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Clinicomorphologic features of a series of 10 cases of malignant triton tumors diagnosed over 10 years at a tertiary cancer hospital in Mumbai, India

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Abstract A rhabdomyoblastic differentiation in a malignant peripheral nerve sheath tumor is unusual and is termed as a *malignant triton tumor*. A series of 10 such cases with their clinicomorphological features, diagnosed over a 10-year period, is presented. The average age of occurrence was 30 years, with the maximum number of cases in the second decade and with male outnumbering female patients. More cases were seen in the setting of neurofibromatosis. On histology, 80% of the cases were of high grade. Distinct rhabdomyoblastic cells were identified in the areas of malignant peripheral nerve sheath tumor. Immunohistochemistry confirmed the neurogenic differentiation with varying S-100 expression and the rhabdomyoblastic differentiation with desmin and myoglobin positivity in all cases. Surgery with adequate margins constituted the treatment mainstay with adjuvant chemotherapy and/or radiotherapy in individual cases. On follow-up with 7 cases, 3 showed local recurrences, including one that, in addition to another 2 cases, showed lung metastasis. One patient died of the disease. This case along with another high-grade case displayed a diffuse Ki-67 and p53 positivity. Malignant triton tumor is an uncommon tumor associated with an aggressive behavior. Surgery with clear margins is the treatment mainstay. Adjuvant radiotherapy is effective.

Keywords: Malignant triton tumor; MTT; Malignant peripheral nerve sheath tumor; MPNST; Uncommon soft tissue tumors

1. Introduction

Malignant peripheral nerve sheath tumor (MPNST) can show an array of dedifferentiation patterns that include osteosarcoma, chondrosarcoma, angiosarcoma, and glandular differentiation, occurring either discretely or in varying proportions [1]. A rhabdomyoblastic differentiation is a rare morphological pattern in an MPNST, known as a *malignant triton tumor* (MTT). This entity was originally described by Masson [2] in 1932. An earlier experiment by Locatelli [3] had shown the growth of neural and muscular elements in the form of a supernumerary limb in the "triton" by transplanting the sciatic nerve of this salamander onto its dorsal surface. An MTT has been seen in the setting of both with and without multiple neurofibromatosis/NF-1 (von Recklinghausen disease) and has been found to behave aggressively [4-9]. A series of 10 cases of MTT diagnosed over a period of 10 years is described in this article.

2. Materials and methods

A total of 10 cases of MTTs were retrieved from the surgical pathology records over a 10-year period between 1996 and 2006. Only those cases of MPNST showing a rhabdomyoblastic differentiation, with or without other differentiation patterns, were included. Of the 10 cases, 7 were in the form of surgical specimens and the remaining 3 cases were in the form of slides with paraffin blocks for

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Table 1
List of primary antibodies used

Antigen	Type	Dilution	Antigen retrieval	Source
Vimentin	Monoclonal	1:50	Microwave	Dako Produkionsveg, Glostrup, Denmark
S-100	Polyclonal	1:300	Pepsin (enzymatic)	Dako
Desmin	Monoclonal	1:50	Microwave	Dako
Myoglobin	Polyclonal	1:600	Pepsin (enzymatic)	Dako
SMA	Monoclonal	1:200	Pepsin (enzymatic)	Dako
CD34	Monoclonal	1:100	Microwave	Dako
CK	Monoclonal	1:100	Pronase (enzymatic)	Dako
Epithelial membrane antigen	Monoclonal	1:100	Pepsin (enzymatic)	Dako
Calponin	Monoclonal	1:50	Microwave	Dako
BCL-2	Monoclonal	1:50	Microwave	Dako
HMB-45	Monoclonal	1:50	Microwave	Dako
MIC-2	Monoclonal	1:50	No treatment	Dako
Glial fibrillary acid protein	Polyclonal	1:500	Pepsin (enzymatic)	Dako
P53	Monoclonal	1:50	Microwave	Dako
Ki-67	Monoclonal	1:50	Microwave	Dako

review. The surgical specimens comprised excision specimens, including wide-excision (4 cases) intracapsular (2 cases), marginal (2 cases), and amputation (2 cases) specimens, following an initial diagnosis.

The criteria for diagnosis of an MPNST were as described by Weiss and Enzinger [10]. Additional discrete rhabdomyoblastic differentiation was necessary to be labeled as an MTT. The panel of immunohistochemical markers used is given in Table 1. Immunostaining was carried out by the avidin-biotin method (Vectastain ABC Kit, Vector Laboratories Inc, Burlingame, Calif) using the immunoperoxidase technique [11].

Tumor grade was assigned on tumor differentiation, mitotic counts, and necrosis [12]. The tumors were classified as low grade or high grade. Any tumor that was not low grade, that is, intermediate grade, was classified as high grade. The detailed clinical findings, hematologic investigations, imaging reports, and follow-up information were obtained from the hospital records.

3. Results

The age of the patients varied from 18 to 55 years (average = 30), with 6 of 10 cases seen in the second decade. There were 6 men and 4 women. Sitewise, 4 cases occurred in the lower limb, 2 in the head and neck region, and 1 case each in the upper limb, chest wall, back, and retroperitoneum.

Clinically, the most common complaint was an enlarging lump with or without multiple nodules (8 cases). The clinical setting of presence or absence of multiple neurofibromatosis (NF-1) was known in 8 cases, with 6 cases showing this setting and 2 cases representing de novo/sporadic-type MTT. The treatment details are listed in Table 2.

3.1. Pathological findings

Grossly, the tumors were gray-white with areas of necrosis; and the size was between 1.5 and 19 cm in the largest dimension.

Histologically, the tumor cells mainly comprised serpentine cells with comma-shaped nuclei, arranged as whorls and fascicles with “hemangiopericytomatous” slit-like vasculature (Fig. 1A). Prominent peritheliomatous arrangements and geographic foci of necrosis were seen in high-grade tumors (Figs. 1B, and 2A, B). At places, the nuclei were plump and showed a characteristic perivascular accentuation (Fig. 2C). Foci of myxoid/chondroid differentiation were also noted, with a few giant cells in some cases. In addition, one case displayed large areas of

Table 2
Clinicopathological features of 10 cases of MTT

No.	Age/sex	Multiple NF	Site	Size[a] (cm)	Diagnosis	Grade	Type[b]	Treatment	Recurr/Mets	Further outcomes
1	21/M	Yes	Thigh	33	MTT + PNET	High	E	Amp + CT	Recurr (1)	NA
2	55/F	No	Neck	13	MTT	Low	E	ICE + RT	NK	NA
3	40/M	Yes	Thigh	19	MTT	High	E	WE + RT	Recurr (2) + Mets	Alive (2 y)
4	25/M	NK	CP angle tumor	7	MTT	High	E	ME + CT	NK	NA
5	25/M	Yes	Forearm	1.5	MTT	Low	E	WE + RT	No	Alive (3 mo)
6	28/F	No	Chest wall	6	MTT	High	E, PM	WE + RT	Recurr (1)	Alive (6 y)
7	18/M	NK	Popliteal	14	MTT	High	E	WE + CT	Mets	NA
8	27/M	Yes	Popliteal	15	MTT	High	E	Amp + CT	Recurr (1) + Mets	Died of tumor (6 mo)
9	23/F	Yes	RP	16	MTT	High	PM	ICE + CT	No Mets	NA
10	38/F	Yes	Back	1.6	MTT	High	PM	ME	NK	NA

NA indicates not available; NK, not known; M, male; E, embryonal; F, female; PM, pleomorphic; ME, marginal excision; PNET, primitive neuroectodermal tumor; Amp, amputation; Recurr, recurrence; Mets, metastasis; RP, retroperitoneum.

[a] Size in largest dimension.

[b] Rhabdomyoblastic differentiation.