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Malignant Fibrous Histiocytoma Arising in a Recurrent Chordoma

Case Report and Electron Microscopic Findings

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Summary. We present the case of a sacrococcygeal chordoma which recurred 15 years after the radical removal as a soft tissue tumor in the gluteal musculature. This tumor consisted of two parts: a chordoma without symptoms of aggressive cellular proliferation and a malignant fibrous histiocytoma. During the following 4 years several local recurrences of the malignant fibrous histiocytoma occurred in the gluteal musculature. The patient finally died of lung metastases. No chordoma tumor tissue was found in the lungs, in the gluteal musculature or in the sacrococcygeal bone area. Histology including electron microscopy revealed no proof of a transition of chordoma into malignant fibrous histiocytoma. It must be assumed that the secondary soft tissue tumor originated from residual chordoma cells which were implanted during the operation of the primary tumor. It remains unclear whether the malignant fibrous histiocytoma arose from mesenchymal stromal cells within the chordoma or directly from primitive neuroectodermal chorda cells which possess the ability to differentiate into a variety of cell types including mesenchymal cells.

Key words: Chordoma – Malignant fibrous histiocytoma – Malignant histiocytoma arising from a recurrent chordoma – Tumors of the neurocrest

Chordoma is a tumor which originates from residual elements of the notochord. Neuroectodermal cells invaginate early from the neural crest and give rise to the development of the chorda. The primitive neural crest cells possess the ability to differentiate into a striking diversity of cells and tissues including melanophores, xanthophores, iridophores, parts of the nervous system but also skeletal and connective tissue components such as mesenchyme in the head and much of the cranial and visceral skeleton (Bolande

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1974; Knese 1979; Weston 1970). Chordoma originates from chorda cell rests in the bone, preferably in the sacrococcygeal and sphenooccipital, occasionally in the vertebral regions. The tumor may occur at any age, it is more frequent in the male sex (2:1) (von Albertini 1974; Doerr 1974; Mikuz et al. 1977; Murad and Murthy 1970). Embedded in a mucinous matrix two cell types have been observed: a) large vacuolated physaliphorous cells and b) stellate cells with larger nuclei and scarce cytoplasm. The latter are the primary cell type, they resemble fibroblasts and contain abundant rough-surfaced endoplasmatic reticulum (Spjut and Luse 1964; Murad and Murthy 1970). They are responsible for reproduction whereas the physaliphorous cells develop from the stellate cells and represent a final cell stage. If stellate cells predominate in a tumor this indicates an aggressive behaviour (von Albertini 1974; Mikuz et al. 1977; Murad and Murthy 1970). Malignant varieties of chordoma with metastases occur, but the majority of cases is characterized by a locally aggressive growth into the adjacent tissues (Poppen and King 1952; Windeyer 1959; Heffelfinger et al. 1973). Heffelfinger et al. (1973) have described a variety which develops chondroid formations (chondroid chordoma) and has a better prognosis. Occasional transitions into chondrosarcoma, fibrosarcoma and osteogenic sarcoma have been observed (Poppen and King 1952; Windeyer 1959; Heffelfinger et al. 1973). To our knowledge a relation between chordoma and malignant fibrous histiocytoma has not yet been mentioned in the literature.

Case Report

Clinical Course

In 1962 the 52-year old man presented with a primary bone tumor of the sacrococcygeal region. The intraosseous tumor was surgically removed and histology revealed a typical chordoma. No additional x-ray therapy was performed. The patient remained free of relapses until 1977 when he observed a nodular tumor in the gluteal musculature. The surgical specimen showed a nodular encapsulated tumor of $10 \times 15 \times 10$ cm. The marginal areas consisted of mucinous whitish tissue, the central parts were partly necrotic, of brownish color with hemorrhages. Histology revealed at the periphery a typical chordoma while the central parts contained a malignant fibrous histiocytoma. Two further encapsulated tumors occurred 4 months later, again in the gluteal musculature, not far from the localization of the first soft tissue tumor. They were removed and in addition treated by x-rays. During the next 4 years several local relapses were surgically treated, but in 1981 the patient died of lung metastases. At autopsy no recurrences of the primary bone tumor or of the soft tissue tumors in the gluteal musculature were found. Histologically the lung metastases consisted entirely of tumor tissue with all the characteristics of a malignant fibrous histiocytoma. Chordoma tumor tissue was not detected anywhere.

Light Microscopy Findings

The sections of 1962 (HZ 4623/62) show a typical chordoma. Well demarcated by a fibrous capsule, the tumor cells are arranged in lobules and alveoli. Vacuolated large physaliphorous cells, sometimes arranged in cords, lie in an abundant mucinous matrix. Trabeculae, continuous with the fibrous capsule, proceed inwards, carrying with them thin-walled blood vessels. Signetring cells are frequent. Stellate cells with larger nuclei and scarce cytoplasm are rarely seen. Mitotic figures are lacking.

The tumor of 1977 (HZ 9469/77) is well demarcated (Fig. 1a). The periphery consists of chordoma tissue (Fig. 1b) which is identical to that of 1962. Again stellate cells are very

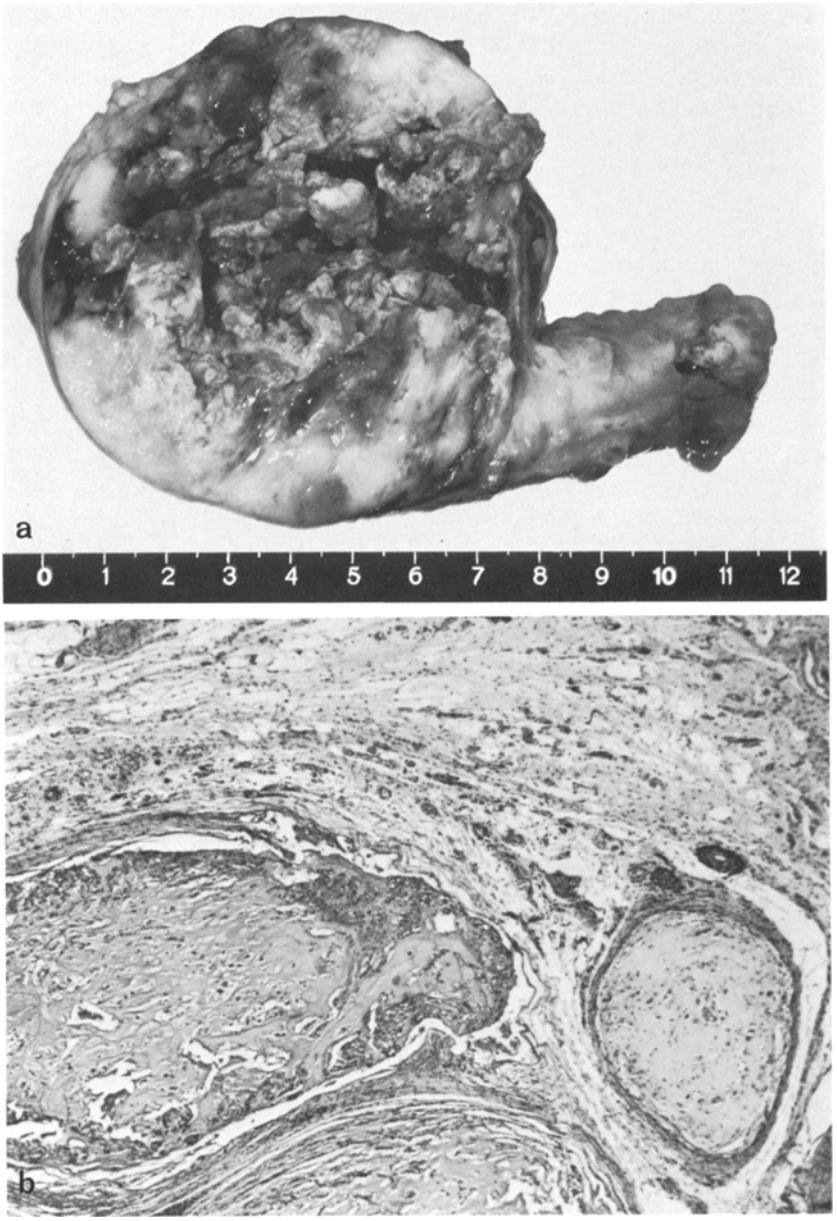

Fig. 1. a Gross appearance of the encapsulated tumor in the gluteal musculature removed in 1977. The whitish areas at the periphery correspond to the chordoma, the central (dark) areas contain the malignant fibrous histiocytoma. **b** Histology of the peripheral area of the tumor with a typical chordoma of nodular appearance. HZ 9469/77. Hemalaun-Eosin, 36×

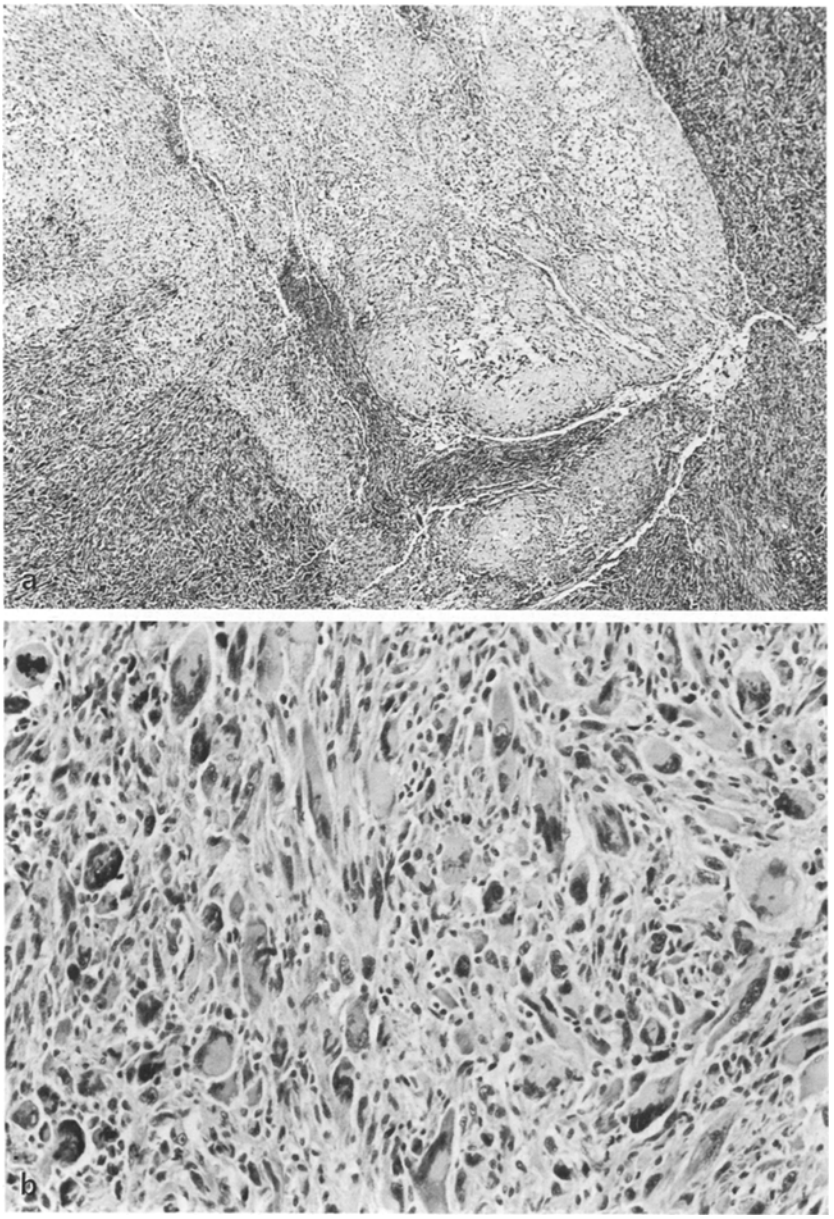

Fig. 2. a Borderline area between chordoma (*bright*) and malignant fibrous histiocytoma (*dark*). HZ 9469/77. Hemalaun-Eosin, 36×. **b** High power of the malignant fibrous histiocytoma with pleomorphic cells including multinucleated giant cells. Mitotic figure at the upper left. HZ 9469/77. Hemalaun-Eosin, 160×

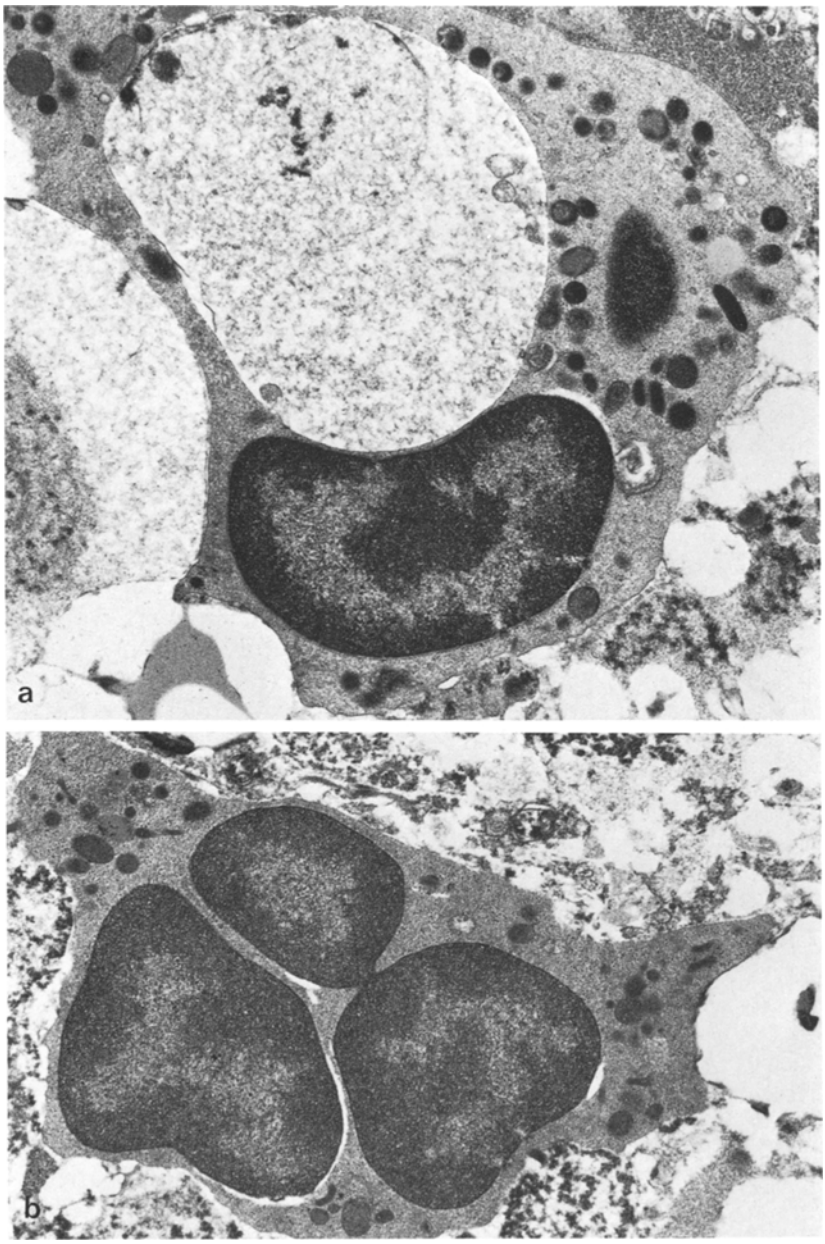

Fig. 3. a Chordoma within the mixed tumor of 1977. Physaliphorous cell with one large and several small vacuoles and lysosomes. 73/77/6. Nr. 1153/81. Phosphate-buffered glutaraldehyde, 11,900 ×. **b** One of the rare stellate cells within the chordoma. Enlarged multiple nuclei and scare cytoplasm. 73/77/6. Nr. 2120/82. Phosphate-buffered glutaraldehyde, 11,900 ×

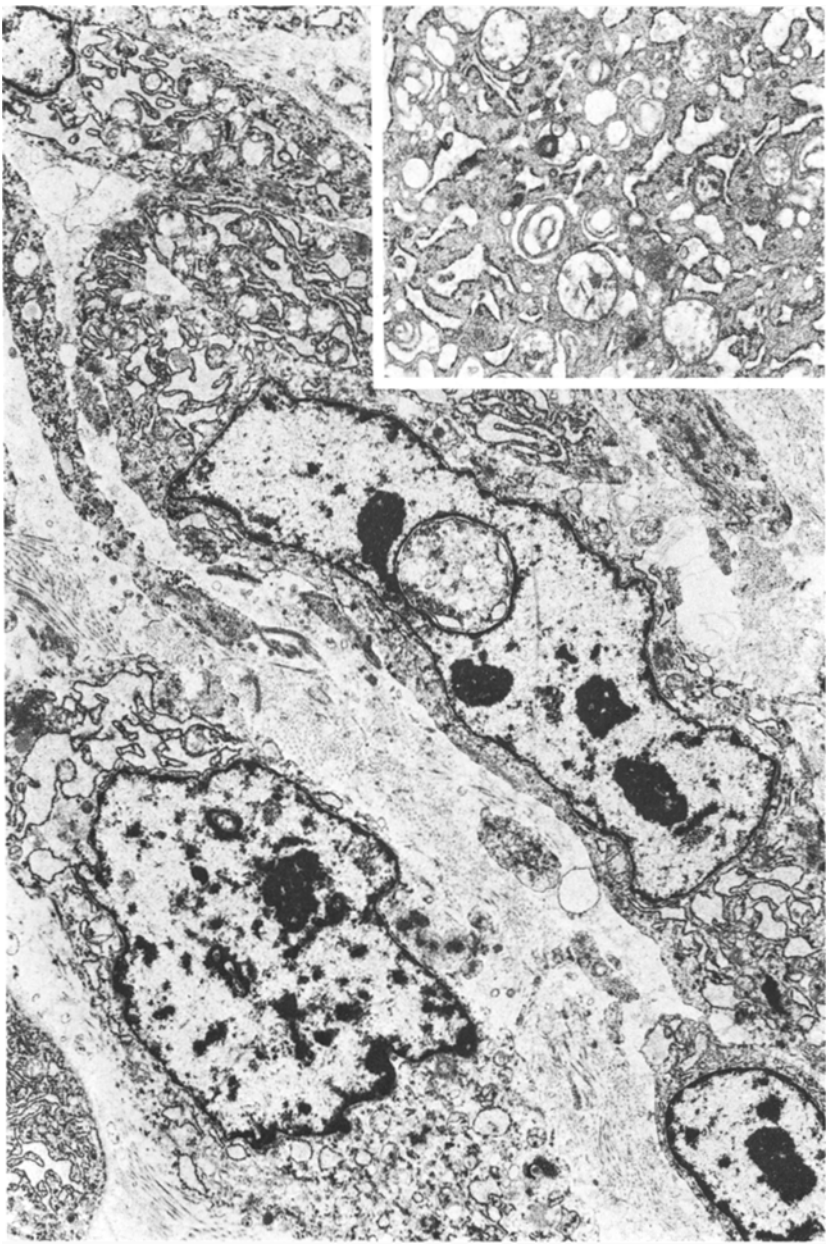

Fig. 4. Malignant fibrous histiocytoma in the mixed tumor of 1977. Fibroblastic cells with abundant rough-surfaced endoplasmatic reticulum and several nucleoli. Collagen fibers between the tumor cells. 22/77/1. Nr. 1133/81. Phosphate-buffered glutaraldehyde, 5,300 × . *Inset:* Detail of the rough-surfaced endoplasmatic reticulm. Nr. 2200/82. 11,900 ×

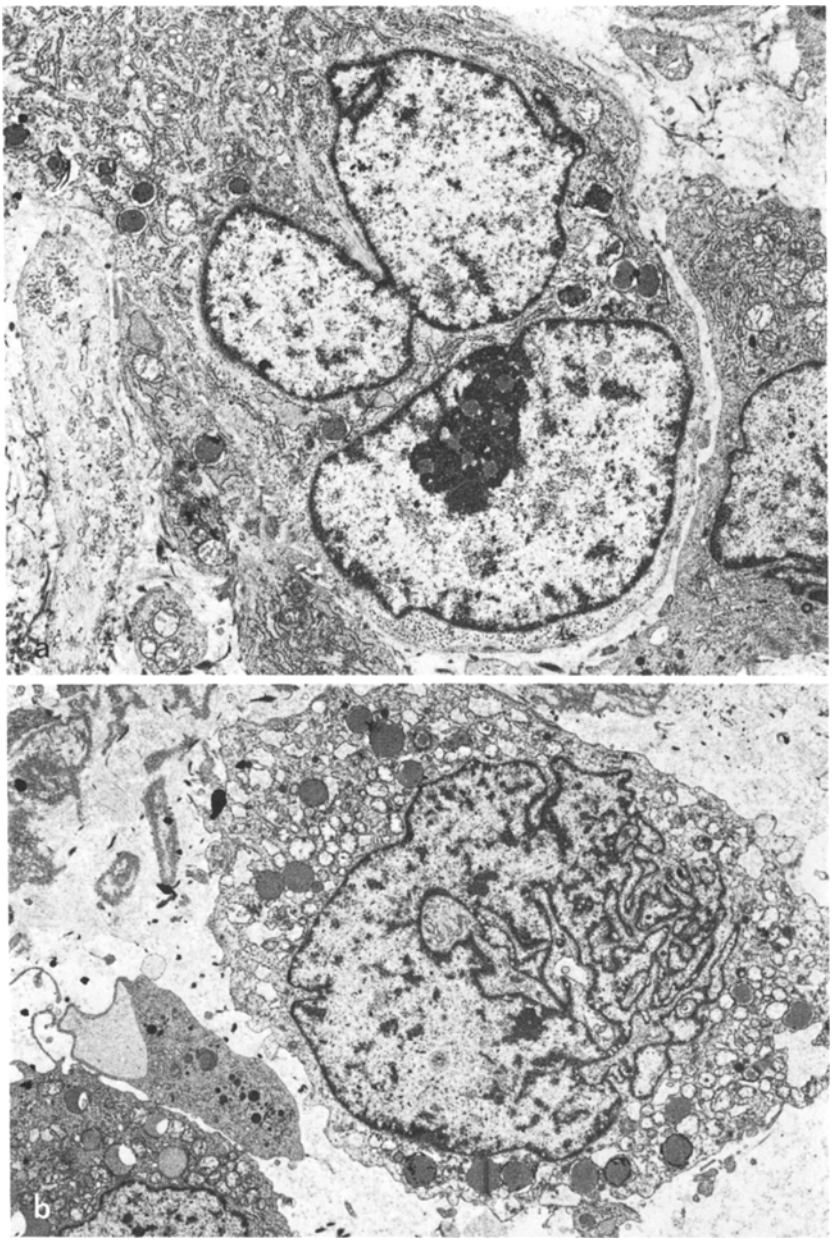

Fig. 5. Malignant fibrous histiocytoma in the mixed tumor of 1977. Histiocytic cells with large, irregularly shaped nuclei, multiple lysosomes and small vacuoles. 73/77/3. Phosphate-buffered glutaraldehyde. **a** Nr. 2087/82, 5,300 ×. **b** Nr. 2083/82, 3,600 ×

rare and mitotic figures are lacking. The central parts of the tumor, however, consist of a quite different tumor tissue. Strands and clusters of pleomorphic, closely packed cells lie adjacent to the chordoma without being separated by connective tissue layers. We distinguish areas with predominately fibroblastic cells which are spindle-shaped and appear as interlacing bands, occasionally forming whorls (Fig. 2a). The nuclei vary from long and thin to plump and irregular, the nucleoli are often prominent. Collagen ist present in variable amounts and often surrounds individual fibroblasts. Other areas contain histiocytic cells in a solid pattern or loosely scattered among the fibroblasts. Some are inconspicuous, others show marked nuclear atypia with irregular chromatin clumping and clearing, hyperchromasia and prominent nucleoli. Bizarre giant cells, often multinucleated, are frequently seen. Mitotic figures occasionally occur (Fig. 2b). Areas of hemorrhage and necrosis lie within the cell-rich areas. Iron stains show the presence of abundant intra- and extracellular hemosiderin. PAS stains and glycogen stains (method of Best) are positive within the chordoma but negative within the sarcomatous parts of the tumor. Lymphocytes, plasma cells and hemosiderin-containing macrophages of normal appearance are loosely distributed within the tumor tissue. These areas correspond to a typical malignant fibrous histiocytoma.

The local recurrent tumors occurring during the next years (19949/77, 19202/78, 19693/79, 8727/81) are uniformly composed of this same tumor tissue but without any traces of chordoma.

At *autopsy* (AZ 631/81) several necrotic metastases of the malignant fibrous histiocytoma are found in the left superior, the right inferior and superior lung lobe together with a necrotizing pneumonia. Their diameter varies between 1 and 4 cm. No residuals of tumor tissue are found in the gluteal musculature. No traces of the original chordoma are left neither in the gluteal musculature nor in the sacrococcygeal bone area.

Electron Microscopic Findings

The chordoma tissue consists of physaliphorous cells scattered widely within a mucinous matrix. This cell type contains abundant cytoplasm including many small and large vacuoles, lysosomal dense bodies, a relatively small nucleus and no organelles. Many of these cells are necrobiotic. The primary cell type of chordoma, the so-called stellate cells, which are characterized by scanty cytoplasm, relatively large nuclei, abundant rough-surfaced endoplasmatic reticulum, a few mitochondria and small vacuoles are practically absent. Mitotic figures are lacking (Fig. 3).

Immediately adjacent to this tissue, without a clear borderline, we find tumor cells which belong to the malignant fibrous histiocytoma. Several cell types can be distinguished. Frequently we find histiocytic cells with abundant cytoplasm containing dilated smooth-surfaced endoplasmatic reticulum and numerous small vacuoles and lysosomes. The nuclei are large, pleomorphic, irregularly shaped, with prominent, often multiple nucleoli. Mitotic figures are occasionally present. Another frequent cell type are the fibroblastic cells. They are spindle-shaped with large oval to elongated nuclei containing one to several prominent nucleoli and occasional mitotic figures. In the cytoplasm vacuoles and lysosomes are lacking or scarce but there is abundant, often dilated rough- or smooth-surfaced endoplasmatic reticulum. Occasionally we find an intermediate cell type between histiocytic and fibroblastic cells with abundant dilated endoplasmatic reticulum as well as lysosomes and small vacuoles. Primitive mesenchymal cells with few cytoplasmatic organelles, as described by Limacher et al. (1978) are not present (Fig. 4, 5). Multinucleated giant cells resembling macrophages and inflammatory cells (lymphocytes, plasma cells) are not rare.

No transitional cells types with either attributes of chordoma cells and histiocytoma cells are observed. Malignant histiocytic and fibroblastic tumor cells lie adjacent to physaliporous cells. No signs of proliferation are detected within the chordoma tumor tissue.

Discussion

The primary tumor of 1962 was a typical chordoma without any characteristics of an aggressive behaviour. There was no abundance of stellate cells

which usually indicates a malignant variety (Murad and Murthy 1970; von Albertini 1974; Mikuz et al. 1977). During the entire observation period of 19 years the intraosseous tumor did not recur.

The chordoma within the soft tissue tumor of 1977 in the gluteal musculature again showed little evidence of cellular proliferation. It consisted of physaliphorous cells which do not possess the ability of reproduction but represent a terminal cell stage (Spjut and Luse 1964; Murad and Murthy 1970; Mikuz et al. 1977; Ashley 1978). Only a few stellate cells could be found.

We detected no cell types which might suggest a transition of the chordoma into a malignant fibrous histiocytoma. Distinction between stellate chordoma cells and fibroblastic cells of the malignant fibrous histiocytoma may be difficult. Both resemble fibroblasts, both contain abundant rough-surfaced endoplasmatic reticulum (Spjut and Luse 1964; Murad and Murthy 1970; Mikuz et al. 1977; Weiss and Enzinger 1978; Droese 1979; Enjoji et al. 1980). The primary chordoma cells are of a stellate shape and are surrounded by mucinous masses, necrotic tissue and physaliphorous cells. The fibroblastic cells of malignant fibrous histiocytoma are spindle-shaped and surrounded by collagen fibers and histiocytic cells.

Both tumors are believed to arise from a primitive cell type. In the malignant fibrous histiocytoma the stem cell is supposed to be a primitive mesenchymal cell (Weiss and Enzinger 1978). Chordoma is supposed to originate from residual cells of the notochord. The neuroectodermal cells from the neural crest differentiate into various cell types including mesenchymal cells which later give rise to the formation of skeletal structures and connective tissue (Weston 1970; Bolande 1974).

The soft tissue tumor in the gluteal musculature occurring 15 years after the surgical removal of the intraosseous primary tumor has no connection with the sacrococcygeal bone. We are convinced that it originated from chordoma tumor cells which were iatrogenically disseminated during the operation of the primary tumor. It took these cells 15 years to grow into a tumor which again was apparently benign. The malignant fibrous histiocytoma arising side by side with the soft tissue chordoma, however, showed a very aggressive behaviour and was responsible for the multiple local recurrences within the gluteal musculature. It finally disseminated into the lungs. At autopsy only tumor tissue belonging to the malignant fibrous histiocytoma was found. No residuals of chordoma could be detected in the sacrococcygeal bone area or in the gluteal musculature. The malignant fibrous histiocytoma contained fibroblastic, histiocytic and giant cells but none of the primitive mesenchymal cells which have been described by Fu et al. (1975) and by Limacher et al. (1978). The diagnosis of a malignant fibrous histiocytoma is verified by the presence of abundant histiocytic tumor cells with their typical ultrastructure. They show phagocytosis of hemosiderin (positive iron stains). We have no proof of a transition of the chordoma into the malignant fibrous histiocytoma. Stains for glycogen were negative within the malignant tumor tissue and positive within the chordoma. Sarcomatous variants of chordoma have been described by Fox et al. (1968)

and by Knechtges (1970). But these tumors were pleomorphic spindle cell sarcomas and did not bear the characteristics of a malignant fibrous histiocytoma. Of course the possibility of a transition of the chordoma into a malignant fibrous histiocytoma cannot be excluded with certainty. On the other hand, the malignant fibrous histiocytoma may have originated from stromal tissue within the chordoma or developped directly from primitive residual chorda cells.

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