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ORIGINAL RESEARCH

A rare case of MPNST of the sciatic nerve in a patient with type 1 neurofibromatosis treated by surgical excision with preservation of nerve functions with review of literature

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ABSTRACT

A 67-year-old man with neurofibromatosis type 1 presented with multiple nodular swelling all over the body and a swelling arising from posterior aspect of right thigh suggestive of neurofibroma arising from the sciatic nerve with malignant potential. The chief complaint of patient was severe excruciating pain into the whole left lower limb. The differential diagnosis of malignant peripheral nerve sheath tumor, neurofibrosarcoma was based on clinical, radiological, and histological evidence. The tumor apparently originated in sciatic nerve at the posterior aspect of the right thigh. The tumor mass was excised completely without neural damage to the sciatic nerve. Patient is relieved of pain and totally asymptomatic after 2 year follow up.

Keywords: Neurofibromatosis type 1; Malignant peripheral nerve sheath tumor; Malignant schwannoma; Von Recklinghausen's disease

INTRODUCTION

Neurofibromatosis 1 (NF1) also called von Recklinghausen's disease is an inherited neurocutaneous disorder. It is characterized by the presence of multisystem tumors throughout the skin and central nervous system (CNS), which carries a risk of malignant transformation.[1] The hallmark clinical features of NF1 include multiple café au lait macules, neurofibromas, intertriginous freckling, osseous lesions, Lisch nodules, and optic pathway gliomas (OPGs). The CNS and skin are primarily involved but other organ systems can also be affected. Since the skin and nervous tissue originate from the same germ layer i.e. the ectoderm, these disorders have been variously called congenital ectodermoses and congenital neuroectodermal dysplasias. Van der Hoeve believed that neurofibromatosis can be found in sciatic nerve.

CLINICAL PRESENTATION

A 67 years old man with history of NF1 presented to the OPD of PGIMS Rohtak with a painful lump over the posterior aspect of right thigh since 12 months with increase in size

since last 3 months. Swelling was gradually increasing in size, nodular, firm in consistency, tender, mobile, non pulsatile, non fluctuant [Fig 1].

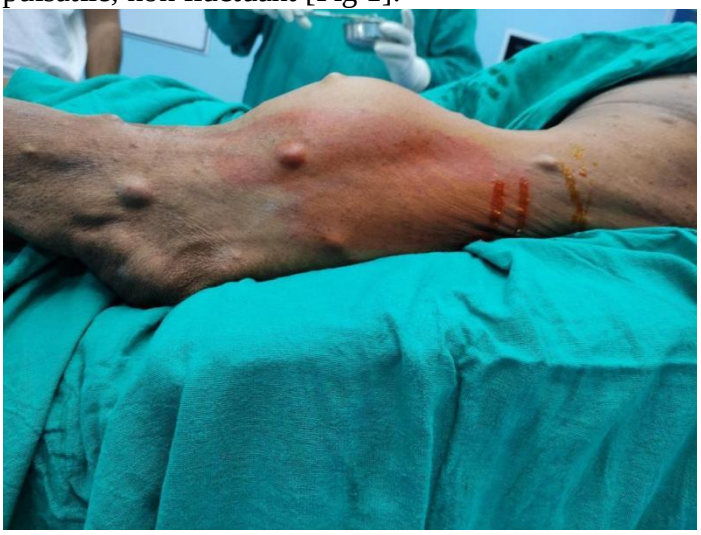

Figure 1: Swelling in the posterior aspect of right thigh.

Two months later he developed weakness and sensory deficit over the right limb which was ascending in nature, more for hip extension, flexion of knee and planter flexion for which he needed assisted walking. There was severe excruciating pain along the course of nerve in right lower limb which was not even relieved by medications. The motor weakness and increasing intensity of pain hampered patient day to day life and finally he reached OPD for removal of this swelling. There was no family history and all the next generations of patients family were clinically normal.

FNAC was done which suggested a neoplastic lesion of mesenchymal origin. MRI suggested a well defined lobulated heterogeneous lesion inseparable from sciatic nerve, likely arising from it [Fig 2].

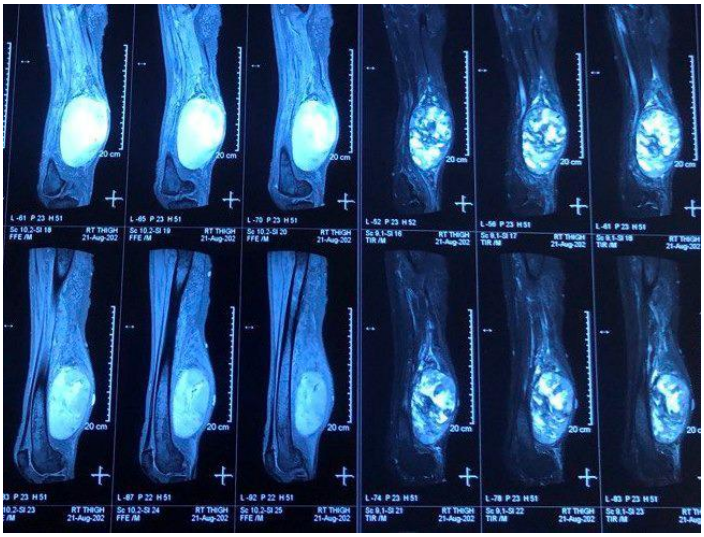

Figure 2: Sagittal sections of T2 and STIR MRI images showing the extent and location of the mass in posterior of thigh

A clinical, radiological and histological diagnosis was made of neurofibroma of sciatic nerve. Patient had multiple nodular swellings over whole body along with a plexiform neurofibromatosis over the face.[Fig 3 and Fig 4].

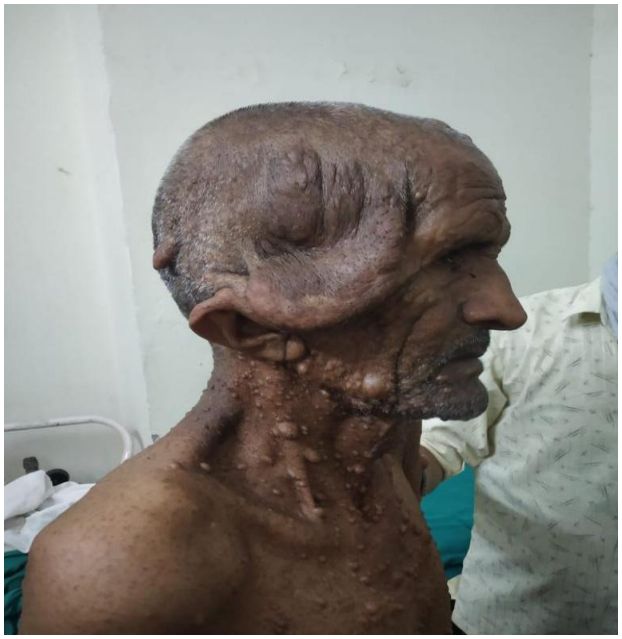

Figure 3: Plexiform neurofibromatosis over face.

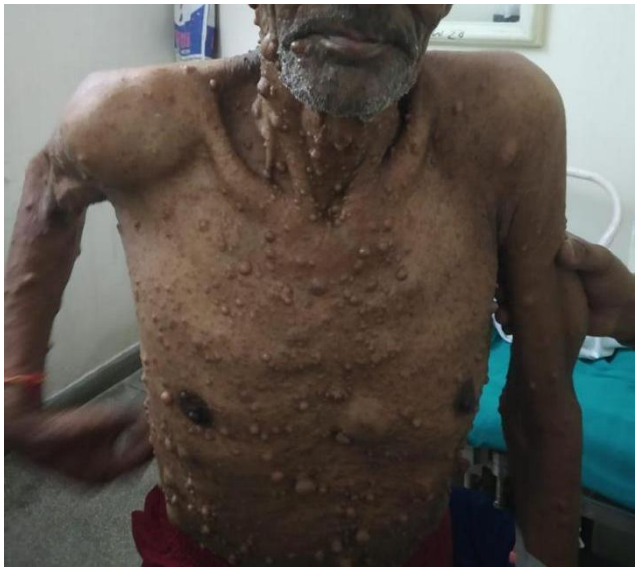

Figure 4: Multiple nodular swelling over the whole body

SURGICAL INTERVENTION

After informed consent of surgical procedure and possible risk of sciatic nerve injury, patient was operated in Spinal anesthesia in prone position. Skin incision was given along the posterior aspect of thigh and after dissecting soft tissues, tumor margins were identified. Sciatic nerve was explored and freed proximally as well as distally.

The tumor was arising from the sciatic nerve (Fig 5) and fibers of sciatic nerve were around it.

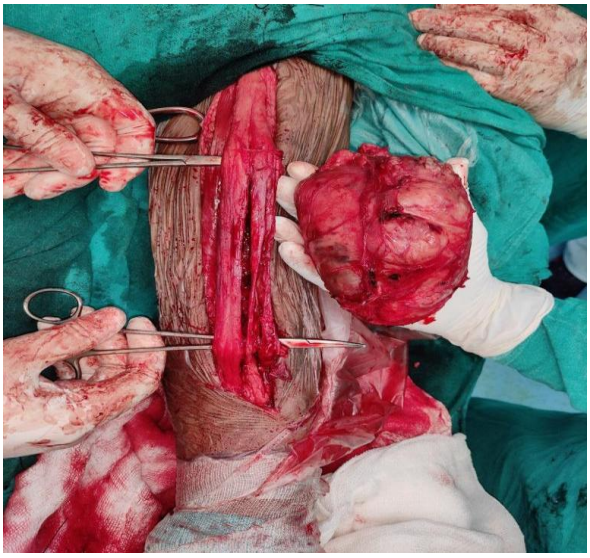

Figure 5: Intraoperative image showing the tumor mass after resection from its origin, the sciatic nerve.

The tumor was completely encasing the sciatic nerve and after dissecting the nerve fibers removed the tumor from its fibre. The nodular encapsulated mass measuring 13*9*8 cm was sent for histopathological examination. It revealed a malignant mesenchymal tumor with closest resemblance to malignant peripheral nerve sheath tumor. On immunohistochemistry it was positive for vimentin and NSE, focally positive for EMA. Postoperative period was uneventful. There was complete relief in pain after the surgery. There was motor recovery in postoperative period from 4th week onwards with almost complete muscle strength after 6 months of postoperative period. Patient is on follow up since last 2 years with no recurrence or any other complaint.

DISCUSSION

Neurofibromatosis (NF) is a disease of defective development of the neuroectodermal tissues that tends to involve multiple systems and occurs in approximately 1 in 4000 to 5000 individuals. Approximately half of the cases appear to be sporadic and the mutation rate has been estimated at 1 in 10000 gametes per generation, one of highest mutation rates in humans. Approximately 50% of patients have affected relatives and in nearly all instances the distribution of cases is consistent with an autosomal dominant mode of inheritance. NF1 is observed in all regions of the world and affects bothmen and women equally.

The inheritance of NF1 is autosomal dominant with 100% penetrance but highly variable expressivity.[1,2,3] The *NF1* gene is located on chromosome 17q11.2.

CLINICAL FEATURES AND ASSOCIATED DISORDERS

NF1 is characterized by cutaneous pigmentation, multiple tumors within the central and peripheralnervous systems and lesions of the vascular and other organ systems.

Focal hyperpigmented areas and café au lait spots, ranging in size from a few millimeters to centimeters, are more commonly found on the trunk than on the limbs, and they are not found on the scalp, soles or palms. These spots are light brown and result from an aggregation of neural crest-derived pigmented melanoblasts in the basal layer of the epidermis. Café au lait spots are present at birth and become more apparent with time. The number of café au lait spots probably does not significantly increase after the first several years of life, although the degree of hyperpigmentation usually does. The presence of six or more café au lait spots larger than 15mm in the greatest diameter is required for the diagnosis of NF, a criterion that

is most useful when applied to postpubertal patients. It should be recognized, however, that approximately 10% of the general population have café au lait spots without other stigmata of the disease. Less frequent cutaneous changes in NF1 include diffuse axillary or inguinal freckling andlarge area of faintly increased pigmentation (melanoderma).

Austrian ophthalmologist Karl Lisch was the first to emphasize what are now called Lisch nodules and their association with NF1 in 1937.[4] Histologically Lisch nodules are melanocytic hamartomas, consisting of a condensation of spindle cells on the anterior iris surface. Stromal iris nevi underlie the pigmented nodules.[5] They are present on the anterior iris surface or in the anterior chamber angle. They are well-defined yellow-brown dome-shaped elevated lesions and can range in size from pinpoint to large.[4,6] Although Lisch nodules do not cause ocular morbidity or disability, they are important because they are one of the diagnostic criteria for NF1. Their presence is age-dependent. Although their presence is unusual before the age of 2 years, they are seen in half of 5-year-olds, 75% of 15-year-olds, and almost 100% of adults older than 30 years.[7]

Neurofibromas are a hallmark feature of NF1, present in almost all patients older than 30 years.[8] They are benign soft tissue tumors of Schwann cell origin that arise on peripheral nerves.[9] In addition to neoplastic Schwann cells, they also contain fibroblasts, macrophages, and mast cells.[10] Clinically, neurofibromas can be further classified as cutaneous, subcutaneous, or plexiform which can be further divided into nodular or diffuse. The morbidity associated with plexiform neurofibromas is 2-fold. In addition to the disfigurement, bony destruction, and pain associated with these lesions, they also carry an 8% to 13% lifetime risk of malignant transformation [malignant peripheral nerve sheath tumor (MPNSTs)].[11,12]

Unfortunately, MPNSTs have a poor prognosis with a 5-year survival of up to 60%, warranting ongoing careful surveillance with a low threshold for investigation. Poor prognosis is associated with early metastasis and poor response to systemic chemotherapy. Delayed diagnosis remains an issue. Features including increased growth rate, irregular contour, and pain in existing neurofibromas are symptoms and signs that may indicate malignant transformation. These symptoms may also be present in benign lesions.[13,14]

Diagnostic Criteria for NF1 includes:

- 6 or more café-au-lait spots, >0.5 cm in prepubertal children >1.5 cm in postpubertal individuals
- Axillary or inguinal freckling
- 2 or more cutaneous neurofibromas
- 1 plexiform neurofibroma
- 2 or more iris Lisch nodules
- An optic glioma
- A characteristic bony lesion (pseudarthrosis, hypoplasia of sphenoid wing, severe kyphoscoliosis)
- First degree relative with NF1

In order to make the diagnosis, at least 2 major criteria are required.

Malignant transformation of neurofibroma to malignant schwannoma occurs in 29% of patients with NF but its origin from a large nerve trunk is less common in patients with NF1.[15,16] Some transformations occur after radiotherapy or previous surgery for a benign neurofibroma.[17] The pleiotropic effect of the NF allele on chromosome 17 is responsible for increasing the risk for both neural crest and nonneural crest malignancies.[18-22] Development of malignant schwannoma from neurofibroma is associated with inactivation of both NF1 (tumor suppressor gene) alleles, and by partial inactivation on the other tumor suppressor gene p53 located elsewhere on the centromere of chromosome 17.[18,23] Neurofibroma increase in size under the conrol of the sex steroids in both sexes, directly or through mediation by

nerve growth factor (NGF) whose receptor is located on the distal arm of chromosome 17.[24,25] The onset of malignant schwannoma may be attributable to the abnormal and continuous stimulation of nerve cells sensitive to NGF.[26]

CONCLUSION

Neurofibroma can turn malignant but involvement of major nerve trunk like sciatic nerve is less likely. Malignant peripheral nerve sheath tumors are a challenging to manage specially if it involves major nerve trunk. Resection of tumor mass and simultaneously preservation of function should be ideal management in such cases but sometimes in cases of MPNST nerves can be sacrificed for complete eradication of tumor mass.

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