OLD FIBRIN COAGULA AND THEIR OSSIFICATION IN SIMPLE BONE CYSTS

N. G. SANERKIN

From the Department of Osteo-articular Pathology and the Bristol Bone Tumour Registry, Bristol

Old calcified fibrin coagula are frequently found in simple bone cysts. They provide a scaffold on which new bone is laid down, in a process analogous to endochondral ossification. It is suggested that these coagula are derived in substantial part from the plasma-like contents of the cyst, after the release of plasma-clotting factors as the result of injury. Major haemorrhage is not involved and in many cases there is no antecedent fracture. The phenomenon is not seen in other common cystic conditions of bone and its recognition is thus helpful in the histological diagnosis of simple bone cyst. Cystic bone infarcts and their possible confusion with simple bone cysts are also briefly discussed.

In simple bone cysts, ossification frequently occurs by an unusual process wherein old flocculent calcified fibrin provides a scaffold, analogous to the columns of necrotic calcified cartilage found in the normal growth plate, on which new bone is laid down.

This process has been inadequately recognised in the literature, and indeed there has been some failure to appreciate the nature of the aged fibrin involved in it. The latter has been variously misinterpreted as "atypical osteoid" (in this Registry), as "a homogeneous hyaline material, in some areas having the characteristics of osteoid" (Spjut et al. 1971), "fibrin-like material or hyalinised or calcified connective tissue" (Schajowicz, Ackerman and Sissons 1972), a "cementoma" (Friedman and Goldman 1969) or the necrotic remains of previous bone grafts (Spjut et al. 1971). Jaffe and Lichtenstein (1942) were aware that fragments of fibrinous clot might be found adherent to the lining of the cyst, often containing some red cells and "undergoing organisation and ossification". Schwimm (1976) mentioned that peculiar areas of ossification occurred not infrequently in "complicated" cases. Dahlin (1978) noted that fibrin deposits often occurred and these might become mineralised in focal masses.

The phenomenon is of intrinsic pathological interest and has obvious diagnostic implications. It is not seen in other common cystic conditions of bone and a certain sequence of events, peculiar to simple bone cysts, would appear to be a prerequisite for its development: the formation of a fibrinous coagulum; its location in an avascular milieu, preventing its early organisation and thus permitting its senescence and calcification; and its eventual vascularisation and ossification.

In this paper the histological features of this mode of ossification will be described and a hypothesis presented concerning its pathogenesis.

MATERIAL AND METHODS

Eighty-five cases of simple bone cyst in the records of the Bristol Bone Tumour Registry were reviewed, with particular attention to any antecedent pathological fracture or operation; to the interval between these and the recent operation; to the description of the contents of the cyst as noted at the operation; and to the macroscopic and histological appearance of the material received in the laboratory.

Histological sections from paraffin blocks, stained routinely with haematoxylin and eosin, were examined and in selected cases special stains were used, including van Gieson's, Martius scarlet blue, phosphotungstic acid haematoxylin and Perls' stain for iron.

For comparison, thirty-four cases of aneurysmal bone cyst, nine cases of intra-osseous ganglion and fifty cases of osteoarthritic subarticular cyst were reviewed.

RESULTS

Antecedent trauma. There was a history of fracture in thirty-seven of the eighty-five cases, and of a previous operation in seven. No such history was elicited in ten of the twenty-eight cases in which old flocculent fibrin coagula were found.

The interval between the antecedent trauma and the recent operation varied greatly, being less than one month in fifteen cases, between one month and one year in twelve cases, and more than one year in ten cases. There was no consistent correlation between the duration of this interval and the demonstration of old flocculent fibrin coagula.

Cyst contents at operation. In many cases no specific mention was made of the contents of the cyst, or the cyst was said to be "empty". Descriptions, when given,
varied considerably and had no consistent relationship to previous trauma: in seventeen cysts there was clear yellow or serous fluid; in nineteen, brown or blood-stained thin fluid; in five, gelatinous fluid which was yellow, reddish or brownish; in two, the cysts were xanthomatous, with a "shower of cholesterol crystals"; and in twelve there were fragments floating in the cavity, described variously as structureless, membranous or "solid" material. In each of these groups there were cases with and without antecedent fracture or operation. In one case, without antecedent trauma, a calcified mass (Fig. 1) was found "lying free" in the cyst cavity.

Macросрoscopic examination. In the vast majority of cases the macroscopic description of the material received in the laboratory was non-specific. Usually mentioned were fragments of cancellous bone, "osteoid", blood clots and strips of cyst lining. In the author's own experience only three cases had special features: a hard calcified coral-like nodule (Figs. 1 and 2) measuring 2.8 × 1.4 × 1 centimetres which was removed from the cavity of a simple bone cyst in the proximal femur of a nine-year-old boy (Fig. 3); calcified friable material, about 0.5 centimetre thick, which was adherent to the lining of the outer shell of a cyst in an ilium (Fig. 4); and an ossified nodule, which was removed piecemeal from the cavity of a simple bone cyst in the calcaneus (Fig. 5).

Histology. Aged flocculent fibrinous structures were found in twenty-eight of the eighty-five cases, in ten of which there had been no antecedent trauma. Sometimes these floccules were uncalcified, and in sections stained with haematoxylin and eosin appeared as pale or lightly eosinophilic fibrillar structures resembling acellular collagen; often they were calcified and appeared as dark
coagula unattached incorporated polarised Gieson's tic haematoxyphil with woman, spaces Radiograph 196 are totally adherent.., O

In most cases, these old fibrin coagula were incorporated into the fibrocellular lining of the cyst. In unattached coagula, and in the more superficial layers of coagula adherent to the cyst lining, the interfloccular spaces were totally avascular, being formed by a loose-textured amorphous substance in which fine strands of old fibrin coursed from one floccule to another (Fig. 6). In the intermediate zone, the interfloccular spaces were permeated by delicate capillaries and sinusoids (Fig. 7), the latter often forming large lakes containing blood, and there might be some extravasation of fresh blood. In the deeper layers there was evidence of organising granulation tissue and of new bone being deposited on the surface of the floccules (Figs. 8–10). Eventually, trabeculae of mature lamellar bone were formed, but some residual floccular fibrin could often be found in these trabeculae (Fig. 11). In this respect they resembled the trabeculae of the growing metaphysis with residual necrotic cartilage. Haemosiderin deposition was found in relatively few of these coagula and in relatively small amounts.

Reactive new bone, without a demonstrable scaffold of old calcified fibrin, was also present in variable amounts in many simple bone cysts and developed in the usual manner through intramembranous ossification. Minor haemorrhages were often present but major haemorrhage was found in only eight cases. Recent haematomata showed organisation by granulation tissue and some underwent intramembranous ossification. Old haematomata showed heavy haemosiderin deposition and abundant cholesterol granulomata (Fig. 12). A composite structure, showing both old fibrin and cholesterol granulomata (Fig. 13), was found in only one case.

In six cases, curettage material contained septa indistinguishable from those of aneurysmal bone cysts, but under radiological examination and at operation these proved to be simple bone cysts, in two of which ossifying flocculent fibrin coagula were present.

Old flocculent fibrin coagula, with or without calcification or ossification, were not found in any of the aneurysmal bone cysts or other cystic intra-osseous lesions examined.
Old calcified fibrin coagulum. Figure 8—Early ossification. The interfloccular spaces contain well-developed granulation tissue; the floccules are being covered with osteoid. (Haematoxylin and eosin, ×130.) Figure 9—A field that is fairly representative of what has been referred to in the literature as "peculiar areas of ossification". (Haematoxylin and eosin, ×60.)

Figure 10—Detail from Figure 9 at higher magnification. Old calcified fibrin floccules provide a scaffold on which osteoid is deposited. Active osteoblasts rim the osteoid. The old fibrin floccules remain sequestered in the osteoid. (Haematoxylin and eosin, ×135.) Figure 11—Relatively mature bone trabeculae formed by ossification of old calcified fibrin coagulum (same case as in Fig. 4). Sequestered fibrin columns lie in the substance of the bone; these have sometimes been mistaken for old bone chip graft. This bone eventually undergoes remoulding and loses all traces of sequestered fibrin. (Haematoxylin and eosin, ×60.)

Figure 12—Old organised haematoma: a typical cholesterol granuloma with abundant cholesterol clefts. These are seen rarely in a simple bone cyst; old calcified fibrin coagula are seen frequently. (Haematoxylin and eosin, ×60.) Figure 13—Old organised haematoma, showing a composite pattern: old uncalcified flocculent fibrin (centrally), cholesterol granulomata (on either side). (Haematoxylin and eosin, ×125.)
DISCUSSION
The absence of old calcified flocculent fibrin coagula from intra-osseous ganglia and osteoarthritic subarticular cysts is understandable, since these do not contain blood or plasma-like fluid. The absence of such coagula from aneurysmal bone cysts is of interest, because haemorrhages and thromboses are to be expected with these cysts: presumably, any fibrin or blood coagula undergo early organisation by granulation tissue and do not persist to undergo senescence and calcification. Thus, haemorrhages or haematomata cannot explain the phenomenon reported and other factors must be involved in its development.

In a simple bone cyst, fibrin coagula might be derived from a haemorrhage into the cavity or from the fluid contained within the cyst, or possibly from both. Histological evidence suggests that the trauma involved in the causation of these coagula is usually minor. Major haemorrhages produce large clots which, in time, contain abundant haemosiderin and cholesterol clefts. Haemosiderosis or cholesterol deposition is a rare occurrence in these old flocculent fibrin coagula; this suggests that they arise mainly from coagulation of the cyst fluid. The cyst fluid has the constituency of plasma (Cohen 1960) and minor trauma or a small haemorrhage could, through the release of plasma-clotting factors, lead to its coagulation. Clinical evidence indicates that major trauma is not essential, because old calcified coagula are often seen in the absence of antecedent fracture.

The fibrin coagulum is formed in an avascular inert chamber, and hence is not subject to early organisation by granulation tissue. It might float free in the cavity or settle on an undamaged part of the cyst lining. In such circumstances it could remain unorganised for some considerable time, undergoing senescence and calcific encrustation. Eventually, the calcified coagulum becomes vascularised from the cyst lining and undergoes ossification.

Ossification, whether in the normal developing skeleton or in other sites and circumstances, occurs in one of two fundamental ways: by direct deposition of osteoid in fibrovascular tissue, or by its deposition on a scaffold of calcified necrotic material. The first process, that of intramembranous ossification, accounts for the development of normal membrane bone and is responsible for fracture callus and most heterotopic ossification (Collins and Curran 1959), including myositis ossificans. The second process, best exemplified by endochondral ossification, accounts for the development of normal bone from the growth cartilage, and is responsible for evolutionary ossification in tumours of the cartilage, both intra-osseous and extra-osseous, and in metaplastic cartilage, as in synovial or periarticular chondromatosis. Calcified necrotic tissue, other than cartilage, may also provide a scaffold for ossification, for instance columns of cornified squames in epidermoid carcinoma (Sanerkin 1968). In simple bone cysts, floccules of calcified fibrin—and not necrotic tissue—provide the scaffold for ossification.

This type of ossification is seen in about a third of simple bone cysts at the time of surgical exploration. Its true incidence may be higher, because traces of calcified fibrous scaffold within the bone trabeculae must eventually disappear during the process of remoulding of bone. These old flocculent fibrin coagula, with or without calcification or ossification, are not seen in other common cystic conditions of bone, and thus provide a valuable aid in the histological diagnosis of a simple bone cyst.

Cystic infarct of bone, if indeed such a condition exists, could perhaps be an exception to this generalisation, because such a cyst might have many features in common with a simple bone cyst. There is no proven example of a cystic infarct in our records, although the iliac cyst illustrated in Figure 4 might arguably be one. Coley (1949), in discussing the possible origin of a simple bone cyst from a bone infarct, stated that “cystic lesions do not follow the aseptic necrosis caused by known infarctions, such as those seen in caisson workers”. Jaffe (1972) believed that “the site of an infarction may come to present, on gross examination, the appearance of a multiloculated cyst”. However, his illustration of a cystic infarct, discovered incidentally in the femoral neck and intertrochanteric region of a seventy-two-year-old man without any history of hyperbaric exposure, could well have been a partly obliterated simple bone cyst, judging by its site and appearance. Dahlin (1978) stated that bone infarcts might be mistaken for cysts and provided a radiological example of an “infarct with cystic change in the os calcis”. This, however, would appear to be a typical simple bone cyst, with a calcified or ossified fibrin coagulum in its cavity, similar to that shown in Figure 5. The subject of cystic bone infarct and its relationship to simple bone cyst remains controversial.

I would like to thank the very numerous colleagues who have referred their cases to the Bristol Bone Tumour Registry with clinical, radiological and pathological material; to Mr M. Findlay, Mr P. J. Hall and Mr A. Wilson for technical and photographic assistance; and to Mrs J. N. Nutt for secretarial help.

REFERENCES
OLD FIBRIN COAGULA AND THEIR OSSIFICATION IN SIMPLE BONE CYSTS


