BONE PRODUCTION IN NON-OSTEOGENIC FIBROMA
An Attempt to Clarify Nomenclature in Fibrous Lesions of Bone

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The lesion in bone named non-osteogenic fibroma by Jaffe and Lichtenstein in 1942 and later—and more satisfactorily—renamed metaphysial fibrous defect by Hatcher in 1945, has been considered by various authors to be a benign tumour of bone (Jaffe and Lichtenstein 1942), the outcome of a circulatory disturbance (Hatcher 1945, Aegerter and Kirkpatrick 1958), a developmental defect (Cunningham and Ackerman 1956, Compere and Coleman 1957), a dysplasia of bone (Ponseti and Friedman 1949) and an abnormal response to injury (Schlumberger 1946). Radiologically it is recognised as a radiotranslucent lesion with a faintly sclerotic scalloped outline, eccentrically placed in the long axis of the metaphysis of long bones in children and adolescents. Histologically it is generally agreed to consist of a stroma of whorled bundles of connective tissue of varying cellularity and vascularity, containing sparsely distributed multinucleated giant cells; occasionally a few lipoid foam cells and haemosiderin granules are present, and the latter may appear also in macrophages. In regard to bone production in this lesion, Jaffe (1958) stated that “absence of bone formation within the lesional stroma tissue is consistent and striking,” and Aegerter and Kirkpatrick (1958) stated that “osteoid is never found and if present, by definition, the lesion cannot be designated ‘non-osteogenic fibroma’.” These authors, and others, will accept the appearance of bone at the periphery of the lesion, describing it as reactive bone or incorporation of bone spicules from the host. We have, however, been able to find two reports, those of Schlumberger (1946) and Adams and Goldner (1953), which recognised that metaphasic bone formation could take place within the stroma of non-osteogenic fibromata. In our own series of fibrous lesions of bone it has become increasingly apparent that non-osteogenic fibroma can often form bone. Since the presence of bony trabeculae within a lesion named rather obviously a non-osteogenic fibroma has in the past deterred the pathologist from this diagnosis, it is important to make this observation more widely known.

NOMENCLATURE

Adams and Goldner (1953) and more recently Stewart, Gilmer and Edmondson (1962) have attempted to clarify the terminology of fibro cystic lesions of bone. For the purposes of this discussion such lesions as unicameral bone cyst, aneurysmal bone cyst, benign osteoblastoma, chondromyxoid fibroma and giant-cell tumour of bone will be accepted as clearly defined entities, recognising that they may be interrelated, as well as related, in some way to non-osteogenic fibromata.

Lichtenstein and Jaffe (1942) clearly established fibrous dysplasia of bone as a definable entity, recognising that it may take polyostotic or monostotic forms. The typical lesion is radiotranslucent, central (medullary), and metaphysial becoming diaphysial; histologically it is represented by proliferation of cellular fibrous tissue which forms metaphasic bone. In its florid phase the diagnosis is rarely questioned now that hyperparathyroid disease and neurofibromatosis are more clearly delineated. But in its monostotic form, distinction from
other solitary fibrous lesions of bone becomes difficult since nests of giant cells, lipoid histiocytes and haemosiderin can also be present. In fact, Schlumberger (1946), on the basis of sixty-seven monostotic lesions in the Armed Forces Institute of Pathology, concluded that "Since... we find no definite clinical, radiological or morphological criteria by which non-osteogenic fibroma of bone and monostotic fibrous dysplasia may be distinguished, we regard the former as a variant of fibrous dysplasia." Most authors who have since written on this subject discount this conclusion of Schlumberger's by stating that he did in fact review sixty-seven cases of non-osteogenic fibromata, and not monostotic fibrous dysplasia. Three cases reported here (Cases 7, 8 and 9) will, we believe, stimulate renewed interest in Schlumberger's statement.

The term ossifying fibroma has long been used for certain fibro-osseous lesions of the mandible and maxilla. Jaffe (1958) concluded that this lesion was identical with fibrous dysplasia, though not all authors (Stewart et al. 1962) are willing to accept this opinion. Certainly there is further reason for confusion with the term osteogenic fibroma introduced by Jaffe and Mayer in 1932, used by Golding and Sissons (1954) and apparently synonymous with the giant osteoid osteoma of Dahlin and Johnson (1954). This lesion apparently has now become known as benign osteoblastoma, a benign osteoid-forming tumour which is slowly becoming more widely accepted. Perhaps Aegerter and Kirkpatrick (1958) have properly buried the term "ossifying fibroma" with this statement: "Within the entire framework of the classification of bone tumours there is no entity which is so nebulous, so ill-defined and so elusive as the one which has been called ossifying fibroma...

Fibrous cortical defect is a term most often encountered in the radiological literature and championed by Caffey (1955). Jaffe (1958) believed this lesion to be a local developmental aberration which heals spontaneously in most instances but in some cases can proliferate to become a true benign tumour, a non-osteogenic, that is, a non-ossifying, fibroma. Certainly both lesions can be traced in the literature to common origins in the papers of Sontag and Pyle (1941) and Hatcher (1945). It seems likely that Caffey's lesion was anticipated by Sontag and Pyle, while Hatcher appears to have been describing the more advanced non-osteogenic fibroma.

The literature has been further confused by introduction of the term periosteal desmoid by Kimmelstiel and Rapp (1951). These authors differentiate their lesion from non-osteogenic fibroma and monostotic fibrous dysplasia but it seems apparent that they were referring to the lesion upheld by Caffey (1955) to be a fibrous (subperiosteal) cortical defect.

In an attempt to clarify this terminology we have no hesitation in discarding the diagnosis ossifying fibroma on the basis of Aegerter and Kirkpatrick's conviction that it is a nebulous, ill-defined and elusive entity. In like manner it seems advisable to drop the term periosteal desmoid since it is undoubtedly the same lesion as subperiosteal fibrous cortical defect, an entity which is more widely known and established.

The cases which we have reviewed shed no light on the relationship of fibrous cortical defect to non-osteogenic fibroma. From accounts in the literature, however, there appears to be a valid clinical distinction in that the former never gives rise to symptoms or signs whereas the latter can do so by virtue of its size and pathological fracture. Radiologically there is a distinction in that the one tends to be subperiosteal, the other endosteal. Histologically there is little to distinguish the two. Jaffe (1958), in fact, believed that fibrous cortical defect is a local developmental aberration which can, on occasion, progress to non-osteogenic fibroma which he considers to be a benign neoplasm.

The relationship between non-osteogenic fibroma and fibrous dysplasia is even more controversial. In the discussion to follow we contend that Schlumberger's view that these two lesions are variations of the same condition gains strength from the frequent demonstration, in our cases, of bone formation in non-osteogenic fibroma. Finally, three cases are reported which we believe still further emphasise this relationship.
MATERIAL

Material available for review totalled ten patients registered in a period of six years with the diagnosis of non-osteogenic fibroma (metaphysial fibrous defect) in the University of British Columbia Bone Tumour Registry. An indication of the incidence of this lesion can be gained from the fact that in the same period forty-five osteochondromata, twenty-one unicameral bone cysts, twelve osteoid osteomata and four aneurysmal bone cysts were registered. All registered cases are required to have full clinical, radiological and pathological documentation.

The lesions occurred in seven males and three females. The ages ranged from six and a half to nineteen years with an average of 13·3 years. The tibia was involved five times, the femur three times and the fibula and humerus once. All of the lesions were metaphysial, nine of them were in the lower extremity, and five were at the knee. Five lesions were found incidentally on radiography and a pathological fracture occurred in three patients. A mass was the primary complaint in two patients and limp occurred in one. The lesion was associated with a clinical diagnosis of Osgood-Schlatter's disease in one patient.

Radiological appearances could be described as typical in all cases. Though the lesions varied in size, all occurred in the metaphysis, occasionally approaching the diaphysis. They appeared eccentrically placed, involving the cortex but expanding into the medulla. The lesion was clearly demarcated by a scalloped, faintly sclerotic outline but was basically osteolytic. The cortex in some cases was eroded from within but there was otherwise no radiological suggestion of malignancy.

The most significant macroscopical feature was the solid nature of the lesion, variously described as pale, yellow-brown, firm, rubbery and occasionally gritty. There was never a soft-tissue mass or cortical penetration.

The histological picture was typical of the classical description of this lesion by Jaffe and Lichtenstein (1942). The tumour tissue was basically fibrous connective tissue of varying cellularity and vascularity, with a moderate sprinkling of rather small multinucleated giant cells which occasionally contained lipoid; macrophages, also sometimes containing lipoid and some haemosiderin, were also present. In four out of the ten cases bone formation was absent except for the occasional reactive spicule of bone or incorporated fragment of host bone seen at the periphery of the lesion. But in the remaining six cases reported below, new bone formation could be seen within, and forming from, the tumour tissue.

CASE REPORTS

Case 1—A girl of thirteen fell, fracturing her right humerus through a lesion in the upper metaphysis. The fracture healed but the lesion persisted and was curetted four months after the fracture. A diagnosis of giant-cell tumour was made at that time. The lesion still persisted (Fig. 1) and three months later it was excised and grafted with autogenous iliac bone. On this occasion a diagnosis of non-osteogenic fibroma was made (confirmed by the Armed Forces Institute of Pathology). The histology was considered typical of this diagnosis, but in a critical search of routine sections isolated areas of bone formation within the stroma of the tumour could be found (Fig. 2).

Case 2—A boy of fifteen complained of pain in both knees and a clinical diagnosis of Osgood-Schlatter's disease was made. Radiographs revealed a lesion considered to be non-osteogenic fibroma. One year later the lesion had enlarged (Fig. 3) and two years later it was curetted. The histological picture was that of non-osteogenic fibroma and again a review of routine sections revealed metaplastic bone formation (Fig. 4).

Case 3—A boy of twelve sustained an injury and fractured the lowest third of his right tibia. Radiographs revealed an adjacent lesion and though the fracture healed the lesion enlarged (Fig. 5). It was therefore curetted and grafted three years after the fracture. A diagnosis of
Case 1. Figure 1—A persistent lesion in the shaft of the humerus nineteen months after the fracture and fifteen months after curettage. Figure 2—Bone spicule formation can be seen in the stroma of the lesion. (× 41.)

Case 2. Figure 3—A non-osteogenic fibroma of the medial femoral condyle. Figure 4—Bone formation can be seen in the tissues of the tumour stroma. (× 41.)
Case 3. Figure 5—A non-osteogenic fibroma of the lower tibial metaphysis three years after a fracture. Figure 6—There are bone spicules in the stroma. (× 41.)

Case 4. Figure 7—A non-osteogenic fibroma of the upper tibial metaphysis. Figure 8—Bone spicules can be seen in the tissue of the tumour. (× 41.)
Case 5. Figure 9—A fracture involving a radiotranslucent lesion of the lower metaphysis of the femur. Figure 10—The histology shows a non-osteogenic fibroma with a large number of lipoid cells and mature bone spicules can be seen. (×41.)

Case 6. Figure 11—A typical lesion in the lower femoral metaphysis. Figure 12—Bone spicules have formed in the collagenous tissue of the non-osteogenic fibroma. (×41.)
non-osteogenic fibroma was made. Recut sections showed small areas of osteoid trabeculae within the typical tumour tissue (Fig. 6).

**Case 4**—A boy of eight noticed a lump on his right leg which had been present for one year before the radiological diagnosis (Fig. 7) of non-osteogenic fibroma was made. This was confirmed histologically when the lesion was later excised. Again, bone spicules could be identified within the stroma (Fig. 8).

**Case 5**—A girl of six injured and broke the lowest third of her left femur through a radiotranslucent lesion (Fig. 9). The fracture healed but the lesion persisted and was curetted eighteen months later. The histology was reported as showing a non-osteogenic fibroma and it was remarkable for the large number of lipoid cells and for the presence of mature, calcified osteoid spicules (Fig. 10). This child is also of interest in that radiographs eight years later revealed a second radiological lesion typical of non-osteogenic fibroma, appearing in the lower end of the same femur.

**Case 6**—A girl of sixteen was diagnosed radiologically as having a non-osteogenic fibroma of the femur (Fig. 11). This was confirmed at operation six months later. Small areas of metaplastic bone were present within the very collagenous connective tissue stroma (Fig. 12).

**DISCUSSION**

It must be obvious that in none of these lesions is bone formation very extensive, but it is for precisely this reason that the diagnosis of non-osteogenic fibroma was originally accepted. The fact that three of these six cases had had fractures or operations previously may be criticised as a possible cause of bone formation. In the author's opinion the illustrations clearly establish that the new bone or osteoid trabeculae are formed from cells of the lesion itself and not from the host bone. The existence of this bone as a reaction of the host to proliferation of the tumour tissue or as resorbing fragments of host bone is similarly discounted. Standard descriptions of non-osteogenic fibromata accept reactive or resorbing bone as part of the lesion. Such bone appears in the periphery, and is clearly seen to be proliferating from surrounding normal bone (Fig. 13) or existing as mature bone spicules which are fragmenting by osteoclastic resorption (Fig. 14).

It seems logical to expect that any lesion arising from bone, whether it is neoplastic, infective, metabolic or simply dysplastic, will have some potential to produce bone. This is certainly true even in the non-bone-forming lesions such as giant-cell tumour and aneurysmal bone cyst. But the acceptance of bone formation within non-osteogenic fibroma has greater significance since it now becomes difficult if not impossible to distinguish it from monostotic fibrous dysplasia. In this regard, three additional cases are of considerable significance.

**Case 7**—A young man of eighteen had noticed a painful, tender mass near his right tibial tuberosity which had existed for three years. The radiological appearance was overwhelmingly one of a fibrous cortical defect or non-osteogenic fibroma (Fig. 15). The upper focus of this double lesion was excised and this tissue was found, surprisingly, to have the typical appearance of fibrous dysplasia (Fig. 16). Seven months later the lower portion was also excised when symptoms persisted and the histological picture was, again, that of fibrous dysplasia. Even though the bulk of the lesion had this appearance, certain fields could nevertheless be interpreted as showing the histology of non-osteogenic fibroma (Fig. 17).

Here, then, was a case which radiologically resembled one lesion, histologically principally resembled another and which clinically could be either. The author is of the opinion that no one aspect of diagnosis should override the others—that is, the clinical, radiological and pathological diagnoses should always be compatible. In this case one was forced to consider the possibility that monostotic fibrous dysplasia and non-osteogenic fibroma arise in the same way and run similar courses, and that their pathogenesis and natural history are the same. If the histological picture does vary, then one lesion might be considered merely a variant of the other.
Case 2. Figure 13—Reactive new bone formation at the periphery of a non-osteogenic fibroma. (41.)
Figure 14—Resorption of host bone spicules at the periphery of the tumour. (41.)

Case 7. Figure 15—Radiological defects in the cortex of the upper tibial metaphysis. Figure 16—The typical appearance of fibrous dysplasia is clearly seen throughout the lesion. (41.) Figure 17—Isolated fields within the lesion show the histological appearance of a non-osteogenic fibroma. (41.)
Case 8—A boy of eight had limped for two years. He had previous admissions to hospital for hyperinsulinism and a subtotal pancreatectomy had been performed but no pancreatic adenoma was found. Though a diagnosis of Zollinger-Ellison syndrome (Moldawer 1962) was entertained, this was never confirmed and no evidence of hyperparathyroidism was found; the alkaline phosphatase was 19 King-Armstrong units, the serum calcium was 9.2 milligrams per cent and the serum phosphorus 4.1 milligrams per cent. Radiographs showed multiple lesions involving the lower end of the left femur, upper and lower left tibia (Figs. 18 and 19), and possibly the first metatarsal bones, all of which were diagnosed as fibrous dysplasia. More critical examination showed them to be cortical lesions rather than medullary. The lower femoral lesion was curetted and "a considerable amount of xanthomatous fibrous tissue typical of fibrous dysplasia" was described. The histology, however, was completely typical of non-osteogenic fibroma (Fig. 20) with, in one or two fields, bone formation within the tumour tissue (Fig. 21).

Case 8. Figure 18—A lesion involving the lower metaphysis of the left femur. Figure 19—Another lesion in the upper tibial metaphysis.

Case 8. Figure 20—The histology is typical of a non-osteogenic fibroma. (×41.) Figure 21—An osteoid spicule is forming in the tissues of the tumour. (×41.)
In this instance radiological opinion favoured a diagnosis of polyostotic fibrous dysplasia principally because of the multiplicity of bony lesions. It is apparent, however, that these lesions do not illustrate the classical medullary ground glass appearance. Their histology is clearly non-osteogenic fibroma. One might coin the name "polyostotic non-osteogenic fibroma" but again the author prefers the view that the two lesions discussed are simply histological variants of the same pathogenetic manifestation.

**Case 9**—A girl of six complained of a painful swelling at the outer side of her left ankle which she had had for four weeks. The radiological diagnosis was monostotic fibrous dysplasia but the appearance of the lesion (Fig. 22) was not inconsistent with a non-osteogenic fibroma which had involved the entire width of the fibula. This was a grey, firm, rubbery lesion which microscopically showed the picture of fibrous dysplasia in most fields (Fig. 23). In several smaller fields, however, the histology was strongly suggestive of non-osteogenic fibroma (Fig. 24).

This final case is one in which it was not possible to distinguish with radiological certainty between monostotic fibrous dysplasia and a large non-osteogenic fibroma. Histologically, the characteristics of both lesions were in evidence.
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SUMMARY AND CONCLUSIONS

1. Six patients have been presented in whom an established diagnosis of non-osteogenic fibroma of bone was made. Metaplastic bone was identified within the tumour tissues.

2. Three other patients are reported in whom the diagnosis appeared to be, on radiological and histological grounds, either fibrous dysplasia or non-osteogenic fibroma.

3. This evidence has convinced the author that the two lesions are frequently not distinctive and that they are, in fact, closely related. Because the natural history of the two conditions, especially in their simple or monostotic form, is also the same, there is good reason to consider them as varying histological manifestations of the same pathogenetic process.

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REFERENCES