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Malignant Peripheral Nerve Sheath Tumour of Thigh in Younger Age Group: A Case Report

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Abstract: Malignant peripheral nerve sheath tumour (MPNST) is relatively rare aggressive tumor which constitutes 5-10% of all Soft Tissue Sarcomas. It occurs either spontaneously or in association with Neurofibromatosis-1(NF1). MPNST is a disease of adulthood, typically between the ages of 20 and 50 years of age. MPNST occurs at earlier age and is associated with NF1. Here in, we have reported a case of 27 year old male, with the complaints of a mass in his right thigh, developed spontaneously, of size 15x7 cm, for a duration of 1 year. Imaging and Fine needle aspiration (FNA) studies were done. A wide excision was done and the specimen was sent for histopathological examination. FNAC and Histopathological findings were towards MPNST. Immuno-histochemical positivity with S100 and Cytokeratin (CK) negativity confirmed the diagnosis and ruled out the differential diagnosis of leiomyosarcoma, monophasic synovial sarcoma, Fibrosarcoma. Besides FNAC, istopathologyand Immunohistochemistry played a major role in the diagnosis of MPNST and helps in ruling out the differential diagnosis.

Key words: Malignant Peripheral Nerve Sheath Tumour · Neurofibromatosis1 · Immunohistochemistry · Sporadic

INTRODUCTION

MPNST is a rare soft tissue sarcoma which originate from peripheral nerves or from cells associated with nerve sheath, such as Schwann cells, Perineural cells or Fibroblasts. The term MPNST replaced previously used names of Malignant Schwannoma, Neurofibrosarcoma and Neurogenic Sarcoma[1]. MPNST is frequently associated with NF1. It also occurs sporadically and in post radiation exposure. Because MPNSTs can arise from multiple cell types, the overall appearance vary greatly, from case to case. This can make the diagnosis and classification difficult. Here in, we Reported a case of MPNST at Right thigh, in an younger individual, not associated with NF1.

Case Report: A 27 Year old male, presented with a rapidly growing mass in his right thigh for a duration of 1 year, with H/O Pain for 2months, in the Surgical out- patient department of Sree Balaji Medical College Hospital, Chennai. There was no clinical evidence or family history of NF1. He had no surgeries in the past. On examination, it was an ill-defined mass over right thigh measuring 15x7cm.

Magnetic Resonance Imaging(MRI) of right Pelvis, showed a heterogenous mass with lobulated margins, abutting the posterior aspect of right iliac wing with diffuse hypointensity noted along the posterior right iliac wing. A diagnosis of soft tissue tumour was considered. Chest X-ray, Ultrasound Abdomen was found to be normal.

FNA Smear showed a spindle cell neoplasm (Fig 1). Incisional biopsy of thigh was sent which was towards Soft Tissue Tumor of Neuronal origin. Wide and local Excision of thigh lesion was done and the specimen sent for histopathological examination.

Grossly, it was an ill-defined soft tissue mass covered by fibro-fatty tissue measuring 18x12x5 cm with elliptical piece of skin measuring 9x4 cm with an incisional biopsy scar of 2.5cm. Cut surface showed a fleshy tumor measuring tumor 12.5cm m with 3x1cm marginal clearance.

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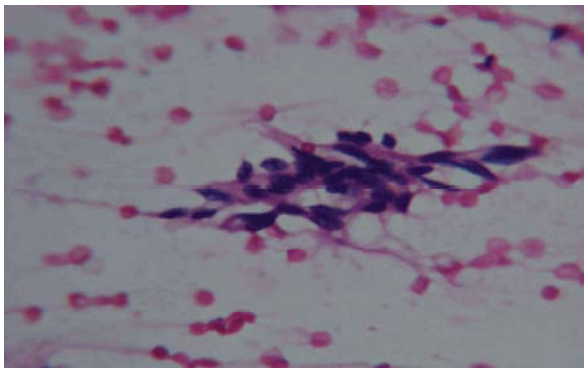

Fig. 1: FNAC Smear showing plump spindle cells with pleomorphic nucle i (H&E 10X view)

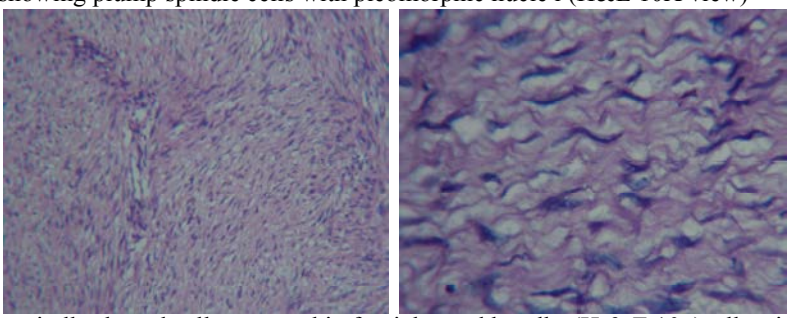

Fig. 2a&2b: Showing spindle shaped cells arranged in fascicles and bundles(H & E 10x)cells with wavy nuclei.(H & E 40Xview)

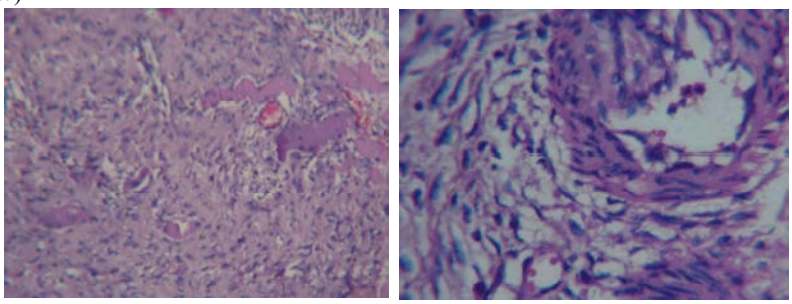

Fig. 3a &3b: Showing tumour cell infiltration into muscle bundles and blood vessels.(H& E 10X& 40X view)

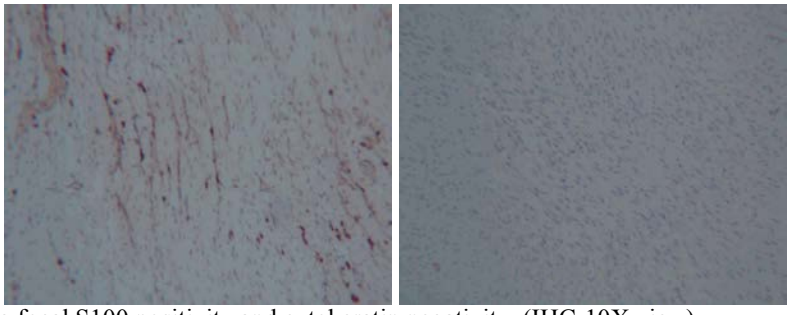

Fig. 4a&4b: Showing focal S100 positivity and cytokeratin negativity. (IHC-10X view)

Microscopic sections showed a cellular neoplasm, composed of spindle shaped cells with elongated, plump, wavy, fusiform nuclei, prominent nucleoli with irregular outline arranged in whorls, fascicles and interlacing bundles with focal myxoid areas. Stroma encloses thin walled capillaries and blood vessels surrounded by tumor cells. Focal areas shows cartilaginous metaplasia, epithelioid cells with occassional mitotic figures. Tumor infiltration is seen surrounding muscle bundles and in focal areas of margin. Adjacent stroma shows nerve bundles with no evidence of tumor necrosis. (Fig 3a,3b,3c).

Impression of Well -differentiated Malignant Peripheral Nerve Sheath Tumor (MPNST). Immuno-histochemistry showed strong focal positivity for S 100 and negative for cytokeratin(CK) (Fig 4&5). This confirmed our diagnosis of MPNST. Our patient is found to be recurrent free for a follow up period of 6 months.

DISCUSSION

MPNST is a very rare tumor, accounting for 5-10% of all soft tissue sarcomas with an incidence of approximately 0.001% in general population [6]. The tumor is more commonly located in the buttocks, forearm, lower leg and neck. It may occur either sporadically in 40% of cases or in association with Neurofibromatosis1(NF1) in 50% of cases, 10% of cases have been reported in patients with history of radiation exposure [2, 3]. MPNST is typically a disease of adult life, seen in the age group of 20 to 50 years of age [1]. However MPNST occurs in earlier age when associated with NF1. The average age at the time of diagnosis for patients with NF1 was found to be 29 to 36 years as against the sporadic counterpart of 40 to44 years, according to the study conducted in Mayo clinic &Memorial Sloan Kettering. MPNST in NF1 shows male preponderance whereas in sporadic cases, the gender ratio is equal.

Genetically both gain and loss of function are seen in MPNST arising from Neurofibroma. Both alleles of NF1 Gene are inactivated. Genomic gain noted in 17q, 7p, 5p, 8q & 12q. Genomic losses noted in 9p, 13q & 1p. 9p includes CDKN2, which is inactivated in MPNST. CDKN2 produces 2 proteins P16 & P19. P16 regulates cell cycling through Rb pathway. P14 regulates Cycling through P53 pathway. Thus P53, a tumor suppressor affected in MPNST.

Clinically, MPNST occurs as a solitary, deep seated palpable mass with sudden enlargement [1]. It may be aggressive, locally invasive and may cause erosion of adjacent bone with high rate of recurrence. Pain is a variable complaint. Mutiple MPNST can arise in NF1 patients. The most common distant metastic site of MPNST is the lung, followed by bone and pleura [1].

Investigations may be proceeded with imaging and FNA methods. Malignant cells can be demonstrated by FNAC but architectural pattern of the tumor cannot be demonstrated in FNAC. This is the reason for difficulty in definite diagnosis of MPNST with FNA smear. As FNAC cannot give a definite diagnosis, incisional biopsy may be done when sarcoma is suspected followed by excisional biopsy as was done in our case. The CT chest and bone scan play a vital role in identifying the metastasis. A Positron Emission Computed Tomography (PET-CT) examination of the whole body can be performed to rule out any possible metastasis or additional lesion. MPNST in NF1 patient may be difficult to detect. Fluorodeoxyglucose(FDG)-PET is sensitive and specific for detecting the malignant transformation in NF1 patients [8].

Grossly, the tumour specimen may be fusiform,oval eccentric mass in a major nerve of size usually more than 5cms in diameter.Cut section may show a fleshy, opaque,white tan with areas of haemorrhage and necrosis.

Histopathologically, MPNST shows areas of dense cellular fascicles which alternate with hypocellular myxoid areas which inter-digitate and swirl to form a " marbleized pattern". The cell may be spindle shaped with irregular contours, rounded or fusiform. The nuclei may be wavy,buckled or comma shaped with lightly stained and indistinct cytoplasm. Nucleur pallisading may be present in 10% of cases. Heterotopic elements may be present in 10 -15% of cases.Islands of cartilage and bone are the most common elements whereas skeletal muscle and mucin secreting glands are rare.

These tumours often create diagnostic difficulties because of their cellular origins and histopathological similarities with those of other spindle cell sarcomas. The differential diagnosis of this tumour is monophasic synovial sarcoma, dedifferentiated liposarcoma, leiomyosarcoma and fibrosarcoma [7]. Immunohistochemical markers such as S100, Vimentin, Leu 7 and Myelin basic protein may be used for the confirmation of the diagnosis and to rule out the differential diagnosis [1]. S100 focal positivity is seen in 50-90% of cases, whereas Leu7 and myelin basic protein positivity seen in 50% and 40% of cases respectively.

Treatment depends on staging, Metastasis and local recurrence. Wide excision with negative margin is the main stay of surgical treatment [5].

Positive tumor margin is most important prognostic marker. Adjuvant radiotherapy should be given in Low, intermediate and high grade lesion with positive margins [4].

Role of Chemotherapy is limited to the case of MPNST with Metastasis. Recurrence rate is around 52 to 88.9% at different sites. Metastasis ranges from 11.1 to 18% [4, 5].

Rate of 5 years survival is reported as 16 to 52%. Longer survival has been co related with complete surgical excision, small tumor size and presence of low grade components [5].

In Metastatic MPNST treated with chemotherapy the survival rate is poor [6].

CONCLUSION

Malignant Peripheral Nerve sheath Tumor can also present sporadically in younger age group. Besides FNAC and Histopathological diagnosis, Immuno Histo Chemistry helps in the confirmation of MPNST, differentiating from other soft tissue sarcomas which mimics MPNST in histological appearance.

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