BENIGN GIANT-CELL SYNOVIOMA AND ITS RELATION TO "XANTHOMA"

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In recent years increasing interest has been taken in tumours of synovial origin whether articular, bursal, or tenosynovial, and the literature has been enriched by many notable contributions. This communication is concerned primarily with the most frequent of these neoplasms, the so-called myeloid tumour of tendon sheaths or, as I prefer to call it, the benign giant-cell synovioma, and especially with its supposed relationship to "xanthoma."

Most of these tumours arise from tendon sheaths, especially those for the flexors of the fingers and thumb. There were forty cases in the routine surgical pathological material of the General Infirmary at Leeds during the years 1914-47. Of these, thirty are available for analysis.

Age distribution—These tumours seldom occur under the age of ten years, or over the age of sixty years.

<table>
<thead>
<tr>
<th>TABLE I</th>
<th>AGE DISTRIBUTION AT THE TIME OF OPERATION IN THIRTY CASES OF BENIGN GIANT-CELL SYNOVIOMA</th>
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<tbody>
<tr>
<td>Age periods .</td>
<td>0-9</td>
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<tr>
<td>Number .</td>
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</tbody>
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It may be remarked that whereas in this series of benign synoviomas twenty-six out of thirty (87 per cent.) were encountered between the ages of twenty and fifty-nine years, in an almost contemporary series of 120 cases of osteoclastoma from the same hospital only seventy-two (60 per cent.) occurred in this age group. This difference is due mainly to the greater frequency of osteoclastoma in the first two decades of life, but in part to the greater delay in seeking surgical aid for a slow-growing and unobtrusive lesion like benign synovioma.

Sex distribution—The ratio of males to females was seventeen to thirteen in the benign synovioma series and forty-three to seventy-seven in the osteoclastoma series.

Site of occurrence—The site of origin was stated, though not always exactly, in twenty-six of the forty cases; nineteen, or nearly three out of four, were situated in the fingers.

<table>
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<tr>
<th>TABLE II</th>
<th>SITE OF TWENTY-SIX CASES OF BENIGN GIANT-CELL SYNOVIOMA</th>
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<tbody>
<tr>
<td>Site . . .</td>
<td>Fingers</td>
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<tr>
<td>Number .</td>
<td>13</td>
</tr>
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</table>

The tumour of the knee was the only one in this series which was related definitely to a joint; but I have seen two others in this situation. It is obvious from these and other published figures that the site of election for this tumour is the digital tendon sheaths, especially of the hands. Malignant synoviomas on the other hand arise mainly from joints and bursae of the lower limbs. In Stout and Haagensen’s collected series of 104 cases, nearly half (forty-nine) originated from the knee joint, almost a fifth (nineteen) in the region of the foot and ankle, and only four in the fingers.
MORBID ANATOMY

The benign giant-cell synovioma is a tumour of slow growth and firm consistency. It has usually been present for many months, or even a year or two, before being removed surgically. Excised specimens from the fingers are small, and seldom more than two or three centimetres in diameter. Almost invariably they are situated on the flexor aspect. They usually show a deep, straight, narrow groove on one side. In this lay the tendon while the tumour was still in situ. Lobulation is often a prominent feature and the tumour is well defined. I have seen one case, however, in which the growth was adherent to, and indeed infiltrating, the overlying skin.

On section the cut surface is grey, but it usually shows yellow or brown flecking towards the periphery. The yellow flecking is due to deposits of cholesterol fat with its associated carotene. The brown pigment is haemosiderin, which gives a strong Prussian blue reaction with hydrochloric acid and ferrocyanide of potassium. Sometimes the whole tumour shows this yellow and brown mottling but more often it is distributed in a patchy manner (Fig. 1). The heaviest grade of siderosis I have ever seen in a benign synovioma was in one from the flexor tendon sheath of the great toe. It had attained an unusually large size and had no doubt been exposed to severe and repeated injury.

![Fig. 1](image)

Slices through two benign giant-cell synoviomas of tendon sheaths. In each instance the upper slice has been treated to show the Prussian blue reaction and is from the same tumour as the lower (unstained) slice. The lower slices show the rusty mottling due to haemosiderin deposits, with opaque yellowish patches of lipoid accumulation. The slices to the left show the groove which contained (in this case) the flexor tendon of the affected finger.

Benign synoviomas of joints and bursae usually take the form of plaques in the capsule, but polypoid formations, often multiple, may project into the joints. It is in this variety that the amount of lipoid deposit is greatest and the histological structure becomes simply an accumulation of foamy cells held together by a delicate collagenous and vascular framework. In chronic villous arthritis on the other hand, the villi, though sometimes of a rich brown or chocolate colour from massive haemosiderin deposits, seldom contain any appreciable amount of lipoid.

HISTOLOGY

The microscopic structure of the benign giant-cell synovioma is usually unmistakable. The fibrous stroma, of variable density and amount, is collagenous and often much hyalinised. In the interstices lie small groups of polygonal cells, arranged either in small masses without intercellular fibres or lining small spaces. Associated with these cells of frankly lepidic* [*“Lepidic” refers to the tissues of lining membranes characterised by the absence of definite stroma between individual cells.—EDITOR.]

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character (and probably derived from them by fusion) are variable numbers of multinucleated giant cells, similar in appearance to osteoclasts or foreign-body giant cells. Large areas of the tumour may be almost completely fibrous; other areas are richly cellular, including both numerous giant cells and lepidic cell-groups.

![Figure 2](image)

**Fig. 2**
Section from one of the xanthic areas in the larger of the two tumours in Fig. 1, showing numerous foamy cells of neoplastic origin.

![Figure 3](image)

**Fig. 3**
Section from one of the areas of rusty mottling in Fig. 1, showing many of the tumour cells charged with haemosiderin granules.

The resemblance to osteoclastoma is remote indeed. That the glandular spaces are usually devoid of mucoid content is I think the only objection to regarding them as of synovial origin. By contrast, the most characteristic examples of malignant synovioma often show mucicarmine-staining material in such alveolar spaces as are present.
In benign synovioma the deposition of lipoid and of haemosiderin are secondary phenomena. Lipoid is deposited in consequence of necrobiotic changes in tumour tissue over the course of months or years. The deposition of haemosiderin is due to siderosis from traumatic effusion of blood. Both the lipoid and the haemosiderin may be taken up by the essential tumour cells (Figs. 2-3). These being synovial, and therefore no more than differentiated histiocytes, still retain many of the more primitive functions of the latter, including phagocytosis. Other non-neoplastic macrophage cells of histiocytic, fibrocytic, or endothelial type are also concerned in the process.
The so-called "Xanthoma" Cell

The occurrence of cholesterol fat in tumours is often observed, but its significance has been misinterpreted. Cholesterol fat is sometimes present within the tumour cells themselves, apparently as a functional manifestation. Examples of this are seen in renal carcinoma of the hypernephroma type, in adrenal cortical adenoma, and in certain types of ovarian tumour. Many fibrous tissue and endotheliomatous tumours of the skin, mostly benign and of slow growth, assume to the naked eye a yellow colour owing to a proportion of the tumour cells undergoing this "xanthic" change. In other instances tumours become infiltrated locally with lipid-filled non-neoplastic phagocytes. Infiltration of this type is common, especially in tumours of slow growth where slow necrobiotic changes occur from a deficient blood supply. The lipid taken up by the phagocytic cells is derived from disintegrating tumour tissue, extravasated blood, or secretory products. The commonest examples are adenomas of the thyroid, adenopapillomas of the kidney (Fig. 4), and the more slowly growing neurofibromas (for example of the acoustic nerve); but all sorts of tumours may show this secondary change.

In the benign giant-cell synoviaoma both types of cell, neoplastic and non-neoplastic, may be concerned in this phagocytic process, as also in the phagocytosis of haemosiderin. In certain articular synoviomas the amount of accumulated lipid may be very great and it is to such tumours that the term "xanthoma" has often been applied.

![Fig. 6](image)

Bilateral xanthomata of choroid plexuses. Specimens from two cases. (Natural size.)

Many writers do not yet realise that the term "xanthoma" is a misnomer. It is no doubt convenient to apply the suffix "oma" in this loose way to any sort of mass or lump (for example granuloma, syphiloma, and tuberculoma), but it should never be so used except on the clear understanding that it does not imply neoplasia. In the three instances quoted no difficulty arises; their non-neoplastic nature is clearly understood. The term "xanthoma" however, is in a different category, because it has been applied not only to frankly non-neoplastic conditions like the cutaneous xanthoma of hypercholesterolaemia and to "xanthomas" of the choroid plexus (Figs. 5–6), but also to genuine neoplasms of various kinds in which the presence of lipid is entirely a secondary phenomenon.

It must be insisted that there is no such thing as a xanthoma in the neoplastic sense of the term any more than there is a neoplastic "tuberculoma" or "sideroma". Twenty-four years ago (Stewart 1924) I endeavoured to introduce the term "xanthosis" on the analogy of "siderosis" to cover this condition of infiltration by cholesterol fat whatever the nature of the cells involved. The seed fell on stony ground.

It is still more unfortunate that "xanthoma cell" should have established itself in our terminology. There is no such thing as a specific xanthoma cell. As I have indicated, many types of cell are capable of becoming charged with cholesterol fat—histiocytes and fibrocytes; serosal, endothelial, and synovial cells; renal epithelium and microglia; not to mention cells of the adrenal cortex, corpus luteum and sebaceous glands; and probably other cells whether
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healthy or diseased. In America, certain writers now speak of pseudo-xanthoma cells when, I gather, they mean no more than lipoid-filled phagocytes. Thus they imply that there is such a thing as a specific and presumably neoplastic cell to which alone the term xanthoma cell is strictly applicable.

All lipoid-filled cells, whatever their nature, are recognisable in paraffin sections by virtue of the foamy cytoplasm, and in fresh frozen sections by the content of doubly refracting cholesterol ester droplets. Their true nature, whether neoplastic or otherwise, can be determined only by other histological characters and by anatomical arrangements and relationships.

The prefix is correctly used in "fibro-xantho-endothelioma" and "xanthic neurofibroma." No doubt "xanthoma" will continue to be used as a convenient name for the infiltrative cutaneous lesion which results from hypercholesterolaemia, and for the "pure" xanthoma of the choroid plexus (usually bilateral), which also is a simple infiltration by "foamy" cells; but there must be no implication of neoplasia. The terms "xanthoma cell" and "pseudo-xanthoma cell" should be dropped.

SUMMARY

Benign giant-cell synovioma, the most frequent example of which is the well-known myeloid tumour of tendon sheaths, is used as a text for the discussion of the true significance of the so-called "xanthoma" cell. These cells are the result of the phagocytosis of cholesterol esters and are of varied histogenesis. Some are undoubtedly of neoplastic origin; most of them are not, being usually histiocytic, fibrocytic, serosal or endothelial. There is no such thing as a specific xanthoma cell.

The term "xanthosis" might well be used to designate this process of infiltration of tissue with cholesterol fat, and the prefix "xantho-" or the adjective "xanthic" in tumour terminology, as for example in "fibro-xantho-sarcoma," "xanthic neurofibroma," and so on.

REFERENCES

