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Case Report

Malignant Giant Cell Tumor of Tendon Sheath

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Summary. A benign, but aggressive, giant cell tumor of tendon sheath developed over a period of 20 years into a metastasizing, histologically malignant giant cell tumor. Ultrastructure of the malignant tumor showed the same five cell types as described in giant cell tumors of tendon sheath. Even the same crystals were identified in the osteoblast-like and osteoclast-like cells.

It therefore appears reasonable to assume that giant cell tumors of tendon sheath indeed are neoplasms with a malignant potential and not an inflammatory reaction of synovial cells as previously suggested.

Both the benign and malignant tumors seem to be of mesenchymal derivation with partial osseous differentiation. No ultrastructural similarities with fibrous histiocytoma were apparent.

Key words: Giant cell tumors of tendon sheath – Soft tissue tumors – Ultrastructure.

Introduction

Giant cell tumors of tendon sheath have been regarded by some as an inflammatory reaction of synovial cells rather than a true neoplasm (Jaffe et al., 1941; Alguacil-Garcia et al., 1978). Consequently, a malignant neoplasm with histologic similarities to a giant cell tumor of tendon sheath has rarely been called a malignant giant cell tumor of tendon sheath (Kahn, 1973) but more frequently a malignant giant cell tumor of soft parts (Alguacil-Garcia et al., 1977; Van Haelst and de Haas van Dorsser, 1976).

This present case demonstrates, however, that malignant giant cell tumors of tendon sheath do exist, can evolve from the benign counterpart and have an ultrastructural appearance similar to giant cell tumors of tendon sheath (Carstens, 1978).

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Clinical History

A 48 year old, black female was first admitted with a mass over the dorsum of the right foot in April, 1964. The lesion, which had been present for one year, was located on the extensor surface of the right great toe and was removed by local excision. Microscopy revealed a giant cell tumor of tendon sheath, with some atypia present in the stromal cells. Additional sections revealed infiltrative growth of the tumor into the submitted bone fragments. The initial diagnosis was an aggressive giant cell tumor of tendon sheath. (The slides were reviewed by Dr. Frank W. Foote, Jr., Memorial Hospital for Cancer and Allied Diseases, who concurred with this opinion.)

The patient was seen one year after the local excision with a recurrence, and involvement of the distal end of the right fibula. The patient refused amputation. The fibula and the recurrence were removed and the patient received radiation to the area.

In August 1970, the patient was admitted with a massive tumor of the right foot and destruction of multiple bones. On this admission the patient was emaciated and almost bedridden because of the tumor. A below-the-knee amputation of the right extremity was performed, and microscopy showed a fully malignant giant cell tumor of tendon sheath extensively invading soft tissue and destroying the calcaneous and metatarsal bones.

The patient remained free of disease until 1974 when three nodules were discovered on the medial aspect of the right thigh, and the groin. The patient received 3000 rads to this area. Because there was no appreciable decrease in the size of the tumor, a wide excision of the tumor mass was performed. The largest nodule in the groin area measured 15 cm in diameter. Microscopy again revealed a fully malignant metastatic giant cell tumor of tendon sheath.

In June 1976, a slowly enlarging nodule in the medial posterior aspect of her amputated stump interfered with wearing of her prosthesis. The lesion was excised and microscopy showed a malignant giant cell tumor of tendon sheath. A chest x-ray revealed no evidence of metastatic disease. In March 1977, multiple masses were again noted on the medial aspect of the right thigh stump. A block dissection was performed and the nodules were diagnosed as metastatic malignant giant cell tumor of tendon sheath.

The patient is currently alive with evidence of recurrences on the right thigh stump.

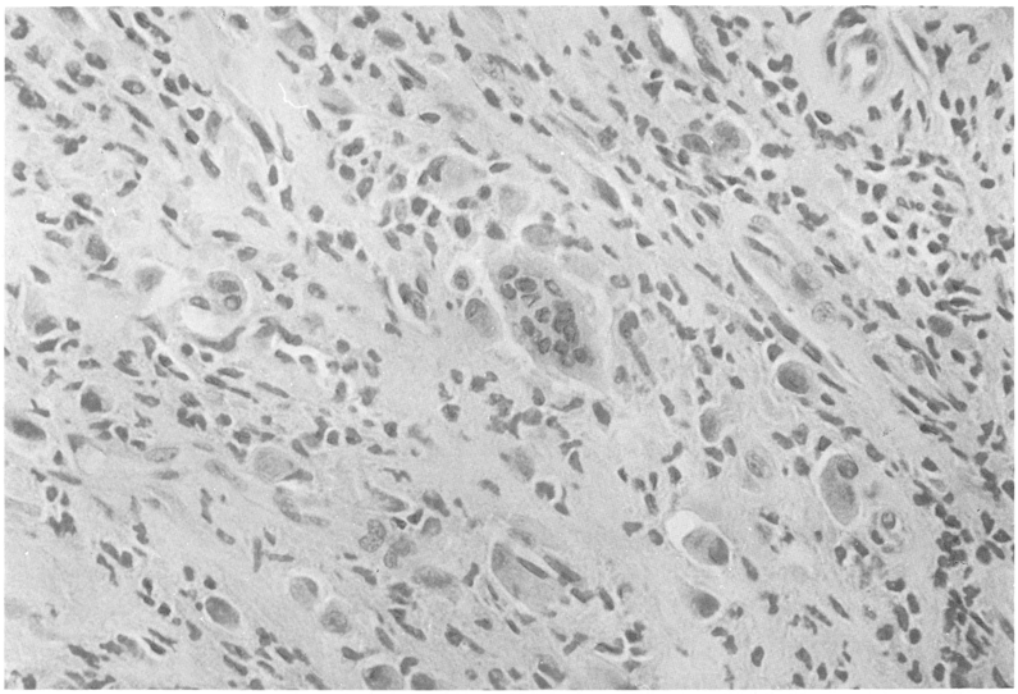
Materials and Methods

Tissue from several different areas of the tumor, removed in March, 1977, was immediately fixed in 3% gluteraldehyde and postfixed in osmium tetroxide. The tissue was dehydrated in graded alcohol and embedded in Maraglas. Thick sections were stained with toluidine blue and used for selection of areas for thin sectioning. The thin sections were stained with uranyl acetate and lead citrate and examined with an Siemens Elmiskop I electron microscope.

Results

Light Microscopy. The first specimen had many multinucleated giant cells embedded in a stroma of mononuclear, mainly histiocytic, cells and abundant fibrous tissue (Fig. 1). Some of the stromal cells had large nuclei with prominent nucleoli. Sections from adjacent bone showed invasion by tumor. The amputation and subsequent specimen had fewer multinucleated giant cells and an increase in atypical mononuclear cells. Many of the stromal cells were in mitosis (Fig. 2).

Electron Microscopy. The tumor consisted of a heterogeneous mixture of predominantly undifferentiated mesenchymal cells, some osteoblast-like cells and few multinucleated giant cells, histiocyte-like cells and fibroblast-like cells separated by scanty collagen and few blood vessels.



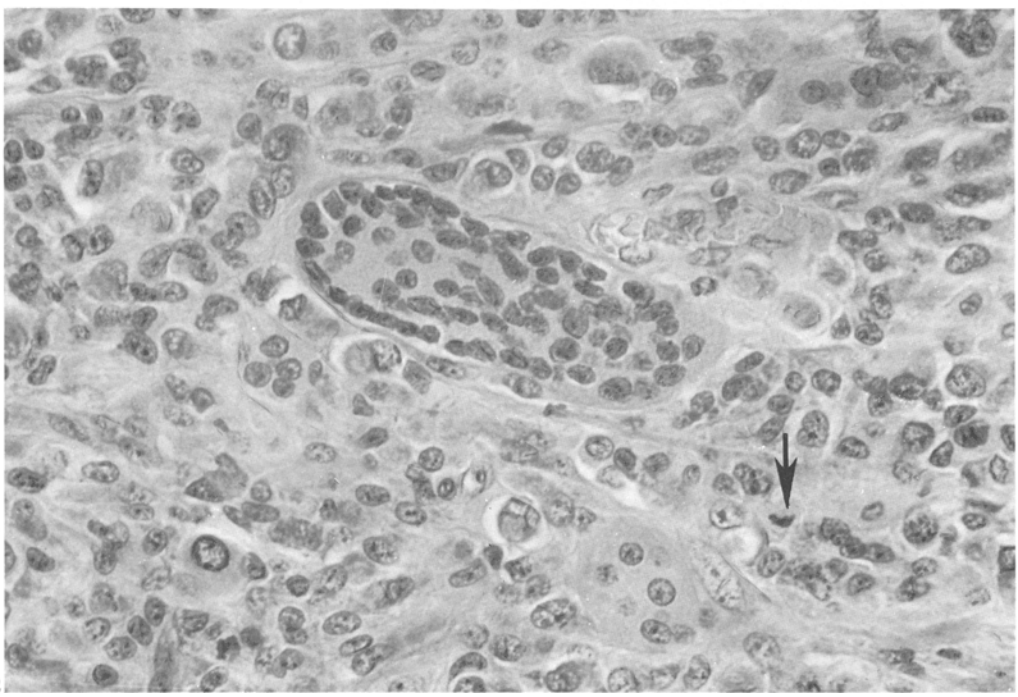


Fig. 1. Giant cell tumor of tendon sheath from the first operation. Numerous multinucleated giant cells are embedded together with various mononuclear cells in an abundant fibrous stroma. (hematoxylin – eosin, ×200)

Fig. 2. Malignant giant cell tumor of tendon sheath from 1976. There are more mononuclear cells, and fewer multinucleated giant cells and little fibrous stroma. Arrow indicates mononuclear cell in mitosis (hematoxylin – eosin, ×200)

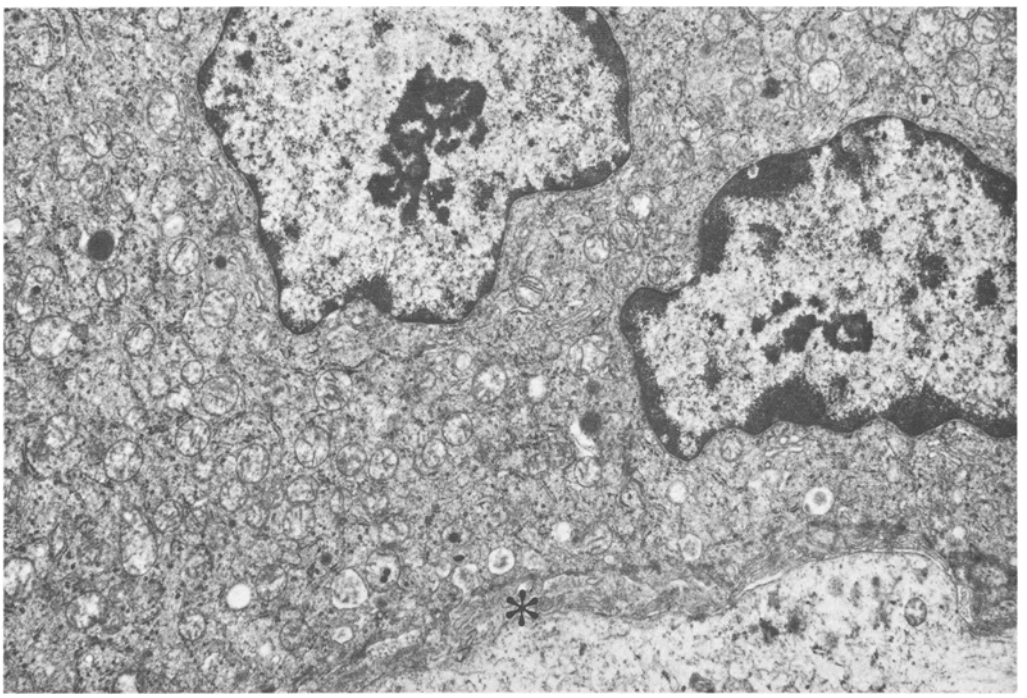


Fig. 3. Giant cell from the tumor removed in 1977. Note abundance of small, round mitochondria, lysosomal bodies and in one area: ruffled border (asterisk) (×2,500)

The giant cells contained a variable number of irregular nuclei with heterochromatin concentrated peripherally and one to two prominent nucleoli. The cytoplasm was occupied by an abundance of small, round mitochondria, a few lysosomal structures, free ribosomes, profiles of rough endoplasmic reticulum and Golgi zones (Fig. 3). The periphery of the giant cells showed, in certain areas, special configurations. In some areas the cell membrane and cytoplasm were arranged in plump microvilli that interdigitated with neighboring cells ("ruffled border") (Fig. 3). In other areas the peripheral cytoplasm was devoid of the normal organelles, i.e. mitochondria, ribosomes, lysosomes, etc. and instead contained a fine granular electron-dense substance ("clear zone").

The osteoblast-like cells were of irregular shape with an indented eccentrically located nucleus (Fig. 4). The bulk of the cytoplasm contained dilated profiles of rough endoplasmic reticulum, round mitochondria and a few lysosomal structures. Some of the giant cells and osteoblast-like cells contained membrane-bound crystals consisting of parallel filaments with a periodicity of approximately 100 Å (Fig. 5). They were identical to the crystals found in the benign giant cell tumors of tendon sheath (Carstens, 1978).

The majority of cells, however, were undifferentiated mesenchymal cells without any distinguishing features. The cells were usually of irregular shape with a prominent large round nucleus and a cytoplasm containing few mitochondria or rough endoplasmic reticulum but many free ribosomes.

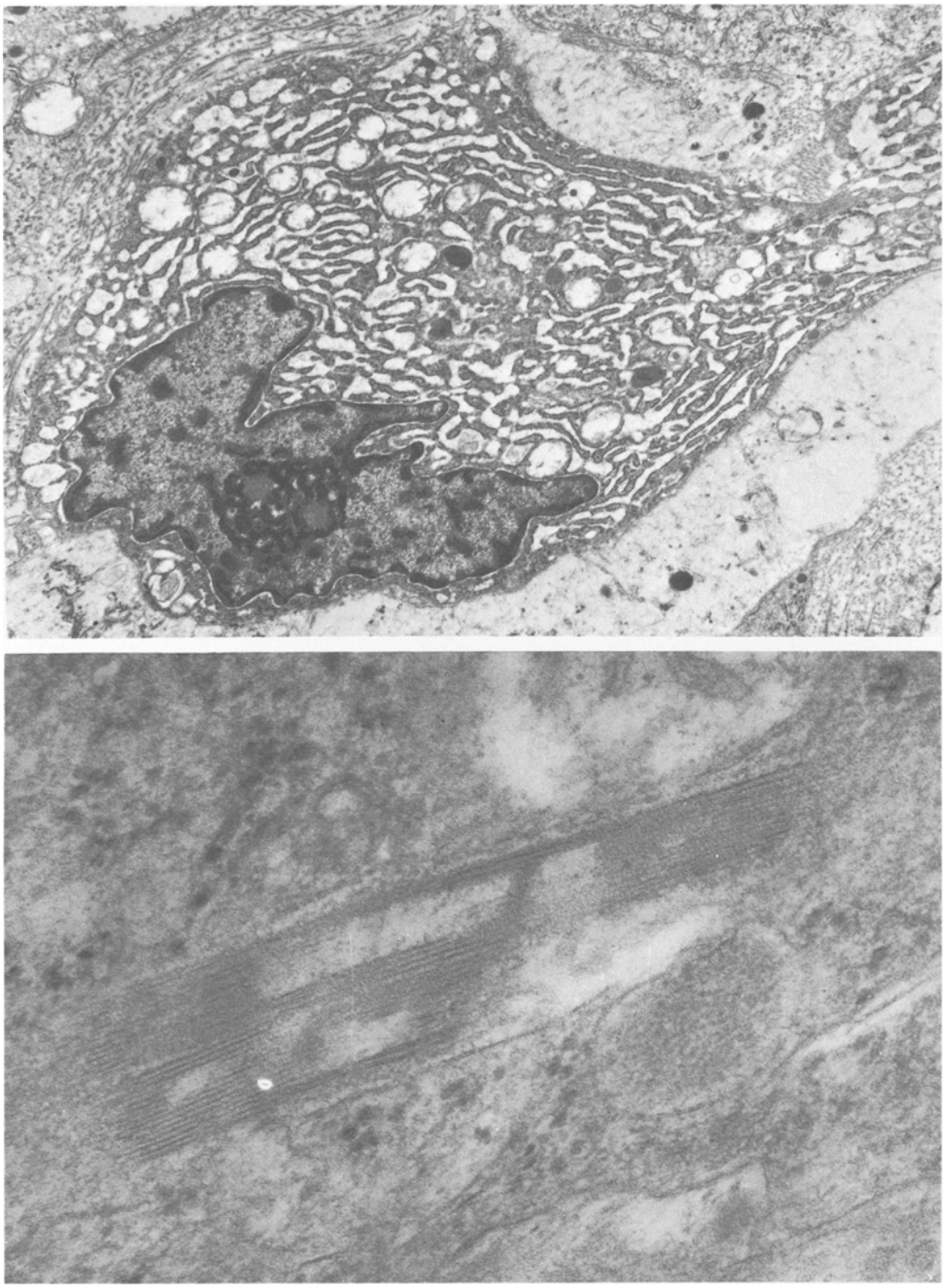


Fig. 4. Preosteoblast-like cell. The indented nucleus is pushed to the periphery of the cell. The cytoplasm is dominated by dilated profiles of rough endoplasmic reticulum ($\times 6{,}000$)

Fig. 5. Partially membrane-bound crystals within the cytoplasm of a multinucleated giant cell ($\times 120{,}000$)

Fibroblast-like cells and histiocyte-like cells containing phagocytized material (hemosiderin) were also noted. The cellular components were separated by a few capillaries, small arterioles, some sinusoids and few bundles of mature collagen. No identifiable osteocytes or areas with hydroxy-apatite crystals were noted in the tumor. None of the described cells was surrounded by a basal lamina.

Discussion

A giant cell tumor or tendon sheath, that over a span of years developed into a malignant, metastasizing giant cell tumor of tendon sheath, has been described. On electron microscopy the same five cell types, as described by Carstens (1978) in his study on giant cell tumors of tendon sheath, were found. Especially the giant cells had great similarity to osteoclasts (Rhodin, 1974). The main cytoplasmic component was small, round mitochondria with a few lysosomal structures and ribosomes. The peripheral portion was specialized into two different zones, namely the "ruffled border" and the "clear zone". In addition, cytoplasmic crystals consisting of parallel filaments were found possessing the same periodicity as in the benign giant cell tumors of tendon sheath (Carstens, 1978).

We postulate, as was the case with giant cell tumors of tendon sheath, that the lesion is a mesenchymal neoplasm with a partial osseous differentiation. In the malignant giant cell tumor of tendon sheath, the giant cells were fewer and the undifferentiated mesenchymal cells were more numerous, compared to the benign giant cell tumors of tendon sheath.

Electron microscopy of synovial membranes (Barland et al., 1962) have demonstrated two different cell types, namely the macrophage-like cell, the A type cell, and the fibroblast-like cell, also called the B type cell.

Some of the previous electron microscopic reports on giant cell tumors of tendon sheath described two cell types as in the normal synovial membrane and therefore supported a synovial membrane origin for this lesion (Alguacil-Garcia et al., 1978; Eisenstein, 1968).

Carstens (1978), on the other hand, found a mixture of five different cell types in eleven giant cell tumors of tendon sheath. He noticed great similarity between the multinucleated giant cells and the normal osteoclasts and less similarity between the different mononuclear cells and fibroblasts, histiocytes, osteoblasts and primitive mesenchymal cells.

Few electron microscopic reports on malignant giant cell tumors of tendon sheath exist. Kahn (1973) studied one case and found only one cell type corresponding to the fibroblast-like cell or type B-cell in the normal synovial membrane. Van Haelst and de Haas van Dorsser (1976) also studied one case and came to the conclusion that the malignant giant cell tumor of soft parts probably was a variant of mesenchymal fibrohistiocytic sarcoma distinct from malignant fibrous histiocytoma by its multinodular pattern. They described five different cell types: undifferentiated mesenchymal cells, cells suggestive of chondro-or osteoblasts, histiocytes, fibroblasts and multinucleated giant cells. They found

the giant cells similar to giant cells in other soft tissue tumors such as leiomyosarcoma, giant cell tumors of the bone, chondroblastoma and even similar to normal osteoclasts. Alguacil-Garcia et al. (1977) studied four cases of malignant giant cell tumor of soft parts. They also found five different cell types present, namely undifferentiated mesenchymal cells, dark monohistiocytic cells, histiocytes, fibroblasts and osteoclast-like multinucleated giant cells. The authors concluded that malignant giant cell tumors of soft parts were bimorphic neoplasms with histiocytic and fibroblastic differentiation. They therfore considered malignant giant cell tumors of soft parts as a distinct subtype of malignant fibrous histiocytoma.

It is interesting to note, that in the last two publications (Alguacil-Garcia et al., 1977; van Haelst and de Haas Van Dorsser, 1976) concerning malignant giant cell tumors of soft parts, a wide variety of cell types was identified. They appear to be the same cell types as described by Carstens (1978) in the giant cell tumors of tendon sheath.

In this study no ultrastructural similarities were found to fibrous histiocytoma (Fu et al., 1975; Taxy and Battifora, 1977).

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