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Synovial Sarcoma of the Abdominal Wall

Light Microscopic, Histochemical and Electron Microscopic Investigations

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Summary. A synovial sarcoma of the abdominal wall in a 56-year old woman showed the typical features of this tumor type. Histologically a characteristic biphasic cellular pattern with epithelium-like cell complexes and sarcomatous spindle cell areas was found. The histochemical examination revealed that tumor cells synthesize glycoproteins and weakly acid glycosaminoglycans (mainly hyaluronic acid). Electron microscopically the tumor cells in epithelium-like cell islets were sometimes arranged in gland-like formations with microvilli at the luminal side, specialized intercellular junctions and a peripheral basement membrane-like condensation of the ground substance. There was no fundamental cytological difference between cells of epithelium-like and spindle cell areas. Generally the tumor cells imitated cells of the synovial membrane and we found no evidence for origin from cells of the nerve sheath. Because of the submicroscopic relationship and histochemical similarities of synovial sarcomas and mesotheliomas we suggest that they should be united in a group of sarcomas with possible biphasic cellular pattern, while preserving their clinicopathologic definition.

Key words: Synovial sarcoma – Abdominal wall – Ultrastructural cytology – Histochemistry of synovial sarcoma – Biphasic cellular pattern.

Introduction

Synovial sarcomas are distinctive tumors with a biphasic cellular pattern forming clefts or acinar structures lined by epithelium-like cells while showing spindle cell areas of varying cellular density (Enzinger et al. 1969). Within these typical features a broad scale of histological phenomena can be seen which depend

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on varying proportions of pseudoepithelial and spindle cell components and on their changing degree of differentiation.

Synovial sarcomas are encountered in different localizations. It is well known that they favour the extremities, but they may also occur in the regions of neck, head and pharynx as well as the trunk (Cadman et al. 1965; Moberger et al. 1968; Lee et al. 1974; Roth et al. 1975; Choux et al. 1978). Usually, these malignant soft tissue tumors do not arise from the proper synovial membrane or tendon sheath, but develop in the periarticular or peritendinous mesenchyme.

It is generally accepted that the term "synovial sarcoma" is without histogenetic implications. It only means the inclination of the sarcomatous tissue to differentiate into a synovial-like pattern (Haagensen and Stout 1944; Pack and Ariel 1950; Mackenzie 1966; Batsakis et al. 1967).

Soft tissue sarcomas of the abdominal wall which fulfil the criteria of synovial sarcomas are extremely rare (cp. Berkheiser 1952; Moses et al. 1959; Moberger et al. 1968). Hitherto it is not known whether this unusual site causes modifications of the ultrastructural cytology when compared with synovial sarcomas of the joints. In addition, ultrastructural examination of such a case might support or refute the new concept that the cells of synovial sarcomas develop from cells of the nerve sheath (Ichinose et al. 1979). For these reasons we examined a synovial sarcoma of the abdominal wall with light microscopic, histochemical and electron microscopic methods.

Material and Methods

A 56-year old woman was admitted to hospital because she had noticed a tumor in the right anterior abdominal wall for some weeks. The tumor showed a rapid growth. Pain or other symptoms were absent. After admission she was operated on, with a provisional diagnosis of myosarcoma. The tumor was the size of an egg, was of grey-whitish colour and possessed a fleshy consistency. It was situated deep in the abdominal wall and infiltrated the musculus transversus and the musculus obliquus internus abdominis. The peritoneum was intact and not involved by the tumor. The neoplasm was completely removed with a rim of healthy tissue and immediately prepared for light and electron microscopic examination.

Light microscopic methods: After fixation in 5% neutral formalin and embedding in paraffin 5 mμ thick sections were made. The following stains were performed: Haematoxylin-eosin, elastica-van Gieson, Goldner's and Mallory's trichrome stain and silver impregnation after Gömöri.

Histochemical procedures: Periodic acid-Schiff reaction (PAS), diastase-PAS, colloidal iron binding reaction after Hale in the modifications of Müller and Mowry, Alcian blue at different pH with and without pretreatment with hyaluronidase (pH 2.5, 1.0 and 0.5), differential staining of acid glycosaminoglycans by Alcian blue in magnesium chloride solution after Scott and Dorling (1965) and Alcian blue-PAS. Furthermore, mast cells were visualized by toluidine blue and by the naphthol-AS-D-chloracetate esterase reaction (histochemical methods s. Pearse 1972).

For the purpose of electron microscopic examination small tissue samples were subjected to a fixation in 2.5% glutaraldehyde (pH 7.2 with 0.1 M cacodylate buffer) for 2 h, postfixed with OsO_4 for 1 h and embedded in Mikropal. Semithin sections were stained with toluidine blue, ultrathin sections were contrasted with uranyl acetate and lead citrate.

Results

Light Microscopy

Histological examination showed that in all tumor regions the typical biphasic pattern of a synovial sarcoma was present. However, the proportions of the two components changed in different areas (Fig. 1). Epithelium-like cell complexes were embedded in a sarcomatous stroma with a high cellular density. The epithelium-like cells were of a moderate size. Occasionally pseudoglandular formations occurred within these cell complexes and the patterns varied from simple clefts to acinus-like structures (Fig. 1b). The content of such cavities was often slightly eosinophilic. In some areas the epithelium-like cells seemed to be clear cells (Fig. 1d). The stromal cells were spindle-shaped and possessed rather chromatin-dense nuclei. Single spindle cells or small cell clusters were surrounded by reticular fibers, which were only observed in the spindle cell stroma (Fig. 2a). Large amount of mast cells were found in areas of spindle cells (Fig. 2d). Collagen fibers were not demonstrable and could only be demonstrated in the focally present pseudocapsule. Occasionally hyalinized areas were seen in regions with spindle cells (Fig. 1e). The frequency of mitoses varied, but their presence was limited to spindle cell areas. Invasive growth of the tumor could clearly be demonstrated in peripheral regions; here and there a pseudocapsule was present, but in other fields infiltration of the adjacent skeletal musculature by both the structural components was obvious (Fig. 1c).

Histochemistry

The results of the PAS reaction were somewhat different in the two structural components of the tumor. In the epithelium-like cell clusters the material within the pseudoglandular cavities was moderately or very positive (Fig. 2b). Large cavities contained thread-like positive material. The epithelium-like cell islets were occasionally demarcated from the sarcomatous stroma by a narrow band of PAS-positive material. Within the regions with spindle cells a network of fine PAS-positive structures could be detected. Hyalinized regions were likewise weakly positive with the PAS reaction.

Acid groups were demonstrated by the colloidal iron binding reaction after Hale and Alcian blue staining at different pH and at pH 5.7 with varying admixture of $MgCl_2$. It was found that the material within the pseudoglandular cavities was clearly positive after staining with Alcian blue at pH 2.5 and with colloidal iron (Fig. 2c). It lost its staining ability with Alcian blue at pH 5.7 between 0.2 and 0.45 M $MgCl_2$ concentration. It is remarkable that some lumina in the epitheloid cell clusters also contained Alcian blue-stainable material at pH 1.0. At pH 0.5 all structures in the tumor were negative after Alcian blue staining, only the mast cells occurring in the sarcomatous stroma were strongly positive (Fig. 2d). Mast cells were also easily demonstrable by the naphthol-AS-D-chloracetate esterase reaction. Acid groups in the spindle cell regions were

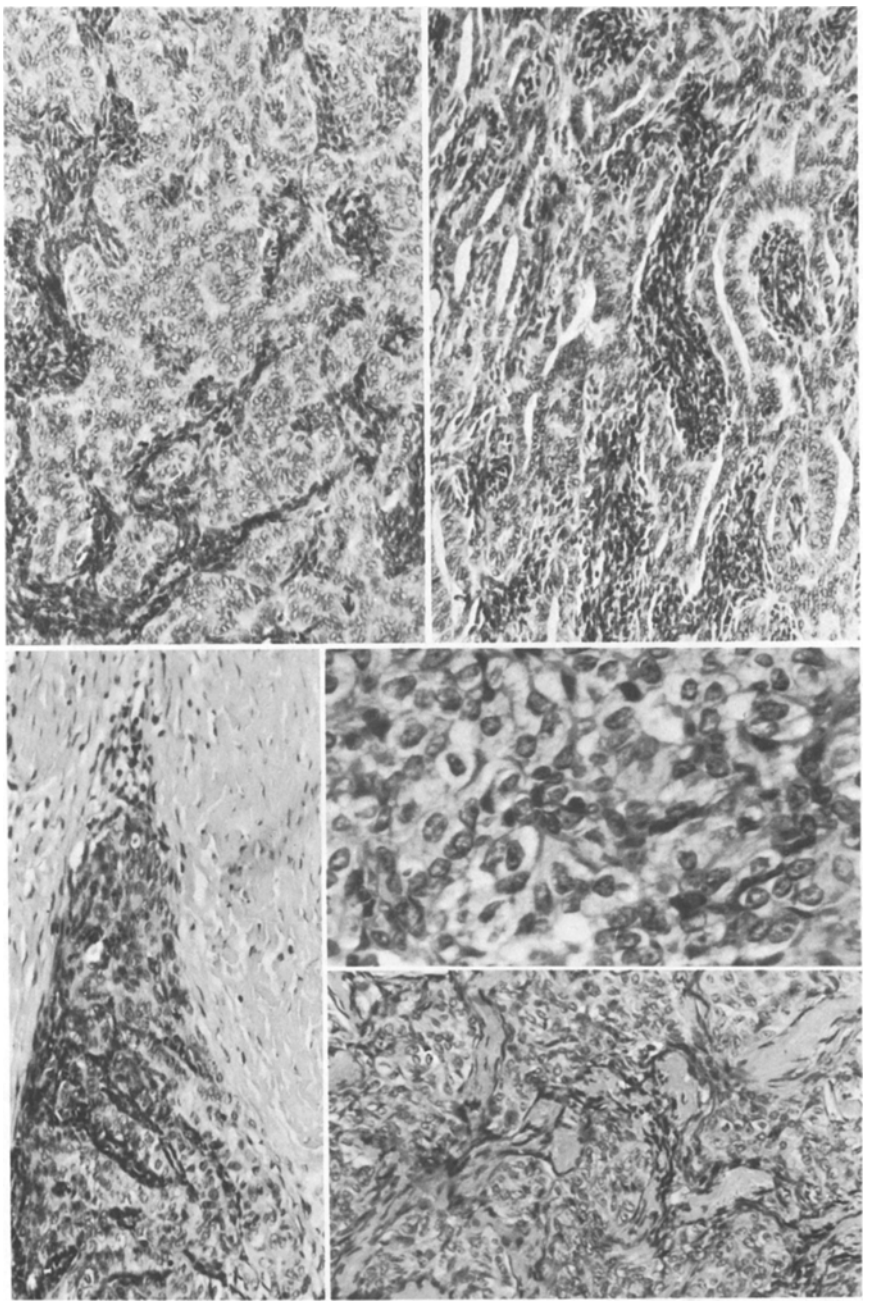

Fig. 1a–e. Light microscopic structure of synovial sarcoma. **a** Typical biphasic cellular pattern with epithelium-like cell complexes and spindle cell areas (HE, 160:1). **b** The epithelium-like cells are arranged in gland-like formations (HE, 160:1). **c** The tumor infiltrates connective tissue structures. Both the structural components are visible (HE, 160:1). **d** A solid area within the sarcoma which shows several clear cells (HE, 380:1). **e** Tumor cell clusters and some hyalinized regions can be seen (HE, 160:1)

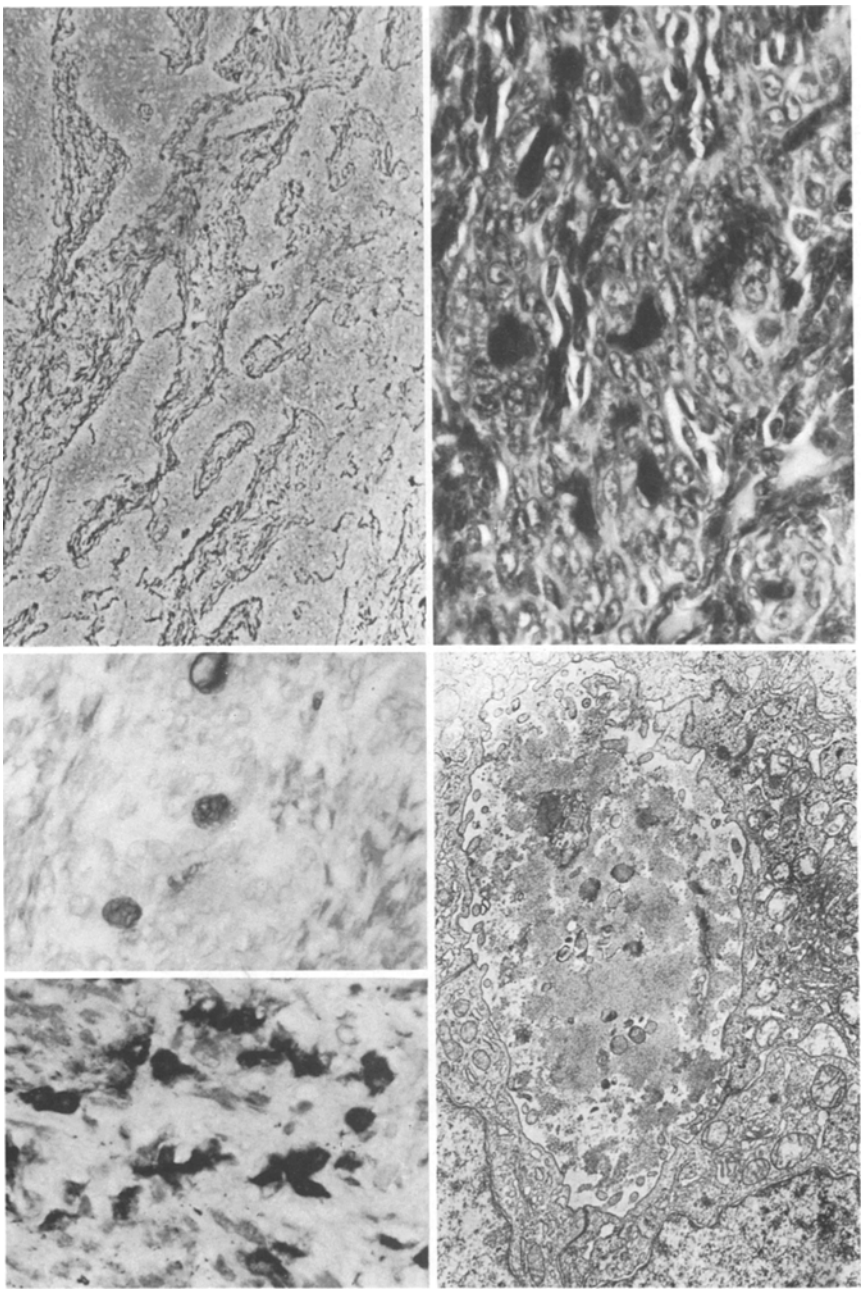

Fig. 2. a Reticular fibers are only present in spindle cell areas, they are lacking in the epithelium-like cell clusters (Gömöri, 160:1). **b** The PAS reaction shows positive substance within the gland-like cavities (380:1). **c** Staining with Alcian blue at pH 2.5 also demonstrates a positive substance within the gland-like lumina (380:1). **d** Alcian blue at pH 0.5 only stains mast cells (380:1). **e** Electron microscopically within the gland-like cavity finely granular and vesicular materials can be shown. Note the microvilli of the lining cells (11,200:1)

identified in moderate quantity by Alcian blue pH 2.5 and weakly by the Hale reaction. Alcian blue staining was negative within the spindle cell areas below 0.45 M $MgCl_2$ and within hyalinized areas below 0.8 M $MgCl_2$. Pretreatment with hyaluronidase prevented a positive reaction after Alcian blue staining, as in Wharton's jelly of the umbilical cord, which was used for comparison.

Electron Microscopy

Electron microscopically both the structural components of the synovial sarcoma could be distinguished by the cellular density, the amount of intercellular substance and the relationship of cells to each other. The cytological features of the single cells did not vary essentially (Figs. 3, 4 and 5).

The cells of the epithelium-like complexes were situated close to each other resulting in parallel orientation of their cell membranes and a paucity of intercellular substance (Figs. 3a, 5a, c and d). Furthermore, interdigitations of cells were often observed. The formation of gland-like cavities was seen. Microvilli-like projections on the luminal side of the lining cells and terminal bar-like intercellular junctions, together with desmosomes, strengthened the resemblance to true glands (Fig. 2d, 3a, 5a, b and c). The distribution and composition of the cytoplasmic organelles, however, was not compatible with true glandular epithelial cells. The cavities frequently contained a fine granular electron-dense material (Fig. 2d). Around these closely packed cellular clusters a narrow zone of condensed amorphous intercellular substance could be perceived relatively often. It had a width of 1,000–1,500 Å and focally resembled a basement membrane (Fig. 3b). Typical basement membranes could not be identified.

The cells in the so-called stroma were of a spindle shape but often clearly irregular (Figs. 3b and 4c). As a rule the cells were separated by intercellular substance although single cells were seen with a certain portion of their plasma membrane in close proximity, leaving only a tiny space between them. Desmosome-like intercellular junctions were few. A basement membrane-like structure around the cells was constantly lacking. The intercellular substance consisted preponderantly of an amorphous moderately electron-dense material although some fine filamentous structures and a few small collagen fibers (600–1,000Å thick) with the typical periodicity of mature collagen were present (Fig. 4c).

The cytological characteristics of tumor cells varied, but in general the organelles in cells of epithelium-like clusters and spindle celled areas was similar. Depending on the number of organelles, light and dark cells could be distinguished, in both epithelium-like islets and in spindle cell areas.

Tumor cells of the epithelium-like clusters possessed a round or polygonal shape and a correspondingly shaped nucleus with frequently deep notchings and indentations. The heterochromatin was visible in either coarse lumps or in a finely despersed distribution. Nucleoli of moderate size and some nuclear bodies evidenced nuclear activity (Fig. 3a). The cytoplasmic organelles consisted of a moderate to large amount of mitochondria, a multicentric and activated Golgi apparatus, free ribosomes which were often arranged as polysomes, some non-dilated tubes of rough endoplasmic reticulum, a varying amount of vesicles

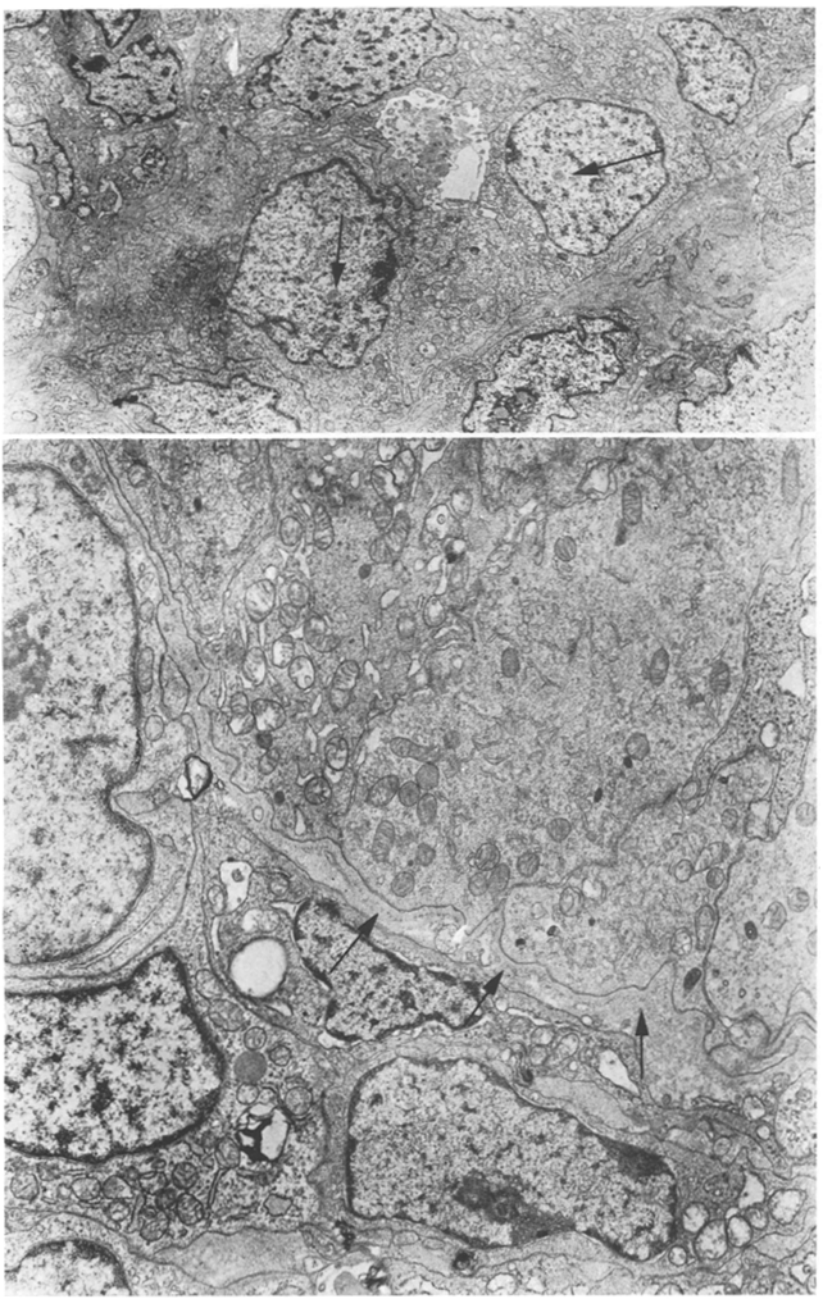

Fig. 3. a An epithelium-like cell cluster with a gland-like lumen is detectable. The nuclei show a somewhat irregular configuration, a moderate amount of heterochromatin and two nuclear bodies (→). The cells are closely packed (4,800:1). **b** Cells of an epitheloid cluster are separated from "stromal" cells by a basement membrane-like condensation of ground substance (→). In the "stromal" cells somewhat more rough endoplasmic reticulum is present than in epithelium-like cells, but there are no fundamental differences in the cytological features (11,500:1)

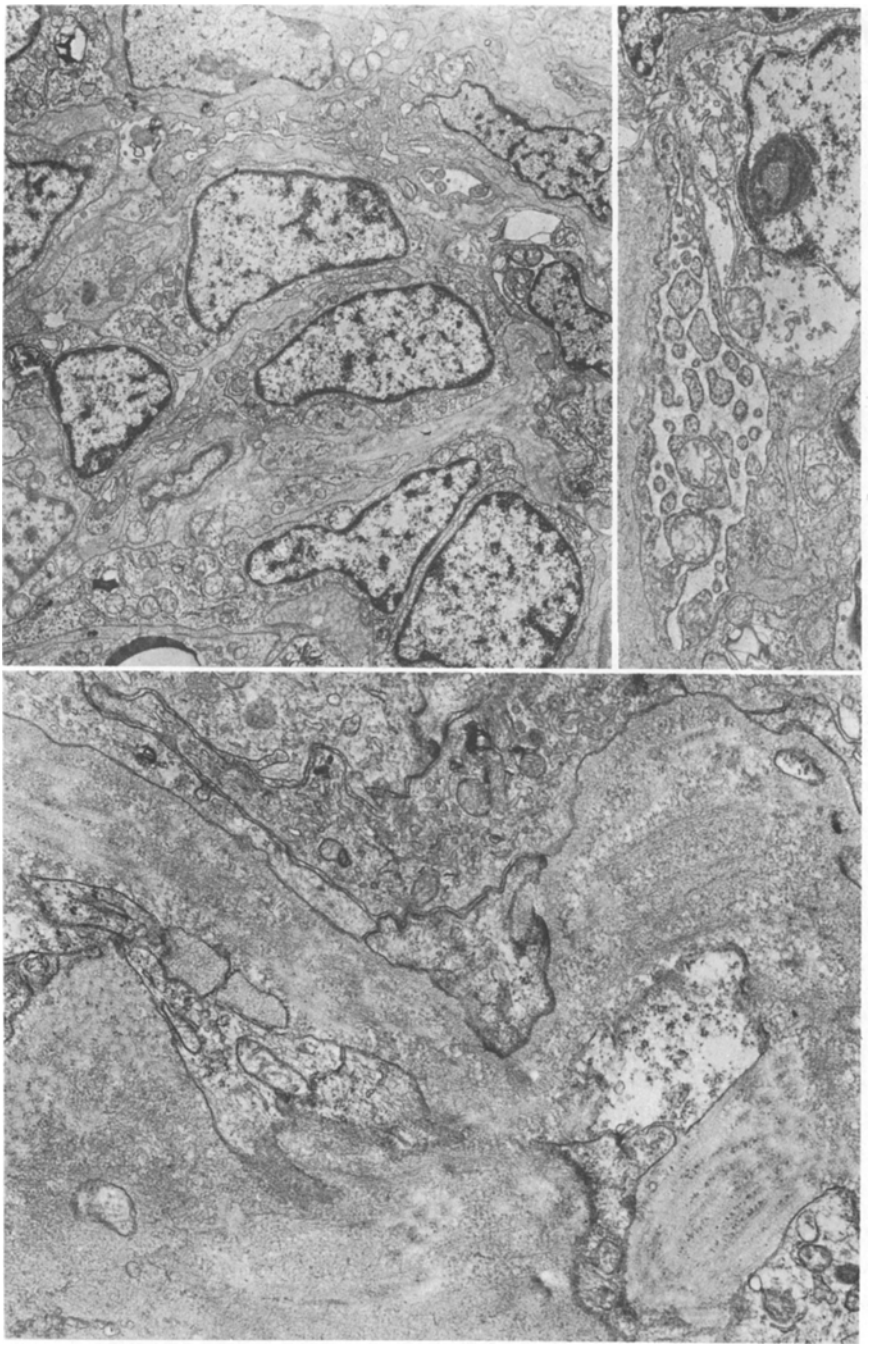

Fig. 4. a Cells in spindle cell areas are less closely packed than in epitheloid clusters. In the intercellular space amorphous ground substance and some collagen fibers are visible. The organelle equipment corresponds to uncharacteristic sarcoma cells (6,900:1). **b** A spindle cell with abundant and partially dilated rough endoplasmic reticulum (12,000:1). **c** Finely granular ground substance, filamentous structures and collagen fibers can be detected between cells (18,000:1).

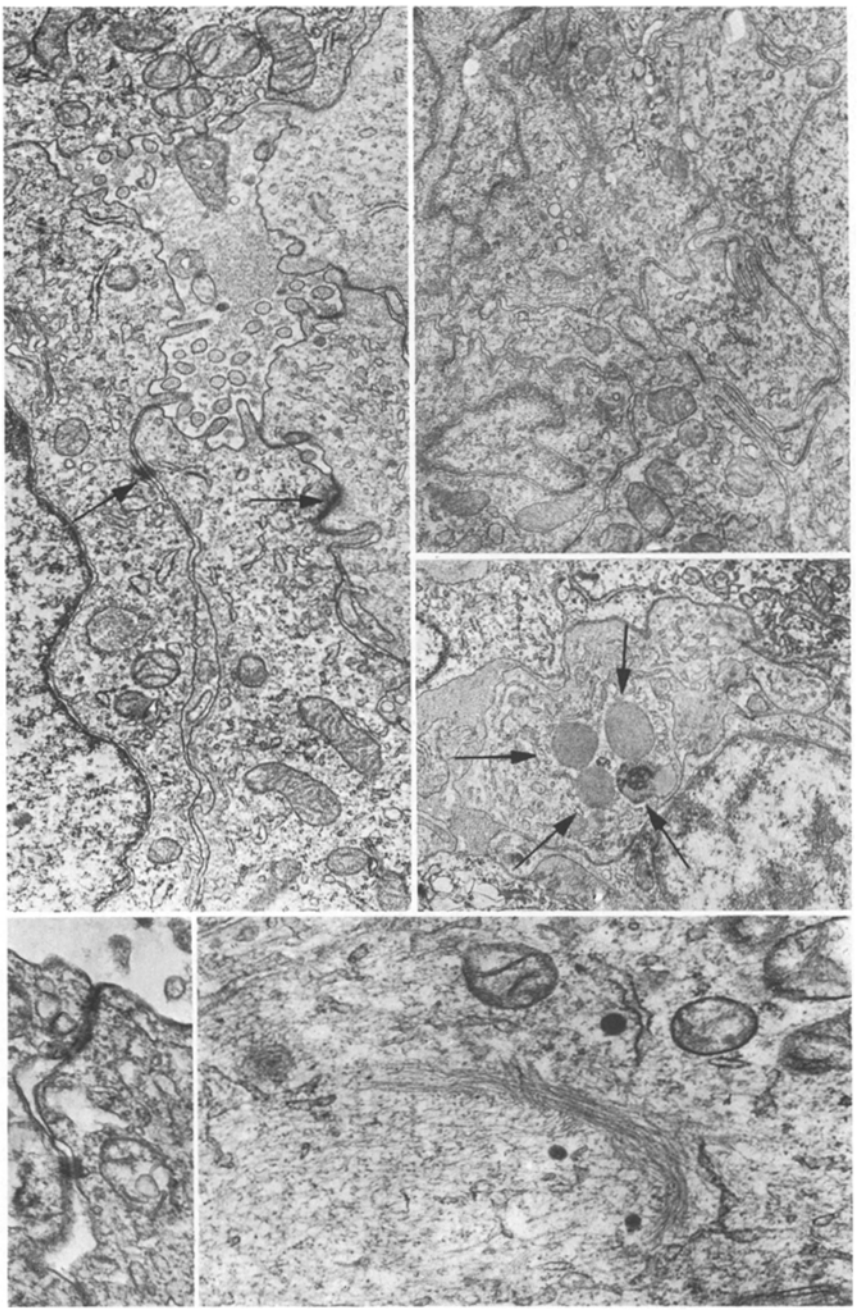

Fig. 5a–e. Details of synovial sarcoma cells. **a** The gland-like cavity is lined by cells with microvilli at the luminal side. These cells are connected by specialized intercellular junctions (→) (18,000:1). **b** Higher magnification of a terminal bar-like and desmosome-like junction, resp. (25,300:1). **c** Interdigitations of cells in an epitheloid cluster (15,000:1). **d** Lysosome-like dense bodies within the cytoplasm (→) (12,000:1). **e** The intermediate filaments within the cytoplasm are partially curved (25,300:1)

and some unordered microfilaments (100 Å thick, so-called intermediate filaments). Sometimes these microfilaments formed small partially curved bundles (Fig. 5e). In the microvilli-like cellular projections actin filaments with the characteristic width of 50–70 Å were encountered. Lipid droplets without a limiting membrane and small dense bodies probably corresponding to lysosomes were also observed in some tumor cells (Fig. 5d).

The nuclei of spindle-shaped tumor cells were almost exclusively equipped with coarse chromatin lumps, "light" nuclei with fine heterochromatin were not seen. It is also remarkable that in comparison with the cells of epitheloid clusters the spindle cells showed a less activated Golgi apparatus, more and partially dilated rough endoplasmic reticulum and more frequent autophagocytosis. These cytological differences were not observed in all cells and most cells seemed to be electron microscopically nearly identical in both the structural components.

Discussion

Synovial sarcomas may show a considerable variability of structure (Mackenzie 1966, Moberger et al. 1968, Hajdu et al. 1977) which occasionally produces diagnostic problems. The synovial sarcoma of the abdominal wall presented here has a typical biphasic structure with pseudoglandular formations with epithelium-like cell complexes and with spindle-cellular sarcomatous areas. The tumor cells synthesize glycoproteins and preponderantly weakly acid glucosaminoglycans, the latter consisting mainly of hyaluronic acid. Electron microscopically the major part of tumor cells correspond to undifferentiated sarcoma cells. There are gland-like cell arrangements with microvilli at the luminal side, specialized intercellular junctions and a peripheral basement membrane-like condensation of ground substance. It must be emphasized that the cytological features of cavity-lining cells were not consistent with true glandular cells (Klein and Huth 1974). These findings as a whole are characteristic for synovial sarcomas of joints (Ghadially and Roy 1966; Gabbiani et al. 1971; Kubo 1974).

Electron microscopic examination shows that tumor cells imitate cells of the synovial membrane. As in the normal tunica synovialis we can find cells with a resemblance to histiocytes and fibroblasts. The majority of the cellular elements, however, correspond to an intermediate cell type with features of both these cellular forms. It might be expected from the light microscopic appearances that ultrastructural examination would reveal great cytological differences between the two structural components. However, the ultrastructural features of the tumor cells suggest a common precursor cell, probably a pluripotential mesenchymal cell. This conception is supported by reports of other authors (Hutchinson and King 1940, Briggs 1942, Hajdu et al. 1977). In contrast, Roth and coworkers (1975) stressed the absence of intermediate forms between the cells in epithelium-like clusters and sarcomatous areas. Although desmosomes and basement membrane-like structures do not occur in the normal synovial membrane (Krey et al. 1971, Klein and Huth 1974) they are known to occur under pathological non-tumorous conditions (Ghadially et al. 1979). Finally,

the almost exclusive synthesis of hyaluronic acid and the frequent occurrence of mast cells are also traits of normal synovial membrane. We did not find any evidence of the origin of synovial sarcomas from neural mesenchyme.

At first sight the name "synovial sarcoma" seems questionable for a malignant tumor of the abdominal wall.

We have emphasised that this term characterizes a particular tendency to biphasic differentiation. Certain electron microscopic features, such as gland-like cavities, microvilli, desmosomes and basement membrane-like structures, and the localization in the abdominal wall may raise the question whether this tumor might be a mesothelioma rather than a synovial sarcoma (cp. Luse 1960). However, the peritoneum was intact and clearly distant from the tumor mass. In this connection the observation that synovial sarcomas may even arise from submesothelial mesenchyme is interesting (Dalton et al. 1979). The finding of intraluminal PAS-positive substances makes the diagnosis of a peritoneal mesothelioma unlikely (Kannerstein and Churg 1977).

Nevertheless there are many common ultrastructural features and histochemical characteristics between synovial sarcoma and mesothelioma. The submicroscopic relationship of both these tumor forms suggests that they may be united in a group of sarcomas with possible biphasic cellular pattern while preserving their clinicopathologic difinition. Future investigations will show whether other tumor types, for example, epitheloid sarcoma (cp. Enzinger 1970) can be included in this tumor category.

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