MALIGNANT ANGIOBLASTOMA OF LONG BONE
So-called “Tibial Adamantinoma”*

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It is to the credit of Bernhard Fischer that in 1913 he isolated a new primary bone tumour, but its histogenetic origin remained a puzzle until recently. Although he realised that it could be an endothelioma of bone, he was misled by conspicuous palisaded quasi-acinar formations with central stellate liquefaction. With some diffidence he derived from these the eye-catching name “primary adamantinoma of tibia.” A number of subsequent authors also noted the peculiar myxoid areas of these tumours, but a few, such as Richter (1930), Rankin (1939), and Anderson and Saunders' unnamed pathologist (1942), recognised that this was not stroma, but an inseparable neoplastic component implying a possible endotheliomatous nature. However, they left their descriptive titles always under Fischer's original name and in this way the misnomer “adamantinoma” survived.

By condensed repetition in text-books a hypothetical ectodermal nature for the tumour became thoroughly entrenched, despite complete failure to show intercellular bridges, keratohyaline granules, enamel, or any source for an intra-osseous epithelium. This narrowed view led to pitfalls even for competent pathologists—for example, Ewing (cited by Ackerman 1956) described one instance which later turned out to be a metastatic squamous carcinoma from bronchus to tibia. Baker, Dockerty and Coventry (1954) introduced the less dogmatic term “adamantinoma so-called of the long bones.”

The tumour remained incompletely categorised until 1957, when Changus, Speed and Stewart published a comprehensive review which paid full attention to the less spectacular mesenchymal component. They traced in detail a gradual transition between solid and palisaded acinar cords of angioblast into sinusoidal vessels with characteristic curlicue arrangements. The puzzling stellate liquefactions were not adamantine in nature but were shown to imitate the normal embryological mode of origin of medullary sinusoids. The tumour is an angioblastoma.

Photomicrographs illustrating previous records have concentrated unduly on the palisaded adamantinoma-like endothelial angioblast, by which these tumours were recognised alone in the past. Both of our cases showed areas of “myxoid stroma” as seen by Fischer (1913), and described later by Baker et al. (1954) as “co-existent fibrous dysplasia” of localised type. This inseparable second diagnostic component, so easily disregarded as a “loose connective tissue carrying blood vessels,” is neoplastic mesenchymal angioblastic tissue, which may also invade.

Here are reported two patients treated surgically who have remained free from recurrence or metastasis for five and a half years and for ten and a half years.

CASE REPORTS

Case 1—The patient was a thirty-six-year-old truck driver who slipped on ice with his right leg beneath him. This was followed by persistent aching in the lower third of his leg. Two months later he had another slight fall and felt the bone break unexpectedly. Radiographic examination showed a spiral pathological fracture through an ovoid radiolucent zone, with complete bone demineralisation, in the lower tibial shaft (Fig. 1). The radiological opinion suggested that the characteristics were those of a benign lesion, such as a solitary bone cyst or fibrous

* Cases reported at the Canadian Orthopaedic Association Meeting, Jasper, June 1956.
Case 1—An oblique pathological fracture extends through the radiotranslucent lesion in the lowest third of tibia. The cortex is completely absent anteromedially. No periosteal reaction is present.

Case 1. Figure 2—Refracture has occurred through the top of the bone graft with slight displacement. Only localised resorption of the graft has occurred. Figure 3—The tumour extends from the tibial fracture at the site of the graft into the sheath of the tibialis posterior and the adjacent fascial plane and almost up to the edge of the amputation.
Case 1. Figure 4—Central stellate loosening in islands of cells, reminiscent of basal cell carcinoma, predominates over the paler mesenchymal angioblasts. (Haematoxylin, phloxine and saffron, ×115.) Figure 5—A high power view contrasts the peripheral palisading of the stellate endothelial angioblasts with the paler staining mesenchymal angioblasts. (Haematoxylin, phloxine and saffron, ×265.)

Case 1. Figure 6—Silver impregnated reticulin occurs only in the mesenchymal angioblasts imitating an epithelial tumour in this area. (Laidlaw's stain, ×50.) Figure 7—Central liquefaction in a palisaded endothelial angioblastic island produces an adamantinoma-like picture. Fusion with mesenchymal angioblasts is occurring. (Haematoxylin, phloxine and saffron, ×115.)
Case 1. Figure 8—Silver impregnated reticulin in a zone of transition between endothelial to mesenchymal angioblast shows a sarcoma-like distribution. (Laidlaw's stain, ×115.) Figure 9—The mesenchymal angioblast predominates, with evolution of adamantinoma-like zones into the characteristic curlicue sinusoids, which points to their endothelial origin. (Haematoxylin, phloxine and saffron, ×50.) Figure 10—Neoplastic mesenchymal angioblastic tissue is infiltrating into, and surrounding, the remnants of the muscle fibres of the tibialis posterior. This is often mistaken for connective tissue. (Haematoxylin, phloxine and saffron, ×50.)
dysplasia. At operation dense bone was unroofed from the anterior surface of the lesion and yellowish-red, friable tumour tissue was found to fill the entire cavity. No invasion of adjacent soft tissues was seen, but the tumour replaced part of the cortex and was adherent to the deep surface of the intact periosteum in the postero-lateral region of the hole seen in the radiographs. As the tumour appeared to lie in a cavity lined by solid, hard bone with occasional trabeculae, it was curetted out and packed with bone chips from an iliac donor site. On frozen section the diagnosis was “adamantinoma” or metastatic carcinoma. Convalescence was uneventful.

Histological preparations were sent to Dr Lauren V. Ackerman, Professor of Surgical Pathology, Washington University, St Louis. His final diagnosis was “adamantinoma, so-called” of tibia. He added that “I do not see how the present treatment could be curative and I suspect this patient is going to get into trouble again. He certainly must be followed with films taken at appropriate time intervals.” This advice was followed.

There was no clinical or radiological evidence of a primary tumour elsewhere. The patient remained well for eighteen months when aching after walking recurred in the operation site. He stepped in a small hole and had sudden exacerbation of symptoms. There was now radiographic evidence of another fracture and tumour growth at the site of the graft (Fig. 2). A Gritti-Stokes amputation of the leg was done. The specimen on longitudinal section showed a surprising amount of tumour which had been unsuspected radiologically (Fig. 3). Much of the graft appeared consolidated, but there was a transverse fracture running through recurrent tumour 2-5 centimetres in diameter which replaced the graft superiorly and the tibial cortex posteriorly. The fracture shown in Figure 3 is accentuated by manipulation during amputation. Continuous with the medullary neoplasm was a large mass of rubbery, glistening, white tumour 18 centimetres long and up to 3 centimetres thick, lying chiefy inside the sheath of the tibialis posterior, and extending along the fascial planes. No fixation to gastrocnemius or soleus was found. A tendency to form confluent nodules with many irregular cystic spaces filled by clear mucinous fluid was also apparent. No vascular or lymphatic permeation was seen microscopically, but tumour extended to within 3 millimetres of the nearest excision margin. Microscopically, most areas showed endothelial angioblastic tissue, imitating adamantinoma, but the characteristic development of curlicue sinusoids was present. Where muscle was invaded mesenchymal angioblastic tissue was more prominent and easy to gloss over as umbilical cord-like connective tissue (Figs. 4 to 10). The patient remained well and without evidence of local recurrence or distant metastasis over the subsequent five and a half years.

Case 2—The patient was a twenty-nine-year-old woman who had had to give up work requiring prolonged periods of standing because of vague recurrent discomfort in the left lower leg over the past four years. In a fall she “sprained” her left ankle, and radiographic examination showed an elongated cyst-like area of medullary bone abscession 8 centimetres long in the lower half of the tibial shaft extending almost to its mid point (Fig. 11). There was cortical expansion, with loss of normal trabecular architecture, some loculation of the wall, and medial cortical erosion, but no periosteal reaction. The superior and inferior margins of the cyst-like lesion showed apparently dense bone formation. A biopsy yielded solid pinkish-tan coloured tissue in the defect and this was reported as “osteitis fibrosa.” The histological slides were submitted to Professor C. F. Geschickter, Georgetown University School of Medicine, Washington, D.C. He reported that “the sections show a fibrous replacement of bone. This fibrous tissue contains numerous loose reticular areas and embedded in this are islands of basal cells. In general, these basal cells grow in a fashion which has been described as cylindromatous. The architecture is typical of adamantinoma of tibia.” He recommended low amputation.

This lesion was explored and no tumour identified outside the tibial shaft. A 16 centimetres length of tibia containing the lesion was then resected and replaced by a corresponding portion of left fibula as a graft and fixed by a Vitallium plate. No soft tissue was resected. On longitudinal section of the specimen the periosteum and outer cortex were intact and soft
Case 2. Figure 11—A multilocular radiotranslucent lesion in the lower tibial shaft has expanded the cortex laterally and has eroded it medially. No periosteal reaction is seen. Figure 12—Radiographs taken fourteen months after operation. The resected segment of the lower tibial shaft has been replaced by a fibular graft and fixed by a long Vitallium plate. There is considerable sclerosis at the sites of union of tibia and fibula.

Case 2. Figure 13—Islands of basal epithelium-like cells evolving progressively into a sinusoidal mesh are embedded in mesenchymal angioblastic tissue to imitate fibrous dysplasia. (Haematoxylin, phloxine and saffron, ×115.) Figure 14—The mesenchymal component of the tumour, which is like fibrous dysplasia, contains a few nests of stellate endothelial angioblasts. (Haematoxylin, phloxine and saffron, ×115.)
greyish-tan coloured tissue was found filling the medullary defect. It showed a few tiny cyst-like spaces filled by jelly-like material. The tumour did not extend to the excision margins. Microscopically mesenchymal angioblastic tissue predominated imitating fibrous dysplasia (Figs. 13 and 14). Radiographic examination fourteen months later showed no evidence of recurrence (Fig. 12). Over the subsequent ten and a half years the patient has remained well and without clinical or radiographic evidence of recurrence or metastasis.

DISCUSSION

Recognition of this tumour in other instances has been aided by peculiar clinical circumstances. The neoplasms were often observed for very many years before giving rise to serious symptoms, by which time it became clear that they were not metastatic. Up to 1942 the tumour is only referred to in the literature as “adamantinoma of tibia,” because the first seventeen cases reported were exclusively from sites within the tibial shaft.

Believing the most prominent tumour component must be a basal epithelial cell, Fischer (1913) speculated that it arose from abnormal epithelial invaginations of foetal skin initiated coincidently with the formation of the dental laminae. It was even proposed somewhat startlingly that perhaps the foetus bent over in the uterus and bit itself in the leg. Ryrie (1932) suggested that basal cells of the mature skin of the shin were implanted into the tibial periosteum much later by injury. In 1942 Anderson and Saunders described the first instance occurring in an ulna but supported the traumatic implantation theory. Even in 1954 Marzet, impressed by previous locations, pointed out that the ulna was a homologue of the tibia. However, it is interesting now to read that the unnamed pathologist fully quoted in Anderson’s unbiased report said that “the stroma... was not unlike the mesenchyme seen in the umbilical cord. . . . Through this course a variety of tubes and cords of endothelial cells forming imperfect vascular spaces, as a matter of fact, cells of the stroma and those forming the cords and vascular spaces seem to be of the same origin and intermediate forms were prevalent.” His diagnosis was mesenchymal endothelioma. This case also was finally recorded under “adamantinoma.” Since then a number of these tumours have been reported in other bones, for example, in the femur by Bell (1942), fibula by Fisher (Baker et al. 1954), again in an ulna by Maier (Petrov and Glasunow 1933), and in a rib. The latter occurred in a man who had a leg amputated twenty-two years previously for a similar tumour occurring in tibia. This intriguing case is very well documented by Morgan and MacKenzie (1956), who chose to regard the rib tumour as metastatic rather than as a probable second primary tumour. Their report is one of the few showing that some of these neoplasms do respond to radiotherapy. It would appear that the supposed predilection for the tibia is at best no more than that of bone tumours in general. It may also reflect a characteristic feature that these tumours often give mild symptoms for very many years, and are only finally detected in weight-bearing bones when they produce pathological fractures. These tend to heal and this has given rise to a belief among earlier authors that the tumour was in some way initiated by injury.

An intriguing suggestion has been advanced by Lederer and Sinclair (1954) that this tumour is one variety of synovial sarcoma. Undoubtedly the latter also may show dual components, with pseudo-glandular structures but on a fibrosarcoma-like matrix. No closer relationship has been proved as yet between such mesenchymal tissues, apart from sharing the mode of cleft formation by central liquefaction. It should be remembered that this was the source of Fischer’s misnomer. Certainly in one unusual case recorded by Mangalik and Mehrrota (1952) as an adamantinoma of long bone, but without detailed photomicrographs, tumour was present in upper tibia, cruciate ligaments and femoral condyles; this may very well have been a synovial sarcoma. Changus et al. (1957) confirmed the vascular origin of their cases by histochemical demonstrations of alkaline phosphatase in the endothelial angioblasts, and contrasted its absence in the true adamantinoma of mandible. Although
they stated that synovial sarcoma also shows an alkaline phosphatase content, they pointed out that these tumours are not characteristically traceable to blood vessels. Morgan and MacKenzie (1956), in comparing so-called adamantinomata with thirty-one synovial sarcomata, "remained unconvinced of the identity of the two growths."

It is likely that this tumour is seldom considered radiologically. For example in one of the standard comprehensive radiological texts by Schinz, Baensch, Friedl and Uehlinger (1952) no description of it is made. Two cases of "adamantinoma of long bone" were incorporated with true oral adamantinoma in a radiological article by DeSaive (1955), who remarks upon the "well vascularized connective tissue stroma" of his tibial tumours. Yet many radiological features of angioblastoma are shared by relatively common lesions such as aneurysmal and other bone cysts, giant-cell tumour, non-ossifying fibroma, and solitary fibrous dysplasia. The neoplasm produces an eccentrically placed, well defined radiolucency anywhere in the diaphysis, slowly expanding the cortex, and later producing honeycomb or loculated extensions apparently confined to the shaft itself. The cortex is slowly eroded in eccentric fashion. The margin is usually definite and later dense, but it is important to realise that the tumour extends beyond these false confines (Figs. 2 and 3). Periosteal reaction does not seem to occur except following fracture, as in fibrous dysplasia. A broad correlation between the radiology and the pathology was given by Marcial-Rojas (1959).

The natural history of this neoplasm is quite unusual. It tends to remain apparently confined inside the bone for long periods without forming distant metastases. For example, Marzet's case (1954) was observed for four decades, Anderson and Saunders' (1942) for thirteen years and Ryrie's (1932) for fifteen years. On the other hand, once the bone encasing the tumour is breached by biopsy or curettage it spreads out extensively into fascial planes. This occurred in our first case, and in every case similarly treated without exception, as was shown by Baker et al. in their excellent review (1954). This review was made to try and determine the best treatment in this uncommon condition. An appreciable number of their patients finally died years later after incomplete resections, with radiological evidence of distant metastases.

Segmental resection with bone grafting has been successful in a few patients, such as those of Cagnoli (1944), and apparently in our second patient. It is interesting to note that Fischer's (1913) original patient was treated in this way. One difficulty in planning such a resection is the known false margin seen radiographically. On the other hand, amputation has often been curative, even after the tumour has invaded the fascia and muscles of the affected limb, such as after curettage, which is always unsuccessful. The angioblastoma of rib reported by Morgan and MacKenzie (1956) showed shrinkage to one-fifth of its original size with a total tumour dose between 6,032 roentgen (maximum) and 4,524 roentgen (minimum) of telcobalt radiation. There is little other information available on the precise response of these tumours to radiotherapy.

Mesenchymal angioblastic tissue has been a very prominent feature of many cases, and the change in describing it over the years is interesting. Fischer (1913) saw it as a slime, Richter (1930) as myxoma-like, Thomas (1939) as loose connective tissue carrying blood vessels, Rankin (1939) as angiomatous material, Anderson and Saunders' unnamed pathologist (1942) as neoplastic umbilical cord-like mesenchyme, Marzet (1954) as osteitis fibrosa with progressive repair, and Baker et al. (1954) as coexistent fibrous dysplasia.

Depending upon the relative amount of mesenchyme present in biopsy material it may easily be mistaken in present nomenclature for recurrent solitary fibrous dysplasia. The penetrating comment of Changus et al. (1957) that this tumour component had been disregarded is clearly justified.

It is hoped that retrospective reviews of similar material will lead to a description of the true incidence for this tumour. There seems no adequate reason why it should have been so selective for the tibia.
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SUMMARY

Two cases of malignant angioblastoma of tibia are described, one finally treated by amputation and the other by segmental resection and grafting. They have remained free from signs of local recurrence or distant metastasis for five and a half and ten and a half years respectively. Both showed prominent areas of neoplastic mesenchymal angioblastic tissue which closely imitates solitary fibrous dysplasia.

The natural history and radiological characteristics of these little-known tumours, long thought to be “adamantinoma” of bone, are described.

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REFERENCES


