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A LARGE MALIGNANT PERIPHERAL NERVE SHEATH TUMOUR (MPNST) OF RADIAL NERVE. - A RARE CASE REPORT

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ABSTRACT

Malignant peripheral nerve sheath tumour (MPNST) are rare, aggressive sarcomatous tumours of peripheral nerve sheaths which can arise from preexisting neurofibroma or de novo. Sporadic origin accounts for nearly half of all MPNST cases, while other cases occur in association with neurofibromatosis type 1 (NF1). The most common site is nerve trunks of extremities like sciatic nerve. On literature search only four case reports of MPNST of radial nerve are published till date. We report a case of 50 years old lady presenting with a large, firm, ovoid swelling measuring 7 cm x 8 cm over her right arm with symptoms of neuropathy. The fine needle aspiration cytology report was a benign neurogenenic tumour. MRI reported as a radial nerve sheath tumour. Core biopsy shows features of neurofibroma(NF).She was subjected to treatment as a benign pathology but the final histopathological report was a low grade - malignant peripheral nerve sheath tumour.

BACKGROUND

Malignant peripheral nerve sheath tumour (MPNST) are rare which accounts 2 % of all sarcomas and incidence only 5 people per million per year and it is an aggressive sarcomatous tumours of peripheral nerve sheaths which can arise from preexisting neurofibroma or de novo. Sporadic origin accounts for nearly half of all MPNST cases, while other cases occur in association with neurofibromatosis type 1 (Nf1). [1,2]. The most common site is nerve trunks of extremities like sciatic nerve. On literature search only four case reports of MPNST of radial nerve are published till date We report here a case of an adult female presenting with a large, firm, ovoid, arm swelling of neural origin that was subjected to treatment as a benign pathology. Post-operative biopsy reported the specimen as a Malignant Peripheral Nerve sheath tumour.

CASE PRESENTATION.

A 50 years old post-menopausal lady presented to the out-patient department with complaints of tingling sensation and numbness over her right forearm and hand towards the thumb side since 10 years. Painless swelling over the back of right arm since 3 years. The tingling sensation and numbness occurred specifically when she does her house hold works. The swelling was initially half the size of her thumb, and grew gradually over 3 years to attain the size of her fist. There were no significant medical and surgical history. None of her family members has similar complaints.

On physical examinations, her vitals parameters were within normal limits. Local examinations revealed a visible swelling over posteromedial aspect of upper half of right arm measuring approximately 6 cm x 8 cm which is ovoid shaped, smooth surface and normal overlying skin Figure 1: Pre-operative markingThere was not local rise in temperature of overlying skin, margins of the lump were well defined, firm consistency, non-tender, measuring 7 cm transversely and 8 cm vertically. The extend of lump was 9 cm below tip of right acromial process and 12 cm above the medial epicondyle of right humerus. Tinel's sign was positive and distal pulses were normal. Rest of general physical and systemic examinations were normal. Her routine laboratory blood parameters where normal.

A fine aspiration cytology, which was done elsewhere showed mild to moderate cellularity and display spindle cells in discrete as well as in short fascicles with fibrilary eosinophilic stromal background. Individual cells have scanty cytoplasm and wavy buckled nuclei. Few cells have mild nuclear atypia without necrosis or mitotic figure. Features suggestive of a benign neurogenic tumor.

Then we have done an MRI of local area which revealed a focal well defined oblong shaped T2W hyperintense and T1W hypointense lesion measuring 4 x 5.5 x 8 cm in the posterior compartment between the medial and lateral head of triceps muscles and along the course of radial nerve. Distally the lesion converses to the radial nerve at the mid arm level. Rest of visualized soft tissues and bone were normal. Features suggestive of Radial Nerve sheath tumour. Further a core biopsy was done and the microscopic findings showed proliferation of bland spindle cells with wavy nuclei and pale cytoplasm intermixed with wire like collagen in a loose myxoid stroma. There were no nuclear atypia, mitotic activity, verocay bodies or nuclear palisading appreciated. It was given impression of Neurofibroma.

Surgical excision was the tumour was planned. Surgery was performed under general anaesthesia, a vertical elliptical skin incision incorporating the core biopsy site was given and a full thickness skin flap was raised all around. The medial and lateral heads of triceps muscle were split and retracted. The tumour was located and dissected nerve fibers. (Fig. 1a & 1b) Intraoperative nerve stimulator was used to check for neural

intact. (Fig. 2) The tumour which measured 7.5 cm x 4.5 cm x 4 cm was completely excised from the nerve sheath without causing nerve damage. (Fig. 3a & 3b). Post-operative periods were uneventful and her motor response was well satisfactory. The final histopathological examination was reported as Low grade malignant peripheral nerve sheath tumour. The surgical margins were free of malignant cells. On 4 weeks of follow up the surgical scar was well healed and power of operated upper limb was 5/5. (Fig. 4) She is on regular follow up.

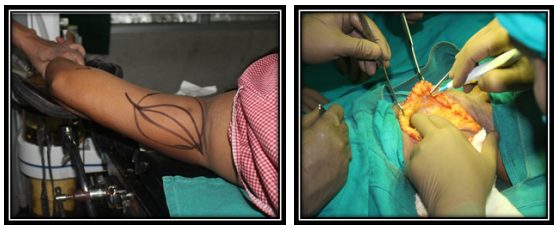

Figure 1a: Pre-operative skin incision marking and rasing of skin flaps

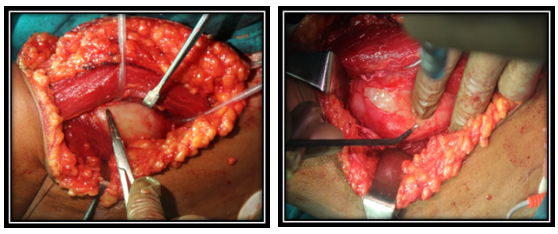

Figure 1b. Exposing the tumour and dissection of the nerve sheath.

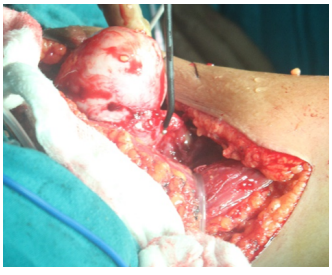

Figure 2 Intraoperative nerve stimulator was used to check for neural intact.

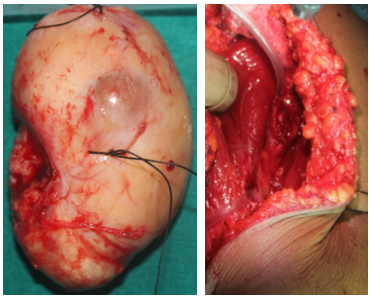

Figure 3a and 3b :- Completely resected tumour and intact Right Radial Nerve trunk

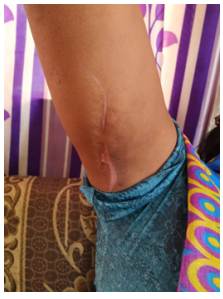

Figure 4:- One month follow-up –Well healed scar

DISCUSSIONS.

Malignant peripheral nerve sheath tumors (MPNST) are defined as nerve sheath tumors arising from a peripheral nerve, from a pre-existing peripheral nerve sheath tumor, or in the setting of neurofibromatosis type 1 (NF1) syndrome. MPNSTs comprise around 2 % of all sarcomas and incidence only 5 people per million per year .MPNST may arise at any age with no gender predilection. The median age for sporadic MPNST is between 30 and 60 years, and that for NF1-associated MPNST is between 20 and 40 years.[3,4] Patients present with an enlarging mass that may be painful or cause local neurological symptoms such as weakness or parae sthesia.

The most common sites of involvement include the nerve roots and bundles in the extremities and pelvis, particularly the sciatic nerve. In most instances, the size of the mass is greater than 5 cm at presentation and up to 50% of patients present with metastatic disease, usually to the lung.[5,6]

Literature search on PubMed online we could fine only 4 case reports of malignant nerve sheath tumour of radial nerve. Pathological diagnosis of MPSNT is that any sarcoma arising from the peripheral nerve sheath is readily diagnosed as MPNST if the tumour clearly has nerve elements or arises in the context of NF1. Otherwise, the diagnosis of MPNST is more difficult, with a broad differential diagnosis of other sarcomas, and requires an extensive clinicopathologic assessment of immunohistochemical (IHC) markers. IHC studies are helpful in distinguishing high-grade MPNST from other sarcomas but are less helpful in distinguishing atypical neurofibroma (ANF) from low-grade MPNST. Few commonly used IHC markers are S100, Ki-67, TP53 and CD34.[3,]

High-grade MPNST are highly cellular with many mitotic figures and areas of necrosis. Low grade MPNST are less cellular, have few mitotic figures and no areas of necrosis, and are difficult to distinguish from benign cellular neurofibromas and ANF. Small biopsies are usually inadequate for clinical decision-making due to this intratumor heterogeneity.[7]

Magnetic resonance imaging is the most useful imaging modality for characterizing the anatomical extent of the tumour for surgical planning. Fluorodeoxyglucose-positron emission tomography (FDG-PET) has been studied to evaluate the key clinical task of differentiating benign neurofibromas from MPNST in patients with NF1. One study demonstrated reliable and replicable differentiation with relatively high specificity this high degree of diagnostic accuracy with FDG-PET remains to be replicated in other series.[6]

In general, MPNST is known to have high metastatic potential and poor prognosis. Reported long-term out comes vary widely across multiple series, with 5-year survival ranging between 15% and 50%. Large tumour size at presentation (typically.5 cm) has been the most consistently determined adverse prognostic factor across all series. Other reported factors include tumour grade, truncal location, surgical margin status, local recurrence, and heterologous rhabdomyoblastic differentiation. Several large series report significantly worse outcomes for MPNST arising in the setting of NF1 compared with sporadic disease, with inferior responses to cytotoxic chemotherapy and 5-year survivals that are up to 50% worse

The only known definitive therapy for MPNST is surgical resection with wide negative margins, which may not be feasible due to variables such as tumour size, location, and/or metastases The role of adjuvant radiation is not defined; however, it is often recommended for high grade lesions > 5cm in size or with marginal excision For these patients, preoperative radiation should be considered. Although radiation has shown improved local control, no effect on

survival has been demonstrated. The risk-benefit profile of adjuvant radiation must be carefully discussed with all patients in view of the heightened risk of radiation-induced sarcomas.[8,9]

There are no randomized data examining adjuvant chemotherapy specifically in MPNST. In a prospective study of chemotherapy (ifosfamide, doxorubicin, and etoposide) in NF1 associated and sporadic MPNST, a lower objective response rate was seen in NF1 patients (18%) compared with patients with sporadic MPNST patients (44%), similar to prior studies however, disease stabilization was achieved in most patients at 4 cycles. The SARC006 phase II trial conducted by the Sarcoma Alliance for Research (SARC) evaluated the role of chemotherapy with doxorubicin, ifosfamide, and etoposide in 48 locally advanced or metastatic MPNST patients. It revealed encouraging disease stabilization and responses accruing from neoadjuvant chemotherapy that rendered subsequent local therapy feasible in the majority of patients with localized disease. There are few phase II and ongoing trails on targeting of both the TOR and hsp90 pathways, which appears to be one strategy of considerable promise based on existing data. The results of this clinical trials employing targeted agents are eagerly awaited, as are those of other combinations involving TOR inhibitors.[9,10]

The future directions of MPNST management is that though the outcome for MPNST has not changed significantly since 2002, the more complete understanding of the natural history of peripheral nerve sheath tumours and of the genomic changes during malignant transformation of plexiform neurofibroma to ANF and MPNST offers hope for the development of more effective diagnostic, therapeutic, and prevention strategies for MPNST. Whole-body MRI and PET imaging may have utility for risk stratification and for implementation of surveillance and medical/surgical interventions as potential preventative therapies and for monitoring treatment response.[10]

CONSLCUSION.

In this case report, we have highlighted a rare and challe nging mesenchymal malignancies to treat, MPNST which was arising from the radial nerve. A suspicion of MPNST should be kept in mind for a swelling despite evidence of benign nature, especially with a tumour size more than 5 cm, as the pathological changes may be present in focal regions. The best approach to treatment is by a multidisciplinary team of surgical, medical, and radiation oncologists, radiologists, and pathologists, all with sarcoma expertise.

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