Malignant Triton tumour of labia majora- a case report

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Abstract:
Introduction- Malignant triton tumour (MTT) is a relatively rare variant of malignant peripheral nerve sheath tumour (MPNST). It is defined as MPNST with rhabdomyosarcomatous differentiation. It is commonly located in head and neck, extremities and trunk. We report a case of Malignant triton tumour occurring in labia majora. Case scenario - A 30 year old female presented with nodules all over the body. The nodules were initially seen in the labia majora and left groin, at the time of birth. She was diagnosed to have neurofibromatosis type 1 in 2011. In view of increased itching and bloody discharge from the labia majora, excision of left majora was done in February of 2013, in a general hospital. We received 7 slides and 8 blocks of that specimen for review. On microscopic and immunohistochemical examination, a diagnosis of malignant triton tumour was made. She was treated with radiotherapy in April 2013 and is disease free till date. Discussion - Primary malignant peripheral nerve sheath tumour involving vulva is extremely rare. Approximately 15 of MPNSTs show heterologous elements such as bone, cartilage and striated muscle. Most of the reported heterologous mesenchymal components are histologically malignant. Along with the histological features, immunohistochemistry aids in the confirmation of MTT. The prognosis of the MTT is worse than that of MPNST. Leiomyosarcoma, Rhabdomyosarcoma, MFH (pleomorphic undifferentiated sarcoma) are most common differential diagnoses for MTT. These are differentiated on the basis of microscopic examination and specific immunohistochemical markers. Conclusion - Malignant triton tumour is a very rare tumour and its occurrence in labia majora is extremely rare, however should be kept in differential diagnosis, particularly in a setting of NF1, as it has worst prognosis compared to MPNST. Keywords: Malignant triton tumour, malignant peripheral nerve sheath tumour, neurofibromatosis, labia majora

Malignant triton tumour (MTT) is a relatively rare variant of malignant peripheral nerve sheath tumour (MPNST). It is defined as MPNST...
with rhabdomyosarcomatous differentiation and constitutes about 5% of all MPNSTs. It is commonly located in head and neck, extremities and trunk. Other rare sites include mediastinum, retropertitoneum, buttock, viscera, parieto-occipital lobe, cerebellopontine angle and lateral ventricle. MTT occurring in labia majora is extremely rare and to our best knowledge this is the first case report of malignant triton tumour of labia majora.

**Case report:**
A 30 year old female presented with nodules all over the body. The nodules were initially seen in the labia majora and left groin, at the time of birth. She was diagnosed to have neurofibromatosis type 1 in 2011. In view of increased itching and bloody discharge from the labia major, excision of left majora was done in February of 2013, in a general hospital. We received 7 slides and 8 blocks of that specimen for review. Microscopic examination showed a tumour arranged in interlacing fascicles, large nests and trabeculae composed of spindle shaped cells with oval to elongated nuclei, coarse chromatin, some with conspicuous nucleoli and eosinophilic cytoplasm. Extensive areas of geographic necrosis were seen. In many areas round to polygonal cells with vesicular nuclei, prominent nucleoli and abundant eosinophilic cytoplasm resembling rhabdomyoblasts were seen. 15-20 mitotic figures per high power field including atypical forms were seen. Some of the tumour fragments were covered by stratified squamous epithelium with focal surface ulceration and the epithelium, infiltrated by tumour cells. On immunohistochemistry the malignant spindle cells were positive for CD56 and focally for S100 and SMA. The rhabdomyoblasts were positive for desmin (Fig 6) as well as myogenin (myf4), the latter being focal and weak. H-caldesmon and TLE-1 were negative. Some sections showed features of classical neurofibroma.

Based on these features, the diagnosis of malignant peripheral nerve sheath tumor with rhabdomyosarcomatous differentiation (malignant triton tumour) was given. She was treated with radiotherapy in April 2013 and is disease free till date.

![Fig 1:Fascicles of spindle shaped cells with areas of necrosis (H&E 100X)](image_url)

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Fig 2: Spindle shaped cells with oval to elongated nuclei, coarse chromatin, some with conspicuous nucleoli and eosinophilic cytoplasm (H&E 400X)

Fig 3: Sheets of Rhabdomyoblasts (polygonal cells with vesicular nuclei, prominent nucleoli and abundant eosinophilic cytoplasm) (H&E 400x)

Fig 4: Classical neurofibromatosis area (H&E 200X)

Fig 5: The spindle shaped cells show positivity for S100( IHC 400X)

Fig 6: The rhabdomyoblasts are positive for desmin(IHC 400X)

Discussion:
Primary sarcomas of the vulva are rare with leiomyosarcoma being the most common type followed by rhabdomyosarcoma and fibrohistiocytic tumours. Primary malignant peripheral nerve sheath tumour involving vulva is extremely rare. Approximately 15% of MPNSTs show heterologous elements such as bone, cartilage and striated muscle. Most of the reported heterologous mesenchymal components have been histologically malignant. Masson first described rhabdomyomatous elements within MPNSTs in patients with neurofibromatosis. The name ‘triton’ was used by Woodruff et al. based on the fact that supernumerary limbs containing muscle and bone were induced to grow on the backs of triton salamanders by transplantation of sciatic nerve into soft tissues of the back. They proposed three criteria for diagnosis of triton tumours: 1) Tumour arising within a peripheral nerve, or in patients with neurofibromatosis (NF1) or representing a metastasis from such tumour 2) Tumour exhibiting the growth characteristics of Schwann cells and 3) presence of rhabdomyoblasts in the tumour that appear to arise from
peripheral nerve tumour and not from metastasis from intrinsic rhabdomyosarcoma. Later in 1984 Daimaru et al. added two more criteria: 1) Tumours containing predominantly rhabdomyoblasts with focal Schwann cells occurring within a nerve or in settings of NF1 and 2) Tumours containing malignant Schwann cells with focal rhabdomyoblasts in patients without NF1. As far as our case is concerned MTT was diagnosed in a setting of neurofibromatosis (NF1). Along with these histological features, immunohistochemistry aids in the confirmation of MTT. Expression of S100, Leu-7 and myelin basic protein positivity in tumour indicates nerve sheath differentiation, while immunoreactivity for desmin, myogenin and muscle specific antigen represents skeletal muscle differentiation. The mean age of presentation of MTT is 31.7 years. More than 40% of these cases are associated with NF1 and these show male predominance, young age at presentation and most common location as head and neck region. In contrast, sporadic cases are seen in older age group, show female predominance and are centrally located. Some cases of triton tumour occur following radiation. Cytopathic studies done in relation to MTT show complex karyotype abnormalities. A break point involving 11p15, the region of gene for myogenic differentiation 1 which is implicated in rhabdomyoblastic differentiation was seen in a proportion of patients. Amplification of c-myc was also observed in some patients explaining the aggressive behavior of MTT. The treatment of MTT is similar to conventional MPNST with surgical excision being the preferred mode of treatment. Use of adjuvant and neoadjuvant chemotherapy and radiotherapy is controversial. As the margins were positive in the present case, postoperative radiotherapy was given. The prognosis of the MTT is worse than that of MPNST with overall 5 years survival rate of 12% and 26% as observed by Brookes et al and Yakulis et al respectively. Yakulis et al observed that tumours located in head and neck, upper and lower extremities had better prognosis compared to tumours located in buttocK, retroperitoneum or trunk. MTT also had high rates of local recurrence (43%) and metastasis (48%).

Leiomyosarcoma, Rhabdomyosarcoma, MFH (pleomorphic undifferentiated sarcoma) are most common differential diagnoses for MTT. Leiomyosarcoma shows a fascicular growth pattern of spindle cells with blunt ended nuclei and eosinophilic cytoplasm and immunopositive for smooth muscle actin, h-caldesmon and negative for myogenin. A proportion of cases can be positive for S100. Rhabdomyosarcoma, especially embryonal or alveolar type has a mixture of round and spindle cells admixed with rhabdomyoblasts which is positive for desmin and myogenin and rarely positive for S100. Malignant fibrous histiocytoma (pleomorphic undifferentiated sarcoma) shows a range of histological types, storiform-pleomorphic type being most common which on microscopy shows plump spindle cells arranged in storiform pattern with high degree of anaplasia, high mitotic activity including atypical forms, xanthoma cells and secondary chronic inflammatory cells. In pleomorphic areas the cells are arranged in more haphazard fashion and contain bizarre multinucleate giant cells. The stroma shows various degrees of collagenisation, myxoid change and metaplastic osteoid or chondroid areas. On immunohistochemistry the cells show vimentin positivity in the absence of lineage specific markers, but there can be focal positivity for keratins.
smooth muscle actin, desmin and EMA.

**Conclusion:**
Malignant triton tumour is a very rare tumour and its occurrence in labia majora is extremely rare, however should be kept in differential diagnosis, particularly in a setting of NF1.

**Bibliography:**


