Sclerosing osteogenic sarcomatosis

LIONEL WOLMAN

From the Department of Neuropathology, Royal Infirmary, Sheffield

SYNOPSIS  A case is reported in which the amputation of a leg for a sclerosing type of osteogenic sarcoma was followed five years later by a metastasis of similar appearance in the skull. This was excised but subsequent necropsy revealed multiple bony tumours in the lungs.

The rarity of multiple osteogenic sarcoma is recalled as shown by a review of the literature. Although some are thought to be of multicentric origin owing to the short history, an early haematogenous spread cannot be excluded and this latter process had certainly occurred in the present case.

The characteristic radiological appearances in the skull are stressed as being diagnostic. The differential points in the histological diagnosis of the condition, especially in the invaded part of the calvarium, are described and should help to exclude a meningioma or other bone tumours.

Osteogenic sarcoma rarely metastasizes to other bones, so that its occurrence five years after the removal of the original growth is worthy of record, especially from the viewpoint of differential diagnosis.

CASE REPORT

A married woman, aged 39, was admitted to the Neurosurgical Department, under the care of Mr. J. Hardman, complaining of a large spherical lump, the size of a half grapefruit, on the left side of the front of her head. It had been present for about six months. She had no other complaints but on direct questioning she said she had experienced some dizziness and occasional diplopia in the previous few months. She had three children, aged 16, 12, and 9 respectively. Her left leg had been amputated five years earlier for 'disease in the knee with some thickened bone'.

On examination there was a firm round bony swelling 6 in. in diameter over the left fronto-parietal region of the skull. It was smooth in contour and free from skin attachment. No bruit could be heard either over the lump or over the vault of the skull. There was gross bilateral papilloedema. No other abnormal physical signs were found, either in the central nervous system, or on general examination. The blood pressure was 140/90 mm. Hg. The left leg had been amputated at the upper third of the thigh and the stump appeared healthy and useful.

A radiograph of the skull showed an intensely sclerotic thickening of the bone in the left fronto-parietal region, interpreted as a large calcified meningioma. In the antero-posterior view the inner surface of the tumour was lobulated and it extended across the midline (Fig. 1). A left-sided percutaneous carotid angiogram (Figs. 1 and 2) showed marked displacement of the anterior cerebral artery across the midline with some downward displacement of the pericallosal and middle cerebral arteries. The tumour displaced the branches of the main vessels, compressing them together, but it did not appear vascular. The branches of the external carotid artery were elevated above the surface of the skull by this tumour. There was evidence of tentorial pressure coning. Although a radiograph of the chest was requested it had not been carried out by the time it was decided to remove the mass in the skull. This was undertaken as an urgent procedure owing to the patient's rapidly failing vision and the onset of vomiting.

OPERATION Under general anaesthesia with hypothermia, burr holes were made in the skull all the way round the tumour and across the tumour mass in the midline sagittal plane. The tumour was then removed by elevating the two bone flaps preserving the superior longitudinal sinus. The underlying dura was firmly adherent to the thickened part of the skull in several places and was diffusely infiltrated by nodules of hard calcified tumour. The infiltrated dura was removed with the bone and several nodules of growth had to be cut through, leaving a small residual amount of tumour which appeared to be invading the underlying brain. A few small nodules of growth were removed from the side of the longitudinal sinus. The defect in the skull was covered with bone from the deep freeze. The patient received 5 pints of blood which more than replaced her loss.

POST-OPERATIVE COURSE Her condition was satisfactory and she was recovering uneventfully till the eighth day.
FIG. 1. Antero-posterior view of the skull showing lobulated bony tumour on the left side with displacement of vessels.

FIG. 2. Left percutaneous angiogram (lateral view) showing bony tumour displacing vessels.

FIG. 3. Lateral view of lower end of left femur showing osteogenic sarcoma.

FIG. 4. Sagittal section through tumour in the skull. Nodules of growth have penetrated the dura on the inner aspect.
Sclerosing osteogenic sarcomatosis

when she suddenly collapsed and died from what was thought to be a pulmonary embolus.

MACROSCOPIC APPEARANCE OF LEFT LEG (1954 SPECIMEN)
The radiograph of the left femur showed a typical osteogenic sarcoma in its lower part (Fig. 3). The leg had been amputated through the upper third of the thigh and about 19 cm. of femur removed. The knee joint appeared normal but for about 10 cm. above the joint the femur was broadened and fusiform. A longitudinal section showed that the marrow was replaced for about 14 cm. to within 3 cm. of the cut end. The subperiosteal thickening of the bone was ivory hard.

SKULL (1959 SPECIMEN) The grossly thickened piece of bone removed from the left fronto-parietal region measured 13 × 12 cm. and was 5 mm. thick in its most affected part. The outer surface was smooth and protuberant while on the inner surface a large area of dura was firmly adherent. Many bony hard nodules of growth projected inwards through the dura. Some of these had a smooth contour, while others appeared roughened and had been cut through at operation. On sawing through the specimen the tumour was ivory hard and was present on both the inner and outer aspects of the vault as well as infiltrating it (Fig. 4). The outline of the vault could still be identified, being very distinct peripherally although rather faint in the centre. The bone of the infiltrated part of the vault was even harder than the tumour.

NECROPSY (21 HOURS AFTER DEATH) The body was that of an obese female with a healed large left frontal skin flap overlying a defect in the skull. This had been partially filled with bone grafts but the underlying swollen brain had herniated through the defect. There was no evidence of residual tumour in the vault of the skull, but several bony nodules of tumour were infiltrating the brain in the left frontal lobe towards the medial border of the hemisphere. The dura had been removed over an area, roughly 4.5 cm. in diameter, in this region. The left hemisphere was more swollen than the right with a tentorial pressure cone. There was ante-mortem thrombus in the superior longitudinal sinus.

Both lungs were studded with small, bony, hard nodules of metastatic tumour both on the surface and in their substance. There was an embolus in the left pulmonary artery at its bifurcation. As the pelvic and femoral veins did not contain any thrombus, the superior longitudinal sinus was thought to be the site of origin of the pulmonary embolus. Apart from a small cyst in the right ovary the other viscera were healthy. The bones of the spine and pelvis were sectioned but appeared free from metastases.

HISTOLOGY

LEFT FEMUR (1954 SPECIMEN) The tumour is made up of round or spindle-shaped cells which are laying down osteoid and bone throughout their extent (Fig. 5). The cells are arranged in small groups widely separated by the bony trabeculae. Several veins contain tumour cells both in their lumina and in clots adherent to their walls. No mitotic figures are seen.

SKULL (1959 SPECIMEN) The tumour has a similar appearance to that seen in the femur. The original bone of the skull is infiltrated throughout most of its extent and the marrow spaces are reduced to minute size by new deposition of bone with scanty scattered tumour cells. Externally the periosteum is elevated by a large mass of solid, well-formed bony trabeculae, often in parallel columns or in rounded masses separating small groups of tumour cells (Fig. 6). These cells are most numerous just beneath the pericranium, which they penetrate in several places. Internally, the tumour forms a large bony mass infiltrating and penetrating the dura. The tumour cells are uniform in appearance and no giant cells or mitotic figures are seen.

BRAIN Coronal sections through the left frontal lobe demonstrate that the residual tumour is confined mainly to the pia arachnoid, which is grossly thickened and compressing the underlying brain. In several places, however, the surface cortex is infiltrated (Fig. 7). The tumour in the pia arachnoid shows similar features to that seen in the skull, with numerous bony trabeculae between groups of tumour cells. Many of the arteries in the invaded pia arachnoid exhibit marked endothelial proliferation with narrowing of the lumen while several pial veins are occluded with fibrin thrombus. In the cortex and superficial white matter of this area is a wedge-shaped infarct, and several petechial haemorrhages have occurred into the softened tissue. The tumour penetrates the pial-glial membrane on the surface in several places and invades the necrotic cortex. It also extends into the perivascular spaces of the cortical vessels. There is a slight tendency for tumour cells to whorl in a few places. Nodules of tumour are present in the dura around the operation site. Tumour cells are seen infiltrating this membrane as well as being present on both its internal and external surfaces and invading its venous channels.

LUNG The nodules in the lung show a similar appearance with groups of tumour cells separated by much bone formation (Fig. 8).

OTHER ORGANS No metastases are seen in the viscera or bones sectioned.

DISCUSSION

REVIEW OF THE LITERATURE Willis (1952) reviewed the literature and collected only 11 reports of cases of sarcomas of bone metastasizing to other bones
FIG. 5. Section of tumour in left femur showing diffuse osteoid formation. Haematoxylin and eosin × 100.

FIG. 6. Section of outer part of tumour in skull showing dense bony trabeculae and scanty tumour cells. Haematoxylin and eosin × 100.

FIG. 7. Section of left frontal lobe showing tumour containing osteoid diffusely infiltrating pia arachnoid and invading the cortex. At the top of the section the pial-glial membrane is still intact. Haematoxylin and eosin × 100.

FIG. 8. Section of lung showing nodule of osteogenic sarcoma. Haematoxylin and eosin × 100.
Sclerosing osteogenic sarcomatosis

(Durham, 1883; von Recklinghausen, 1885; Nunokawa, 1908; von Roznowski, 1915; Roedelius, 1915; Joll, 1923; Martin, 1925 (2 cases); Bird, 1927; Dresser and Dumas, 1930; Dyke, 1931; Geschickter, 1932). To these 12 cases he added one of his own (Case 59).

Although White (1922) described a case of multiple pulsating bone tumours which he thought were probably alveolar sarcoma, the variability of the appearance suggesting either an epithelial growth or an angiosarcoma led to the omission of this case by Willis. A further 12 cases have been found in the subsequent literature.

In a series of over 500 cases of primary bone sarcomas, Geschickter (1936) found the cranial bones involved in only 12. In this series osteolytic sarcomas were twice as common as the sclerosing type. All except one of the patients in this series died of metastases but in only one case did these occur in bone, viz., the spine and the ilium.

Silverman (1936) reported the case of a man aged 27 dying with multiple osteogenic sarcomata 11 weeks after the first symptom. Owing to the growths occurring almost simultaneously and showing similar appearances and stages of osteogenic development, a multicentric origin was postulated, especially as osteogenic sarcomas do not metastasize extensively to bone.

Ray and Galstaun (1938) reported a case with multiple bone tumours but their diagnosis was made on radiological grounds without histological confirmation.

Busso and Schajowicz (1945-6) recorded the case of an 8-year-old girl with sclerotic tumour foci in many bones without pulmonary involvement.

Two cases were reported by Ackerman (1948). They were both male aged 27 and 10. After the first bone tumour was recognized, other bone lesions developed at sites characteristic of primary osteogenic sarcoma. Thus only the metaphyseal ends of the shafts were involved, the rest being intact. As metastases from other types of tumours are encountered in other parts of the shafts of long bones, their absence in these two cases together with the simultaneous appearance of bone lesions and their analogous stages of osteogenic development were regarded as supporting Silverman's idea of multicentricity, although insufficient to prove it.

Halpert, Russo, and Hackney (1949) regarded the numerous bone sarcomata seen in a child aged 8 as being of multicentric origin. The history was very short as death ensued within four and a half months of the initial symptoms. The multicentricity of origin was supported by Lichtenstein (1952), who described two further cases.

Finlayson (1953) recorded a case with multiple bone and pulmonary tumours in a girl aged 12. Death occurred 20 months after the onset of symptoms. He pointed out that even in the cases with a very short history in which multicentricity of origin was suggested, the extremely rapid development of haematogenous skeletal metastases from one initial growth could not be excluded.

Moseley and Bass (1956) stressed the characteristic radiological appearances of the sclerosing type of osteogenic sarcoma, reporting a case of multiple bone tumours in a girl of 5, dying four months after the initial symptoms. No decision as to the explanation of the multiple growths was reached but Price and Truscott (1957) favoured the multicentric origin in their case.

METASTATIC ORIGIN OF SKULL TUMOUR Apart from the sarcoma arising in bones affected by osteitis deformans, where the frequency of association has been reported as varying between 0·9 and 30% (Porretta, Dahlin, and Janes, 1957), with the majority of authors reporting an incidence of 7 to 11% (Esposito and Berne, 1960), tumours considered to be of multicentric origin are very rare, occurring in young patients with a relatively short history (four weeks to 19 months). Even when the multiple bone tumours develop almost simultaneously, however, early haematogenous spread cannot be excluded. In the case reported in this paper the haematogenous spread cannot be doubted in view of the widespread invasion of blood vessels in the initial growth and the presence of pulmonary metastases. There was no evidence of Paget's disease, which is the commonest basis for bone sarcoma in the skull.

Although the majority of metastases of osteogenic sarcoma appear within two years of the onset (Willis, 1953), much longer periods may elapse, e.g., 13 years in one of the cases of Badgley and Batts (1941). The osteoblastic or sclerosing types of osteogenic sarcoma (classification of Geschickter and Copeland, 1936) usually has the best prognosis and the interval of five years between the amputation and the appearance of the skull mass was sufficiently long to suggest other pathological lesions in the differential diagnosis of the present case.

DIFFERENTIAL DIAGNOSIS A meningioma was considered a likely possibility when the patient was first seen, especially in view of the rarity of multiple osteogenic sarcoma and the absence of Paget's disease. The radiological appearances were striking, and not typical of an osteoblastic meningioma. In the hyperostosis associated with meningioma, bone is laid down in parallel trabeculae close to the tables of the vault to form both an enostosis and exostosis,
and from these columns of bone radiate inwards and outwards with an external cap of a thin layer of fluffy bone (Rowbotham, 1939). The irregular, fusiform and rather fluffy thickening contrasts markedly with the densely sclerotic mass seen in the present case. The intense sclerosis, giving the impression of a snowball thrown into the calvarium, is characteristic of this type of osteogenic sarcoma. The lobulated inner border extending across the midline, as seen in the antero-posterior radiograph, also contraindicated a meningioma.

Although the morphological character of meningioma cells and osteoblasts is very similar (Russell and Rubinstein, 1959), there were histological features in the present case differing from those of a meningioma. Thus the tumour cells were small, round, or spindle-shaped, with fairly well-defined borders arranged in small groups in contrast with the larger, more spheroidal, poorly defined cells arranged in sheets in the endotheliotomatous type of meningioma. In only a few places was there any tendency for the cells to form compact whorls and these were separated by osteoid formations. Although the latter superficially resembled psammoma bodies in several areas, the majority were devoid of concentric lamination. In bone invaded by meningioma, groups of endothelial cells, frequently in compact whorls, can often be seen diffusely ramifying the wide medullary spaces between the trabeculae (Cushing, 1922; Phemister, 1923). In contrast, in the case described, the affected part of the vault, which was harder than normal, showed intense new bone formation causing reduction of the spaces between trabeculae to minute channels usually devoid of cells.

My thanks are due to Mr. J. Hardman, F.R.C.S., for allowing me full access to his clinical notes and for the details of the operation. His helpful suggestions and advice are gratefully acknowledged. I should also like to thank Professor D. H. Collins for his interest, useful criticism, and help with the text; Dr. J. L. Edwards for his description of the original specimen and loan of the histological section; Dr. J. L. A. Grout for the radiographs of femur, and Dr. J. Wilkie for the cerebral angiograms.

REFERENCES