CASE REPORT

Malignant peripheral nerve sheath tumours in a patient with Neurofibromatosis-1

Fatima Iqbal[1], Muhammad Jamaluddin[2], Fakiha Bukhari[3], Omama Subul Islam[4]

Abstract

Malignant peripheral nerve sheath tumour (MPNST) is an uncommon type of soft tissue tumour which most commonly arises in the setting of Neurofibromatosis-1 (NF-1) or in the presence of another nerve sheath tumour. NF-1 is an autosomal dominant syndrome which is diagnosed based on clinical criteria. People suffering from NF-1 are at a higher risk of developing tumours, especially MPNST. MPNST can occur anywhere along the distribution of nerve roots but most commonly involves the limbs and trunk. The prognosis of MPNST in the setting of NF-1 is grave as the distant metastasis develops earlier than non-syndromic cases. Pre-operative diagnosis is difficult as there is no gold standard radiologic technique or characteristic radiological features. The diagnosis is established after histological evaluation supplemented by immunohistochemistry of the tumour tissue. We present a case of a 38-year-old female, a known case of NF-1, who presented with a single, irregular, cystic swelling in the left flank which was increasing in size. The patient underwent complete surgical excision of a 6cm tumour which was diagnosed as MPNST after histopathological examination. The rare nature of this tumour makes the diagnosis and treatment extremely hard. Awareness regarding this disease should be increased so that proper treatment plans can be made.

Keywords: Malignant peripheral nerve sheath tumour, Neurofibromatosis-1, Immunochemical staining, Histopathology.

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Introduction

Malignant peripheral nerve sheath tumour (MPNST) is an aggressive, well-known sarcoma of peripheral nerve sheath origin, comprising 5-10% of all soft tissue sarcomas.[1] It may arise sporadically or in patients affected by Neurofibromatosis-1 (NF-) syndrome. MPNST can occur in patients over a wide age range; however, it usually occurs at a younger age as compared to other types of sarcomas. It has no gender or racial predisposition.[2]

[1,2,4]Department of Surgery, Abbasi Shaheed Hospital, Karachi, Pakistan; [3]Final Year MBBS Student, Karachi Medical and Dental College, Karachi, Pakistan
Correspondence: Fatima Iqbal. e-mail: drfatimaiqbal90@gmail.com
ORCID ID. 0000-0002-3001-5073

NF-1 is an autosomal dominant syndrome with an occurrence of 1 in 2,500 births and a prevalence of 1 in 4,000 individuals.[3] NF-1 is characterised by acoustic neuromas, café-au lait spots, Lisch nodules, and skeletal deformities.[4] The risk of developing MPNST in patients with NF-1 is approximately 2-4%. It is also seen to arise in patients previously treated with radiotherapy.[5]

Case Report

A 38-year-old female, a known case of NF-1, presented to the OPD of Abbasi Shaheed hospital on May 25, 2021, with complaint of painful swelling at the left flank for one month. The swelling was initially pea-sized, however, it increased to the size of a lime. It was associated with sudden onset, severe pain which was non-radiating, non-shifting, aggravated on lying down and relieved spontaneously. No association with fever, weight loss, discharge, functional impairment or numbness was noticed. There was no complaint of headache, vertigo, earache, blurring, tinnitus or seizures. The patient had multiple swellings all over her body due to NF-1. Her mother also suffered from NF-1 and had died due to some unknown cause.

On examination, the patient was a middle-aged female of normal height and weight. Her vitals were within normal range. She was afebrile. Multiple neurofibromas of various sizes and café-au-lait spots were seen all over her body. Ophthalmic examination also revealed Lisch nodules.

A solitary, irregular swelling, 6x5cm in size, was seen in the

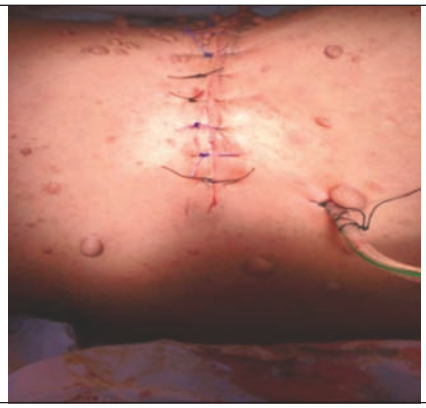

Figure-1: Postoperative picture showing multiple neurofibromas.

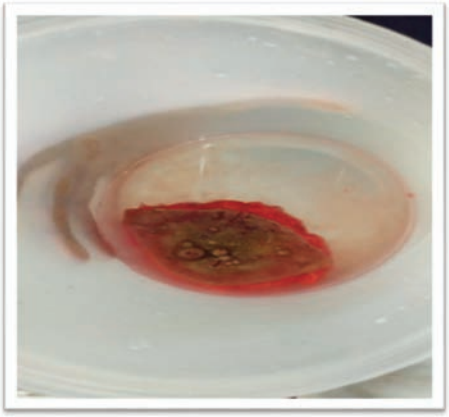

Figure-2: Excision biopsy sample of Neurofibroma.

left lumbar region in posterior axillary line which was fixed to the overlying skin. The adjacent skin also showed neurofibromas. This postoperative picture showing multiple neurofibromas. (Figure 1). There were no scar marks or prominent veins. The swelling did not move with respiration. Cough impulse was negative. On palpation, the temperature above the swelling was normal. The swelling was also adherent to underlying structures and was non-compressible, non-reducible and non-fluctuating. No regional lymphadenopapthy was observed. Ultrasound revealed a cystic swelling. Pre-operative diagnosis of dermatofibrosarcoma was made. An excisional biopsy was done using elliptical incision and the tumour was sent for histopathological evaluation (Figure 2). The morphological and immunohistochemical (IHC) features were consistent with the diagnosis of low grade MPNST.

Discussion

Mutations of the neurofibrin 1 gene, which is located on chromosome 17q11.2, causes NF-1. According to NIH guidelines, two or more of the following clinical features must be present for the diagnosis of NF-1: -

1. Multiple neurofibromas
2. Café-au-lait spots
3. Lisch nodules
4. Intertriginous freckling
5. Distinctive bony lesions
6. Optic pathway gliomas
7. A first-degree family relative with neurofibromatosis.[6]

Our patient had café-au-lait spots, Lisch nodules, multiple neurofibromas, and a family history of NF.

Patients suffering from this genetic disorder are at a higher risk of developing various tumours, such as pheochromocytoma, leukaemia, glioma, and MPNST. The lifetime risk of developing MPNST in NF-1 patients is 8-13%.[7] Thirty percent of the cases diagnosed with MPNST are affected by NF-1.[8] The chances of developing MPNST in general population is 0.017 per one million persons per year, whereas in patients with NF-1 it is 0.1%.[5] MPNST can also arise in the setting of previous radiation exposure (therapeutic radiotherapy for other tumours) or microdeletions in NF-1 genes.[9]

MPNST can occur anywhere along the nerve root; however, they occur most commonly in the nerve of trunk or limbs.[10] The most common nerve root to be involved is sciatic nerve roots.[11] Our patient had MPNST in the left flank which most likely originated from the lumbar nerve roots.

Pre-operative diagnosis of MPNST is difficult as there is no single imaging modality which is considered gold standard for the diagnosis. However, the diagnosis is confirmed after histopathological and IHC evaluation.[10] Histopathological examination generally shows fascicles of spindle cells with variable pleomorphism. Few cells with wavy nuclei having tapered ends are also seen. Tumour cells show positive expression for SOX-10, S100, CD56 and PGP 9.5. IHC stains.[12]

The patient under discussion was diagnosed clinically with NF-1, therefore, MPNST was already a differential. Histopathology report showed S100 and CD56 positivity and a mitotic score of 2 was observed. All these features were consistent with MPNST.

MPNST is generally recognised as a biologically malignant tumour with high rate of metastasis and grave prognosis.[2] Its relapse is also high with 40% people developing local recurrence. The five-year and 10-year survival rates of patients with MPNST are 26-60% and <45%, respectively.[13]

The prognosis of MPNST is poor and depends upon several factors with tumour size being the most critical factor. Larger size (>5cm), high grade of tumour, and rhabdomyoblastic differentiation are poor prognostic features.[2] MPNST with NF-1 is linked with grave prognosis as compared to MPNST without NF-1 (Radiation or sporadic).[7]

Treatment of MPNST is complete surgical excision with negative margins. However, it is successful only in cases where the tumour is resected and treated early.[9] In some instances, neoadjuvant chemotherapy is administered in large-sized tumours. This helps in reducing the relapse of tumour.[11] However, its use is still disputed. Single dose Anthracycline has been used palliatively, in cases where tumour has extensively metastasized.[9]

Conclusion

MPNST is a highly aggressive and uncommon tumour whose prevalence has been increasing and more cases are being reported as this case is reported and managed early which reduces the mortality of patient. Its clinical and radiological features and treatment modalities should be described more frequently so that it can be diagnosed easily and treated at an early stage. Further studies should be conducted to evaluate the effectiveness of different treatment options for patients with poor prognosis.

Follow up: Patient's follow up was taken she is fine with no new swelling. Previous swellings are present with same size and number.

Consent: Patient consent was obtained for publishing her data and pictures.

Disclaimer: None.

Conflict of Interest: None.

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