TWO TYPES OF SOFT TISSUE SARCOMA OF UNCERTAIN HISTOGENESIS

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SUMMARY.— A brief account is given of two types of rare soft tissue sarcoma of uncertain histogenesis. The danger of mistaking the epithelioid sarcoma for a benign lesion is emphasized.

ENZINGER (1965, 1970) delineated two rare types of sarcoma arising in soft tissues. Although the cell of origin is unknown in both types, these neoplasms have a characteristic histological appearance and natural history. The clear cell sarcoma of tendon and aponeurosis is unlikely to be mistaken for a benign tumour, but the epithelioid sarcoma is a sinister entity liable to be misdiagnosed as a benign granulomatous proliferation or, alternatively, as a carcinoma. There may seem little justification for recording a very few further cases, but in the last 9 months I have seen three cases of the epithelioid sarcoma all diagnosed as benign. In two of these the diagnosis was granuloma annulare. Therefore, a brief report of these cases in an English Journal and of several others found in the files of Westminster Hospital seemed justified. For comprehensive accounts readers are referred to Enzinger's definitive papers on the subject.

Clear Cell Sarcoma of Tendons and Aponeuroses

Enzinger (1965) described 21 cases of this rare and unusual neoplasm. Kubo (1969) described the electron microscopic appearances of a case arising from the patellar tendon. Dutra (1970) recorded three further cases. In his Cases 1 and 2 there were considerable differences of opinion regarding the nature of the neoplasms and the photomicrographs are not entirely convincing. These tumours, which can occur at any age, usually present as a slowly growing painless mass. They are slightly more common in women. They arise from tendinous structures in the extremities and are commonest in the foot and ankle region. They pursue a slow but relentless clinical course with a tendency towards repeated recurrences and eventual metastases. In Enzinger's series 14 cases died with metastases particularly in the lungs and lymph nodes.

Pathology

The tumours are usually firm, roughly spherical, with a smooth, nodular or coarsely lobulated surface. A pseudocapsule may be present. They are intimately associated with a tendon or aponeurosis. The size usually ranges between 2 cm. and 6 cm. They have a grey, white or matted cut surface and small cysts may be seen in a minority of cases.

TABLE I.—*Clear Cell Sarcomas*

Case	Age	Sex	Site	Recurrences	Metastases	Treatment	Follow-up	Length of initial history	Initial diagnosis
1	27	M	Ankle	0	Inguinal nodes, lungs, pleurae, ribs	Excision, radiotherapy, later amputation	Died after 6½ years	Not known	Synovial sarcoma
2	51	M	Ankle	0	Multiple metastases.	Excision, radiotherapy	Died after 3 years	1 year	Synovial sarcoma
3	19	M	Ankle	2	No P.M. Inguinal nodes, lung	Excision, radiotherapy	Alive with metastases 22 years	6 months	Synovial sarcoma
4	30	M	Ankle	0	Popliteal fossa	Excision followed by amputation	Alive and well 6 years	Not known	Clear cell sarcoma
5	40	F	Thigh	—	Lost to follow up		—	—	Clear cell sarcoma
6	19	F	Lower back	0	Inguinal nodes	Excision	Alive with metastases	3½ years	Clear cell sarcoma

TABLE II.—*Epithelioid Sarcoma*

Case	Age	Sex	Site	Recurrences	Metastases	Treatment	Follow-up	Length of initial history	Initial diagnosis
1	21	F	Upper arm	0	Lungs	Excision and radiotherapy	Died after 1 year	7 months	Synovial sarcoma
2	29	M	Hand	1	—	Excision and later radiotherapy	Alive and free of disease 15 years	2 years	Synovial sarcoma
3	24	F	Hand	1	—	Excision and radiotherapy	Alive and free of disease 10 years	Not known	Synovial sarcoma
4	42	F	Finger (tip)	1	Nodule at base of same finger	Excision and later amputation of finger	Alive and free of disease 3 years	1 year	Granuloma annulare
5	23	M	Forearm	1	Skin, lungs	Excision and radiotherapy and amputation	Alive with metastases 4 years	3 years	Sclerosing angoma
6	18	M	Finger	1	—	Excision	Alive and well 1 year	Not known	Granuloma annulare
7	63	F	Near knee	1	Lymph nodes	Excision and radiotherapy	Alive and free of disease 1½ years	Not known	Epithelioid sarcoma
8	35	F	Forearm	—	A recent case	—	—	—	Epithelioid sarcoma
9	2½	F	Hand	1	A recent case	—	—	—	Epithelioid sarcoma

Histologically the tumours are made up of nests and fascicles of pale fusiform cells of epithelioid appearance which often have prominent nucleoli. Connective tissue septa often enclose these cellular aggregates. Multi-nucleated giant cells have been described in over half the cases. The characteristic picture is shown in Fig. 1–6. In one of my own cases the histological picture suddenly changed to a pattern markedly reminiscent of an alveolar rhabdomyosarcoma (Fig. 4). No cross striations were identified and Enzinger who was kind enough to examine the sections regarded the change as being due to “tissue shrinkage, compounded by the effect of muscle infiltration and fibrosis” (personal communication, 1970).

In his experience the typical histological picture may be lost in recurrent or metastatic lesions. Diagnoses which have been applied to this neoplasm in the past include synovial sarcoma, fibrosarcoma, alveolar soft part sarcoma and malignant melanoma. A detailed discussion is given in Enzinger's original paper.

I have had the opportunity of studying six cases. The details of these are shown in Table I.

Epithelioid Sarcoma

Enzinger (1970) gave a comprehensive account of this unusual neoplasm and his findings are summarized briefly.

One of the most remarkable things about this neoplasm has been the multiplicity of diagnoses applied to it. Enzinger lists 11 different benign diagnoses to which must be added granuloma annulare and 20 different malignant ones. The most frequent diagnoses were granuloma and synovial sarcoma.

These tumours can occur at any age but 70% occur between 10 and 34 years. The male/female ratio is approximately 3 : 1. They tend to arise as firm subcutaneous nodules or as chronic ulcers of the skin. Pain is a variable feature. In Enzinger's series of 62 cases all occurred in the extremities except two which arose in the scalp. The commonest site was the volar aspect of the fingers. The tendency was towards recurrences and ultimate metastatic spread. Follow-up information on 54 patients (87%) revealed slow, relentless clinical course with frequent recurrence (85%) and late metastasis (30%). The lungs and the scalp were the commonest site for metastases.

Histologically these tumours are characterised by the nodular arrangement of the tumour cells, their tendency to undergo necrosis and in many cases by the

EXPLANATION OF PLATES

- FIG. 1.—Case 1. Clear cell sarcoma. Showing nests and fascicles of pale fusiform cells. H. and E. $\times 145$.
 FIG. 2.—Case 1. Clear cell sarcoma. Showing cells with pale cytoplasm and well defined nucleoli. H. and E. $\times 410$.
 FIG. 3.—Case 1. Clear cell sarcoma. Bundles of cells outlined by reticulin. Gordon and Sweets. $\times 150$.
 FIG. 4.—Case 1. Clear cell sarcoma. Showing an appearance reminiscent of an alveolar rhabdomyosarcoma. H. and E. $\times 95$.
 FIG. 5.—Case 4. Clear cell sarcoma. A similar appearance to Fig. 1. H. and E. $\times 150$.
 FIG. 6.—Case 6. Clear cell sarcoma. Showing sheets of pale cells interspersed by thin fibrous trabeculae. H. and E. $\times 205$.
 FIG. 7.—Case 3. Epithelioid sarcoma. Showing epithelioid-like cells surrounding an area of necrosis. H. and E. $\times 165$.
 FIG. 8.—Epithelioid sarcoma. A similar picture. H. and E. $\times 145$. (By courtesy of Dr. F. M. Enzinger.)
 FIG. 9.—Case 5. Epithelioid sarcoma. A metastatic nodule modified by radiotherapy. H. and E. $\times 145$.
 FIG. 10.—Case 6. Epithelioid sarcoma. An area devoid of necrosis. H. and E. $\times 185$.

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eosinophilia of the cytoplasm when stained with haematoxylin and eosin. The cells themselves range from plump spindle cells to large round or polygonal cells resembling epithelioid or squamous cells. Considerable desmoplasia resulting in the deposition of considerable birefringent collagen about the tumour cells is also a feature. Characteristic appearances are shown in Fig. 7-10.

Nine cases have been seen at Westminster Hospital. Two cases were diagnosed originally as granuloma annulare, one as a sclerosing angioma and three as synovial sarcomas. The details are given in Table II.

DISCUSSION

Knowledge of the exact cell of origin of any neoplasm is clearly desirable. Nevertheless, by defining the clinicopathological characteristics of both these neoplasms with great accuracy, Enzinger has made possible a rational approach to diagnosis and treatment. Kubo (1969) considered that the electron microscopic appearance of the clear cell sarcoma showed a resemblance to synovial lining cells and he suggested that this neoplasm might be a variant of synovial sarcoma. In this connection it is of interest that electron microscopic studies of three cases of the epithelioid sarcoma also showed some features suggestive of both synovial cells and histiocytes (Enzinger, 1970). At the moment, however, there is no conclusive evidence as to the cell of origin of either of these neoplasms.

Both show a marked tendency to recurrence and both are capable of ultimate metastatic spread. The epithelioid sarcoma is the more dangerous of the two because misdiagnosis is more likely. This is particularly true when it presents as a dermatological problem. This brief summary of their main characteristics is an attempt to bring these rare neoplasms to the attention of clinicians and pathologists.

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ADDENDUM

Since the completion of this paper a personal communication has been received from Dr. F. M. Enzinger. He has seen about 30 additional cases of clear cell sarcoma since 1965. Two showed melanin pigmentation and in one case this was confirmed by electron microscopy. This observation suggests a neuroectodermal origin for these tumours.