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# A Case of Malignant Peripheral Nerve Sheath Tumor with Rhabdomyoblastic Differentiation: Malignant Triton Tumor

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## Key Words

Malignant triton tumor · Malignant peripheral nerve sheath tumor · Rhabdomyoblastic differentiation · Desmin · Neurofibroma

## Abstract

Malignant peripheral nerve sheath tumors (MPNST) constitute a rare variety of soft tissue sarcomas thought to originate from Schwann cells or pluripotent cells of the neural crest. Malignant triton tumor (MTT), a very rare, highly aggressive soft tissue tumor, is a subgroup of MPNST and is comprised of malignant Schwann cells coexisting with malignant rhabdomyoblasts. We herein report the case of a 24-year-old man who presented a subcutaneous mass in his right thigh. The mass was removed surgically in its entirety and radiation therapy was applied locally to prevent tumor regrowth. Nonetheless, the patient died 10 months after surgery from metastases to the lung and brain. He presented neither café-au-lait spots nor cutaneous neurofibromas. The histopathology showed a transition from a neurofibroma to an MTT, making this the second report of an MTT arising from a neurofibroma without neurofibromatosis type 1, an autosomal dominant disorder with which 50–70% of tumors reported in previous studies were associated. A histopathological examination using immunostaining with desmin confirmed this diagnosis. MTT has a poorer prognosis than MPNST and should therefore be regarded as a distinct clinical entity.

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## Introduction

Malignant peripheral nerve sheath tumors (MPNST) account for 5–10% of soft tissue sarcomas [1] and are thought to arise from Schwann cells or nearby cells with perineural differentiation. Malignant triton tumor (MTT), a subtype of MPNST presenting rhabdomyoblastic differentiation, takes 2 principal forms: the sporadic form and the neurofibromatosis type 1 (NF-1)-associated form. The majority of reported cases are of the latter variety. Direct transformation of malignant Schwann cells or neural crest cells into striated muscle is the most plausible explanation for the presence of rhabdomyoblasts within the tumors. Immunohistochemically, the rhabdomyoblastic elements are typically positive for skeletal muscle markers such as desmin, myoglobin, or muscle actin. When MTT occurs in the sporadic form, other spindle cell sarcomas such as the fibrosarcoma, rhabdomyosarcoma, osteosarcoma, chondrosarcoma, and liposarcoma should be included in the differential diagnosis.

## Case Report

A 24-year-old man presented with a subcutaneous mass in his right thigh, which gradually enlarged over 8 years, then grew rapidly 1 year prior to consultation. His medical and family histories were unremarkable. Physical examination revealed a firm, movable, painless, subcutaneous mass measuring 10 × 8 × 7 cm (fig. 1). Palpation revealed no inguinal lymphadenopathy. The patient presented neither cafe-au-lait spots nor cutaneous neurofibromas. T2-weighted magnetic resonance imaging revealed a solid, subcutaneous mass containing a cystic lesion (fig. 2). Computed tomography of the chest, abdomen and pelvis showed no evidence of metastasis. The tumor was totally excised under general anesthesia, with a 3-cm margin including the muscle surface. The resected margins were clear.

The resected tumor was not connected to the nerve tissue. Histopathological examination revealed the tumor's tissue origin as well as cystic degeneration and central necrosis. In 1 region, the tumor was composed of spindle cells occurring among collagen bundles or in a loose fibromyxoid stroma corresponding to a neurofibroma (fig. 3). Elsewhere, it was composed of spindle cells with hyperchromatic nuclei, together with some rounded or oval and strap-like cells possessing deeply eosinophilic cytoplasm in variably interlacing fascicles or whorls with a herringbone appearance or nuclear palisadings (fig. 4). Mitoses were also observed (fig. 4).

Immunohistochemically, the majority of spindle cells intensely expressed S-100. Cells with deeply eosinophilic cytoplasm are often positive for desmin (fig. 5). The MIB-1 (Ki-67) labeling index was less than 1% in the region corresponding to the neurofibroma, but had increased to 25% in the most mitotically active portion of the tumor. Postoperative radiation therapy was administered to the affected area. However, the patient died of brain and lung metastases 10 months after surgery.

## Discussion

MTT is a rare tumor arising from peripheral nerves or a pre-existing neurofibroma in patients with NF-1, an autosomal dominant disorder. 50–70% of the MTT cases observed were associated with NF-1. Masson [2] first described neurogenic tumors with rhabdomyoblasts, and categorized them as rhabdomyomas of the nerve. In 1973, Woodruff et al. [3]

proposed the classification of MTT and established the following 3 criteria for its diagnosis: (a) the tumor is related to a peripheral nerve or occurs in a patient with NF-1, (b) most of the tumor consists of Schwann cells, and (c) the tumor contains rhabdomyoblasts. Since then, Daimaru et al. [4] have broadened the definition of MTT to include sporadic cases by removing the first of the 3 criteria proposed by Woodruff et al. [3]. The present case, who displayed neither cafe-au-lait spots nor cutaneous neurofibromas, conforms to Daimaru's criteria.

The histopathology showed a transition from a neurofibroma to an MTT, making this the second report of MTT arising from a neurofibroma without NF-1. Less than 170 cases of MTT are known [5], most are among younger individuals. The age of the present patient is consistent with the tendency of the sporadic type to manifest first at the average age of 35 years [6]. MTT can arise in almost any site of the body. However, patients presenting symptoms on the trunk are more numerous than those with symptoms in the extremities. The prognosis of MTT depends on its location, grade, and the completeness of the surgical margins and is generally good for the head, neck, and extremities, but worse for other sites including the trunk, buttocks, and retroperitoneum [7].

The pathogenesis of MTT is unknown. One hypothesis states that malignant Schwann cells differentiate into rhabdomyoblasts [8], while another states that both cell lines arise from less differentiated neural crest cells with ectodermal and mesodermal potential [9]. Chromosomal abnormalities, reported in several cases, probably play a role in the pathogenesis or the progression of MTT [9, 10]. It is still unknown why the partial differentiation of the rhabdomyosarcoma should make the tumor more aggressive.

There are no guidelines for treating MTT yet. The most frequently performed treatments are a radical excision followed by postoperative radiotherapy and chemotherapy, or excision combined with radiotherapy. Radical excision followed by high-dose radiotherapy is the conventional treatment, although McConnell et al. [11] reported that, while this treatment reduced the risk of death, it was not associated with either reduced recurrence or progression.

There was no difference between MTT and MPNST in terms of the rate of local recurrence and the rate of metastasis. However, the 5-year survival rate for MTT is only 11% in contrast to 39% for MPNST [12]. A number of reasons account for the distinctly lower survival rate. MTT is fast growing, and in its early stages, prone to local recurrence and blood-borne metastasis. Compared to MPNST, MTT occurred more often in older patients, developed more often in the trunk area, and produced larger tumors [13]. In addition, MTT patients had a shorter metastasis-free interval as well as a shorter survival [13]. In summary, MTT is therefore more aggressive than MPNST and is important as a differential diagnosis.

### Disclosure Statement

The authors declare no conflict of interest.

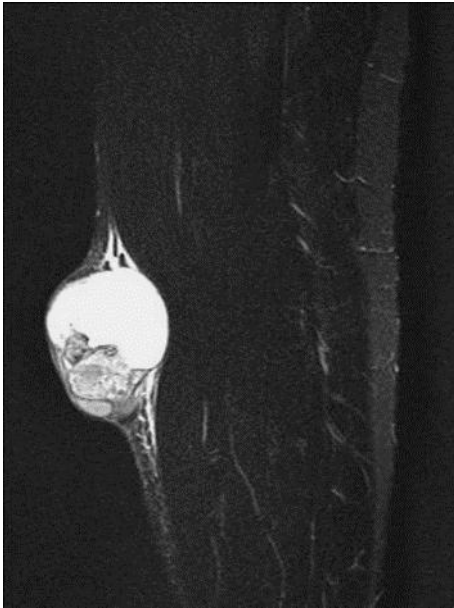
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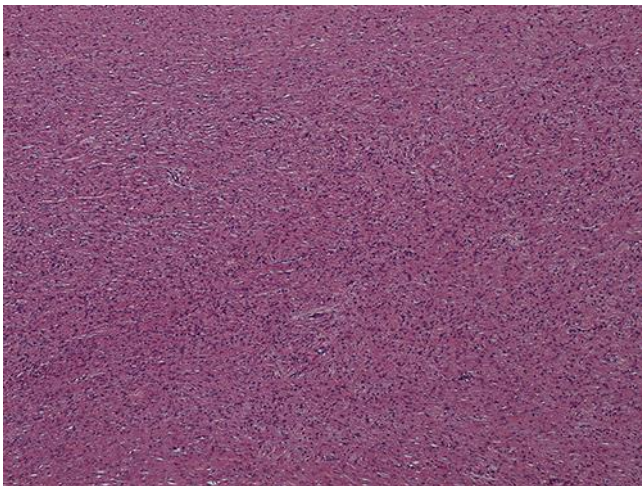
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**Fig. 1.** Clinical photograph of the firm, movable, painless, subcutaneous mass, measuring approximately 10 × 8 × 7 cm in the patient’s right thigh.

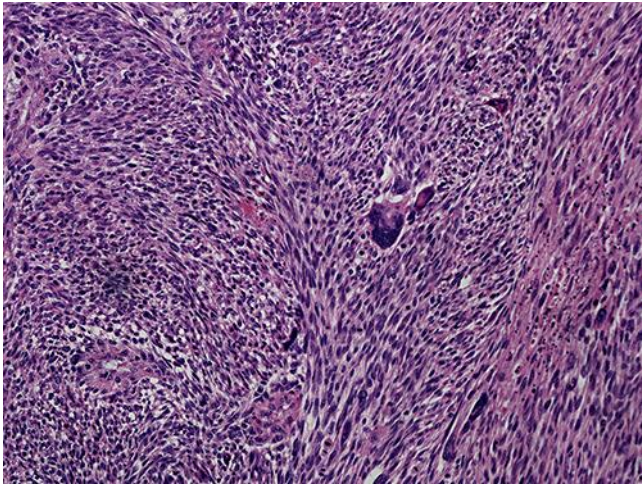


**Fig. 2.** T2-weighted MR imaging shows a solid subcutaneous mass containing a cystic lesion.

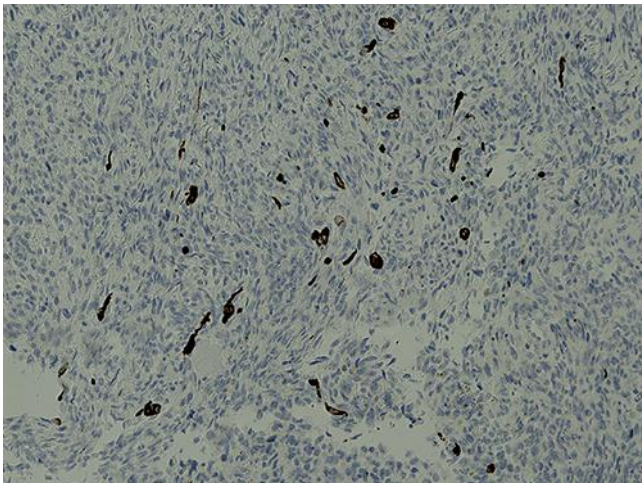


**Fig. 3.** Spindle cells arranged in interlacing and woven fascicles.





**Fig. 4.** In one region, the tumor was composed of a dense, tightly packed proliferation of spindle cells with elongated nuclei and prominent mitoses.



**Fig. 5.** Lesional tissue stained with desmin showing focally stained tumor cells.