Giant malignant peripheral nerve sheath tumor with cauda equina syndrome and subarachnoid hemorrhage: Complications in a case of type 1 neurofibromatosis

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Abstract

Type 1 neurofibromatosis (NF1), which mainly involves ectodermal tissue arising from the neural crest, can increase the risk of developing malignant peripheral nerve sheath tumors (MPNSTs), soft tissue sarcomas and subarachnoid hemorrhage. We describe a patient with neurofibromatosis type 1 who developed soft tissue sarcoma, MPNST, and subarachnoid hemorrhage. A 22-year-old male reported right focal seizures consequence to severe headache. He had a weakness in both legs, could walk only with the support of a stick for the last 3 months and suffered from constipation and intermittent urinary retention for the past 1 week. The patient had a history of swelling in the back of left thigh for which surgical resection was done 6 months back. Cutaneous examination revealed multiple nodules of varying sizes all over the body, along with many café-au-lait spots and Lisch nodule in iris. Patient had weakness in bilateral hip abduction, extension, knee flexion, extension and ankle dorsiflexion and plantiflexion. Bilateral ankle reflexes were absent while other deep tendon reflexes were sub-optimal. A noncontrast computed tomography brain indicated subarachnoid hemorrhage in left perisylvian region. Ultrasound of left thigh showed a hypoechoic solid lesion in the posterior aspect of left thigh in muscle plane. Histopathology of the lesion following resection showed features suggestive of a low-grade pleomorphic rhabdomyosarcoma. Histology of cutaneous nodules was consistent with neurofibroma. Magnetic resonance imaging of the lumbosacral spine demonstrated a tumor arising from cauda equina. Histopathological examination of the tumor suggested high-grade MPNST. Unfortunately, the patient’s MPNST was inoperable, and he received palliative radiotherapy for local control of the disease. The care of a patient with neurofibromatosis requires a comprehensive multisystem evaluation. MPNST occurs in 8-13% patients with neurofibromatosis. Early diagnosis and surgical resection are key to prolong survival. Though rare, rhabdomyosarcoma can occur with a higher frequency in NF1, necessitating through clinical investigation. Subarachnoid hemorrhage can occur due to aneurismal rupture or vascular friability in NF1 patients.

Key words: Malignant peripheral nerve sheath tumor, neurofibromatosis, rhabdomyosarcoma, sarcoma, subarachnoid hemorrhage
INTRODUCTION

Type 1 neurofibromatosis (NF1) is an autosomal dominant disorder with an incidence of 1 in 3000-4000 individuals.[1] It affects the skin, skeletal system, and cerebral function. The disease mainly involves ectodermal tissue arising from the neural crest and is diagnosed by the presence of two or more of the following features: Six or more café-au-lait spots, two or more cutaneous neurofibromas, axillary or groin freckling, optic pathway glioma, two or more Lisch nodules, a characteristic bone dysplasia and/or a first-degree relative with NF1 patient. Patients with neurofibromatosis have an increased risk to develop malignant peripheral nerve sheath tumors (MPNSTs), which tend to be more aggressive then in patients without neurofibromatosis. Furthermore, these patients also have a predisposition to develop soft tissue sarcomas and vascular aneurysms, which may lead to subarachnoid hemorrhage. To best of our knowledge, there hasn’t been a report of all these complications in a single patient. We describe one unusual patient with NF1 who developed soft tissue sarcoma, giant MPNST causing cauda equina syndrome, and subarachnoid hemorrhage.

CASE REPORT

A 22-year-old man was brought by his relatives in an emergency department following partial seizures involving right half of the body, which occurred after a severe headache a few hours prior to admission. After initial stabilization patient was shifted to the neurology ward where a formal clinical evaluation was performed. He had weakness in both legs and required support to walk for the last 3 months. He had constipation and intermittent urinary retention for a week. He had a history of swelling in the back of left thigh, which was surgically resected 6 months back. His blood pressure was normal with no history of addiction or any other major illness. Cutaneous examination revealed multiple nodules (firm to rubbery in consistency) of varying sizes all over the body [Figure 1] along with many café-au-lait spots [Figure 2]. Ocular examination was significant for a Lisch nodule in iris [Figure 3]. Clinical examination for higher neurological functions and cranial nerves did not reveal any abnormality. Patient had weakness in bilateral hip abduction, extension, knee flexion, extension and ankle dorsiflexion and plantiflexion. He had impaired sensation for pain, touch, and temperature in L5 to S3 distribution. Bilateral ankle reflexes were absent whereas other deep tendon reflexes were sub-optimal. Since the patient satisfied 3 out of 7 diagnostic criteria for neurofibromatosis type 1, a diagnosis of NF1 was made.

Patient’s complete hemogram, kidney and liver function tests were within normal limits. Chest X-ray was normal. An urgent noncontrast computed tomography brain revealed subarachnoid hemorrhage in left perisylvian region [Figure 4]. His previous hospital records were reviewed, in which the preoperative ultrasound of left thigh showed a hypoechoic solid lesion in the posterior aspect of left thigh in muscle plane, measuring 10.9 cm$^3 \times 3.4$ cm$^3 \times 5.8$ cm$^3$. Histopathology of the lesion after resection showed features suggestive of a low-grade pleomorphic rhabdomyosarcoma. The cutaneous nodules were also biopsied, and histology was consistent with neurofibroma. Magnetic resonance imaging of the lumbosacral spine [Figure 5] demonstrated a large soft tissue mass displaying mixed signal changes on both T1 and T2 weighted images with a heterogeneous postcontrast enhancement. The tumor was seen arising from sacrum with surrounding bony destruction, extending from anterior abdominal wall to glutal muscles. Imaging features were consistent with an MPNST arising from cauda equina. Histopathological examination of the tumor biopsy showed the presence of spindle-shaped cells with marked nuclear pleomorphism and giant cells. It had increased cellularity and a high mitotic activity, features suggesting a high-grade...
Patient was closely monitored during the initial period for subarachnoid hemorrhage and received mannitol, acetazolamide, and nimodipine. Unfortunately, the patient's MPNST was inoperable, and he received palliative radiotherapy for local control of the disease. Patient's neurodeficit was persistent at 6 months follow-up and he was dependent on caregivers for his daily routine.

**DISCUSSION**

Neurofibromatosis type 1 (von Recklinghausen's disease) is an autosomal dominant genodermatosis with global incidence of 1 in 2500-3000 individuals.\(^2\)\(^,\)\(^3\) The principal and defining manifestations of NF1 are café-au-lait patches, neurofibromas (benign peripheral nerve sheath tumors), skin-fold freckling, iris Lisch nodules (hamartomas diagnosed on slit-lamp examination), optic nerve gliomas and characteristic bony dysplasia of the long bones and sphenoid wing.\(^4\)

The overall risk of cancer is 2.7 times higher in NF1 patients than in the general population. The cumulative risk of a malignancy by age 50 years is 20%\(^,\)\(^3\) MPNST is one of the most aggressive tumors associated with NF1 and reported to occur in up to 8% to 13% of patients.\(^6\) The lifetime risk of developing an MPNST has been calculated to be 5.9-10.3%.\(^7\) Outcome of treatment of MPNST remains poor. The 5 years survival of NF1 patients with MPNST is reported to be 16%, compared with 53% for non-NF1 patients with metastases of 39%. Prognosis has correlated with tumor size and extent of resection, but not with radiation or chemotherapy.\(^8\)\(^,\)\(^9\) In patients with MPNST, median survival of 18 months overall, 53 months in peripheral locations, and 21 months in axial locations are reported.\(^10\) Hence, only early detection and surgery appears to be vital for improving survival of patients with MPNST.

Our patient had a low-grade rhabdomyosarcoma in left thigh. Rhabdomyosarcomas are reported in patients with neurofibromatosis 1 with a disproportionately higher frequency.\(^1\)\(^,\)\(^11\) However, studies regarding treatment outcomes of rhabdomyosarcoma in patients with neurofibromatosis are lacking. Hence, again early diagnosis and timely surgical intervention are key elements in the management.

The subarachnoid hemorrhage in our patient can be explained by probable rupture of an intracranial aneurysm, which is reported with a higher frequency in patients with NF1.\(^12\)\(^-\)\(^18\) Such higher vascular manifestations may be due to endothelium and smooth muscle dysfunction secondary to neurofibromatous tissue at these sites. Neurofibromatous tissue are observed in the wall of the aneurysm as well as
in small veins, where they alter neurofibromin function\textsuperscript{[13]} and often make the surgery difficult due to the risk of excessive bleeding.

**CONCLUSIONS**

The care of a patient with neurofibromatosis requires a comprehensive multisystem evaluation. MPNST occurs in 8-13\% patients with neurofibromatosis. Early diagnosis and surgical resection are key to prolong survival. Although rare, rhabdomyosarcoma occurs with a higher frequency in NF1, requiring comprehensive clinical investigation. Subarachnoid hemorrhage can occur due to aneurismal rupture or vascular friability in NF1 patients.

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