of pubic and ischio-pubic bone (Fig. 31). Aspiration biopsy

FIG. 25

FIG. 26

FIG. 27

Case 6. Figure 25—A radiograph showing an osteolytic lesion like giant-cell tumour. Figure 26—A photomicrograph of the resected specimen showing many giant cells of osteoclastic type but with formation of osteoid and immature woven bone trabeculae. ($\times 100$.) Figure 27—Osteoid trabeculae (a) are seen surrounded by compact groups of hypertrophic plump osteoblasts and some osteoclasts. ($\times 360$.)

FIG. 28

FIG. 29

FIG. 30

Case 6. Figure 28—A lateral radiograph showing local recurrence of the tumour. Figures 29 and 30—Photomicrographs of the amputation specimen showing abundant osteoid trabeculae surrounded by hyperchromatic plump osteoblasts and several osteoclasts. The stromal cells show nuclear atypia but atypical mitoses are absent. (Both $\times 100$.)

local recurrence appeared, but the patient refused further operation until April 1974. By this time the tumour had destroyed the upper end of the tibia (Fig. 28). Mid-thigh amputation was performed. The gross specimen showed an enormous soft, friable mass of tumour which had totally destroyed the cortex, invaded the soft tissues and ulcerated the overlying skin. The tumour was in part greyish-white but mostly brownish with extensive haemorrhages (Figs. 29

followed by wide resection was performed in April 1973. The tumour was soft and greyish in colour, with several cystic cavities (Figs. 32 to 35). Because one of the surgical incisions ran through tumour tissue radiotherapy was given post-operatively. The patient was free of disease two years after admission.

Case 8—A man aged sixty-seven attended because of pain

FIG. 31

FIG. 32

FIG. 33

Case 7. Figure 31—A radiograph showing the osteolytic lesion. Figure 32—A photomicrograph showing a highly cellular area rich in giant cells with some osteoid trabeculae (a). ($\times 100$.) Figure 33—A photomicrograph of an area of the periphery of the tumour where more mature bone trabeculae produced a bone shell (b). Abundant osteoid and immature woven bone trabeculae (a) are present. ($\times 100$.)

FIG. 34

FIG. 35

Case 7. Figure 34—A photomicrograph showing evident atypism of the stromal and osteoblastic elements with formation of a few osteoid trabeculae (a). ($\times 400$.) Figure 35—Showing several typical giant cells separated by mononuclear cells with evident atypism. An isolated atypical mitosis can be seen. ($\times 400$.)

deep in the region of the ilium for two months with a swelling in this area. The radiographs showed a rounded osteolytic lesion 5 centimetres in diameter with peripheral sclerosis, suggesting an osteoblastoma. After an aspiration biopsy wide excision of the lesion and neighbouring sclerotic bone was performed in July 1973. Several large fragments of dense bone surrounding an irregular cavity containing haemorrhagic friable tissue were removed. The patient is alive and well more than one and a half years after this treatment.

CLINICAL CHARACTERISTICS

The clinical data of the eight cases are summarised in Table I. There were more females than males (six to two). The age of the patients varied from six to sixty-

seven years, an average of thirty-four. The localisation was more in the long bones (six) than in short and flat bones (two). The duration of symptoms before consultation varied from two weeks to one year, but was three to five months for most cases.

RADIOGRAPHIC FEATURES

Radiologically the appearances were extremely variable and not diagnostic. In contrast to conventional osteoblastoma, the long limb bones and different segments of them were more often affected, but no lesion had the characteristic classical appearance of osteosarcoma. In

TABLE I
CLINICAL FINDINGS IN EIGHT CASES OF MALIGNANT OSTEOBLASTOMA

Case number	Age (years)	Sex	Location	Symptoms and duration	Treatment	Progress
1	47	Male	Femoral neck	Pain in left hip, 4 months	Curettage. Internal fixation by nail	Recurrence after 6 months. Radiotherapy. Death from peritonitis at 16 months
2	19	Female	Left humerus, upper end	Pain and swelling, 1 year	Resection and bone grafts	Well 11 years after treatment
3	46	Female	Left tibia, lower third	Pain and swelling, 3 months	Resection	Recurrence at 2 years, further wide resection. Well 9 years after first resection
4	44	Female	Left tibia, upper third	Pain and swelling, 6 months	Curettage	Recurrence at 4 months. Amputation 4 months later. Well 4 years after admission
5	6	Female	Lumbar spine (L.1), spinous process and lamina	Pain and swelling, 3 months	Extirpation	Well 3½ years after excision
6	14	Female	Right fibula, upper end	Pain and swelling, 6 months	Resection	Recurrence at 2 years but refused treatment. Invasion of tibia and amputation 6 months later. Well 4½ years after initial treatment
7	33	Female	Pubis	Pain, several months	Resection	Well at 2 years
8	67	Male	Left ilium	Pain and swelling, 2 months	Extirpation	Well at 1½ years

most cases there was a rather large area of osteolysis, initially well limited, with expansion and thinning of the cortex. Giant-cell tumour was closely simulated in three cases (Figs. 8, 23 and 31). Some lesions showed spotty calcification, dense at times (Figs. 10 and 15). One lesion, of the ilium, was indistinguishable from genuine osteoblastoma. In the more advanced or recurrent lesions there was destruction of the cortex and extensive invasion of the surrounding soft tissues or of a neighbouring bone (Fig. 28).

PATHOLOGICAL FINDINGS

Gross pathology—In four cases the material received for examination consisted of numerous irregular fragments obtained by curettage or excision, but the other five were complete resection specimens.

The macroscopic appearance varied greatly. The tumour was generally of grey or reddish colour with extensive brownish or haemorrhagic areas mainly of soft consistency occupying the medullary cavity, and expanding and thinning the cortex like a giant-cell tumour. Greyish-white areas of gritty consistency were frequently observed, most extensive in the recurrence in Case 3, but never of the hardness of the sclerosing zones observed in osteosarcomas. In both amputation specimens the tumour widely destroyed the cortex and invaded the soft tissues, with a predominance of haemorrhagic, sometimes cystic, areas.

Microscopic appearances—In all cases, with few differences, these were essentially those of osteoblastoma but suggestive of malignancy. The lesion was highly cellular, with some areas of dense conglomeration of osteoblasts

and others with abundant formation of osteoid, besides trabeculae of immature woven bone. In all cases multinucleated giant cells of osteoclastic type without any trace of malignancy were always present. In the cases of tumour of the humerus (Case 2) and upper end of the fibula (Case 6) this gave rise to problems of differential diagnosis from malignant giant-cell tumour. However, though giant cells may be dominant in certain areas, the bulk of the tumour is constituted by osteoblasts and osteoid tissue. We have observed characteristics of malignancy only rarely in the stromal cells of areas where giant cells predominated, but generally in relation to the osteoblasts. Giant cells of osteoclastic type, osteoblasts and osteoid tissue may be found homogeneously distributed throughout the tumour or may form individual predominating areas. The presence of immature tumour bone ("spiculated blue bone") identical to that observed in conventional osteosarcoma is of great value for the diagnosis. We found this type of new bone in most of the eight cases and often in abundance. The presence of areas like fibrosarcoma beside others like typical osteoblastoma, as seen in the tibia of Case 4, seems to indicate a possible transformation into a fibrosarcoma.

DIFFERENTIAL DIAGNOSIS

The presence of nuclear atypism and frequent typical mitoses, or even of a few atypical mitoses alone, is an important, though not absolutely conclusive, finding for a diagnosis of malignant osteoblastoma. Special care is necessary in the evaluation of nuclear atypism because in some osteoblastomas of benign evolution the osteoblasts can be large with plump nuclei and prominent

nucleoli, and nuclear hyperchromatism may be evident. In two cases of typical osteoblastoma, in a femur and in a vertebral body, we found osteoblasts with large, bizarre and hyperchromatic nuclei in some areas, but not in sufficient numbers to suggest malignancy because the characteristic "blue spiculated bone" and areas rich in multinucleated giant cells were lacking. However, the most important problem is the distinction from malignant giant-cell tumour on the one hand and osteosarcoma on the other.

Malignant giant-cell tumour—The hall-mark of osteoblastoma is the predominance of osteoblastic proliferation with fairly abundant osteoid and bone formation. Multinucleated giant cells can be abundant in large fields of microscopic sections, but they never dominate the lesion when enough tissue for study has been obtained. In genuine giant-cell tumours we can occasionally find osteoid or bone formation, but generally of the reactional type and never as conspicuous as in osteoblastoma. On the other hand, most of the malignant cells in osteoblastoma are indisputably osteoblasts and not similar to the fibroblast-like stromal cells of giant-cell tumour. The osteosarcoma that arises from malignant transformation of a giant-cell tumour occurs commonly after one or more recurrences, which is quite different from the rapid evolution of an osteoblastoma that is malignant *ab initio*. However, we cannot be sure that some cases of malignant osteoblastoma do not represent a special mixed type of neoplasm, with some features of osteoblastoma and others of giant-cell tumour.

Osteosarcoma—Malignant osteoblastoma is histogenetically related more to osteosarcoma than to any other bone tumour. If we understand by the term osteosarcoma a malignant tumour forming osteoid or bone, then malignant osteoblastoma has to be classified as an osteosarcoma. However, we believe that these tumours must be differentiated from conventional osteosarcoma because the clinico-radiographical features and the histological pattern are different. We never found the intense cellular

pleomorphism and atypism, the extensive areas of necrosis and the great number of atypical mitoses that are found in genuine osteosarcoma. There is no formation of tumoral cartilage or chondroid tissue, and the abundance of osteoid tissue seems to be characteristic. The uniform distribution of multinucleated giant cells of osteoclastic type is another aspect uncommon in genuine osteosarcoma. The clinical evolution demonstrates the restricted malignancy of a malignant osteoblastoma which is locally aggressive. Thus none of our patients had metastases, and five of the eight were free from disease three years after the initial treatment.

DISCUSSION

On the basis of our actual experience we believe that the term *malignant osteoblastoma* is the most appropriate for this group of tumours. Besides the characteristic features of genuine osteoblastoma (formation of abundant osteoid and immature woven bone trabeculae, and a large number of osteoblasts and osteoclasts) they present fields with numerous multinucleated giant cells of osteoclastic type and more or less extensive zones showing formation of bone spicules of irregular shape, stained dark blue with haematoxylin and closely resembling those observed in osteosarcoma but generally surrounded by typical osteoblasts. In all cases the osteoblasts are more abundant and larger in size, presenting often plump hyperchromatic nuclei and a greater nuclear atypia and more frequent mitoses than we habitually find in conventional osteoblastoma. According to the World Health Organisation classification of bone tumours they are osteosarcomas, but of low, probably only local, malignancy. The term *malignant osteoblastoma* links the tumour to osteosarcoma and at the same time to osteoblastoma as its malignant counterpart. We think it should be separated from conventional osteosarcoma mainly because of its peculiar histological pattern and much better prognosis.

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