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# MALIGNANT PERIPHERAL NERVE SHEATH TUMOUR PRESENTING AS SCIATICA IN A PATIENT WITH NEUROFIBROMATOSIS TYPE 1: IS MAGNETIC RESONANCE IMAGING AN EFFECTIVE SCREENING TOOL?

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## ABSTRACT

Peripheral malignant nerve sheath tumours (MPNST) are rare and aggressive soft tissue sarcomas often associated with neurofibromatosis type I (NF-1). We describe a case of 26-year-old female with NF-1, initially misdiagnosed as sciatica, who was later found to have a malignant spindle cell peripheral nerve sheath tumour of the right sciatic nerve. Magnetic resonance imaging (MRI) proved to be a valuable tool for diagnosis. This case illustrates the importance of considering the transformation of neurofibromas into MPNST as a potential cause of worsening neuropathic pain in patients with NF-1. Given the overlap in clinical presentation with benign conditions, we analyse the utility of MRI for early screening for. Early detection is crucial to improve the chances of cure and prolonged disease-free survival.

## KEYWORDS

Malignant peripheral nerve sheath tumor, MPNST, neurofibromatosis type I, NF-1, magnetic resonance imaging, sciatica

## LEARNING POINTS

- Malignant peripheral nerve sheath tumours can occur in patients with neurofibromatosis and present as sciatica.
- Magnetic resonance imaging screening should be considered early on in this patient population.

## INTRODUCTION

Peripheral malignant nerve sheath tumours (MPNST) are rare but highly aggressive tumours with an incidence of 1 in 100,000 in the general population, but they are more common in patients with neurofibromatosis type 1 (NF1). Close to 25-50% of MPNSTs are diagnosed in patients with underlying NF-1 with the lifetime risk of developing MPNST in these individuals being 8 to 13%[1,2]. They are associated with a poor prognosis. Early diagnosis is the most important factor impacting prognosis but is often challenging due to non-specific symptoms often mimicking sciatica. Therefore, a high index of suspicion is crucial in patients with underlying predisposing factors. Diagnosis typically involves tissue biopsy (preferably surgical) of a suspicious lesion identified

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on imaging studies such as positron emission tomography/computed tomography (PET/CT) scan or magnetic resonance imaging (MRI)[2,3]. MRI is essential in distinguishing between benign and malignant lesions.

We describe a rare presentation of a malignant peripheral nerve sheath tumour of the right sciatic nerve in a young patient with NF-1 and explore the role of MRI in a NF-1 patient with new or worsening neuropathic pain, potentially aiding the early diagnosis of MPNSTs and improving patient outcomes.

## CASE DESCRIPTION

A 26-year-old female patient with a medical history of neurofibromatosis type 1 (NF-1) presented to the emergency department (ED) complaining of a 1-week history of progressively worsening lower back pain that radiates to her right leg. The pain started about 9 months before but became especially severe over the week before her ED visit. During this time, she experienced weakness, numbness, and paraesthesia in her right leg. She also had difficulty during urination which she describes as needing to strain to initiate flow. The patient had visited multiple hospitals for her chronic back pain and was treated with gabapentin and baclofen for sciatica with no significant improvement.

At presentation, the patient was mildly hypertensive (blood pressure: 148/92), with otherwise normal vital signs. On physical examination, she was in a moderate degree of pain and was found to have reduced strength on hip flexion on the right side (3 out of 5). A neurological exam revealed intact sensation, however, the patient was noted to walk with a significant limp. Skin examination was remarkable for numerous skin-coloured neurofibromatosis nodules. Initial blood workup with complete blood count (CBC) and comprehensive metabolic panel (CMP) were without significant abnormalities (*Tables 1 and 2*, respectively). CT scan of the thoracolumbar spine was done to rule out spinal cord compression which revealed lobulated peripherally enhancing right pelvic mass with suspected associated pelvic sidewall adenopathy *(Fig. 1)*. These findings were further evaluated with MRI of the pelvis with contrast, revealing a 6.2 cm centrally non-enhancing and peripherally avidly enhancing lesion of the right greater sciatic foramen likely representing centrally necrotic mass. The mass was also found to involve the posterior aspect of the right obturator internus, right levator ani, and proximal gluteus minimus and medius *(Fig. 2)*.

A biopsy of the mass was taken under CT guidance and showed a high-grade spindle cell tumour with geographic necrosis and marked mitotic activity *(Fig. 3)*. Further evaluation with immunohistochemistry indicated high-grade spindle cell neoplasm, consistent with malignant peripheral nerve sheath tumour. The H3K27me3 epigenetic marker of histone-3 protein was found to be retained by immunohistochemistry. On metastasis workup, the patient was found to have bilateral upper lobe metastasis lesions of the lungs for which she underwent video-assisted bilateral apical segmental resection. She was also started on neoadjuvant chemotherapy and discharged to follow up with neurosurgery as an outpatient.

| Test | Result | Reference Range |
|---|---|---|
| White blood cell count ($10^3$/µl) | 9.4 | 4-10 |
| Neutrophils (%) | 88.9 | 34-71.1 |
| Lymphocytes (%) | 8.8 | 19.3-51.7 |
| Monocytes (%) | 1.6 | 4.7-12.5 |
| Eosinophils (%) | 0.1 | 0.7-5.8 |
| Haemoglobin (g/dl) | 13.6 | 11.2-15.7 |
| Platelets ($10^3$/µl) | 338 | 150-450 |

*Table 1. Complete blood count with differentials in the emergency department.*

| Comprehensive metabolic panel | Result | Reference Range |
|---|---|---|
| Sodium (meq/l) | 133 | 135-145 |
| Potassium (meq/l) | 4.7 | 3.5-5.3 |
| Chloride (meq/l) | 99 | 96-108 |
| Carbon dioxide (meq/l) | 25 | 23-30 |
| Glucose (mg/dl) | 108 | 70-99 |
| Calcium (mg/dl) | 9.5 | 9.2-11 |
| Urea nitrogen (mg/dl) | 17 | 8-23 |
| Creatinine (mg/dl) | 0.8 | 0.6-1.2 |
| Total protein (g/dl) | 7 | 6-8 |
| Total bilirubin (mg/dl) | 0.6 | 0.1-1.2 |
| AST (U/l) | 17 | 9-33 |
| ALT (U/l) | 16 | 4-36 |
| Alkaline phosphatase (U/l) | 48 | 38-126 |

**Abbreviations:**
AST, aspartate aminotransferase; ALT, alanine aminotransferase.

*Table 2. Initial comprehensive metabolic panel in the emergency department.*

## DISCUSSION

Although neurofibromas remain the most common neoplasms associated with NF-1, malignancies such as MPNST, pheochromocytomas, gastrointestinal stromal tumours (GISTs), and gliomas can also occur. MPNSTs typically arise from the malignant transformation of neurofibromas and are associated with significantly poorer

outcomes compares to those with sporadic MPNSTs[4,5]. Our patient had been misdiagnosed with sciatica which delayed treatment, highlighting the challenges in diagnosis and management of NF-1 patients presenting with neuropathic pain.

MPNST arising from sciatic nerve often presents as painless swellings, with a progression in symptoms as the swelling increases in size. In a case series, Zhao et al. noted that, a sciatic nerve tumour can also cause clinical manifestations similar to lumbar disc herniation or sciatica, making the diagnosis difficult[5]. The presence of benign neurofibromas in NF-1 patients often make it difficult to distinguish malignant lesions from benign ones. On imaging, while benign neurofibromas are usually well defined, malignant transformation leads to irregular margins and invasion of surrounding tissues. Early use of MRI in at-risk patients, like those with NF-1 can help identify cause of neuropathic pain as well as differentiate between benign neurofibromas and malignant transformations. Haemorrhage and necrosis on T1-weighed images and intra-tumoral cystic changes on T2-weighed images are often indicative of malignant transformation. Benign neurofibromas often display a "target sign" on MRI, defined as a central hypointense region surrounded by a rim of T2 hyperintensity. The absence of a target sign may suggest malignant transformation, although this sign is not always present in benign neurofibromas. Thus, MRI remains the preferred imaging modality in the assessment of MPNSTs because of its high soft tissue resolution and ability to characterize different tumour components[3,6,7].

Similarly, our patient had progressively worsened lower back pain that radiating to her right leg and was being treated for sciatica. MRI of the pelvis with contrast revealed a 6.2 cm centrally necrotic mass in the right greater sciatic foramen. The MRI of the pelvis without contrast also showed adjacent oedema. These features were suggestive of malignancy and the patient subsequently underwent a CT-guided biopsy. Histopathological examination revealed a high-grade spindle cell neoplasm with marked mitotic activity and necrosis, along with H3K27me3 retention on immunohistochemistry. The tumour also showed patchy positive staining for SOX10 and was negative for pan-cytokeratin AE1/AE3, leading to the diagnosis of MPNST[8]. Although biopsy remains the gold standard for definitive diagnosis, MRI can be used as an ideal screening too in at-risk patients due to its ability to detect early signs of malignant transformation.

The prognosis for MPNST remains poor with a 5-year survival rate of 21%[5]. The primary therapy for MPNST involves surgical resection with clear margins. Radiation therapy plays an important role in enhancing local control while the role of chemotherapy is still under debate[6]. Prognostic factors include a tumour diameter of 5 cm, positive resection margins, and tumour size for tumours outside the extremities, such as the trunk, head, or neck. Our patient had a tumour size of 6.2 cm which is generally considered a good prognostic factor. Additionally, MPNSTs without loss



*Figure 1. A CT scan of the lumbar spine with contrast showed a lobulated peripherally enhancing and likely centrally necrotic right pelvic sidewall mass incompletely seen.*
*The mass measures approximately 5.9 x 5.6 by at least 5.4 cm. There is suspected right pelvic sidewall adenopathy. The pelvic mass is not separable from the right internal iliac artery and vein. It may also be contiguous with the right S1 nerve root.*




*Figure 2. Axial and coronal images of MRI of the pelvis with contrast demonstrated a large right pelvic mass which was centrally non-enhancing and peripherally avidly enhancing lesion in the greater sciatic foramen likely representing a centrally necrotic mass.*
*The mass was seen locally infiltrating adjacent muscular structures including the right obturator internus, levator ani, gluteus medius, and minimus.*

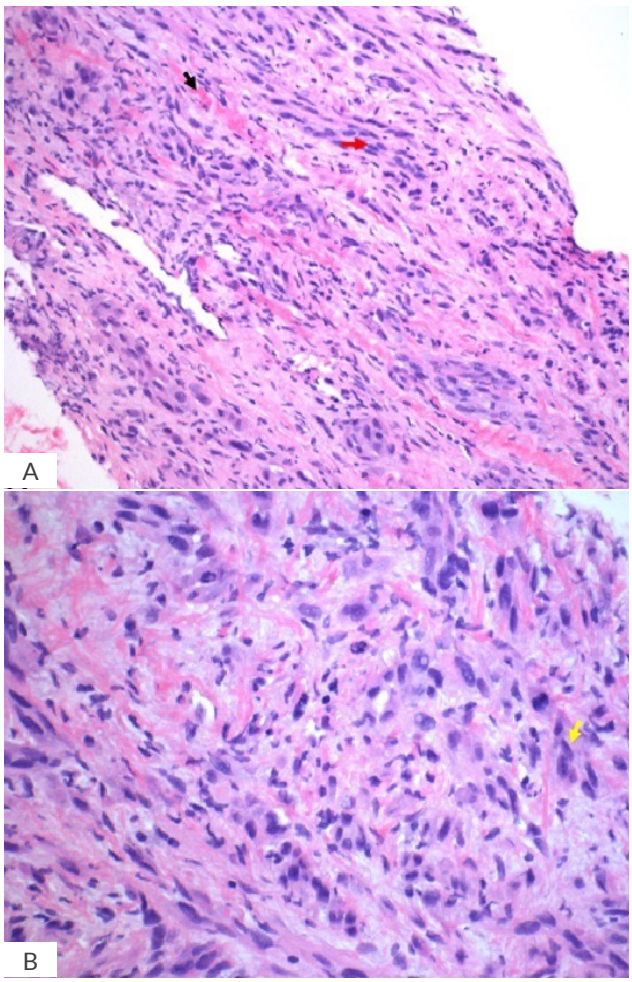



*Figure 3. A) Light microscopy picture of biopsy specimens from the pelvic mass revealing multiple geographic areas of spindle cells with a high number of mitotic figures (red arrow). Intermixed are areas of necrosis (black arrow); B) More magnified light microscopy view of the tissue specimens revealing the typical spindle cell tumours with a high number of mitotic figures characteristic of malignant peripheral nerve sheath tumours.*

of H3K27me3 are associated with less aggressive behaviour, as many low-grade MPNSTs retain this expression, which is consistent with our case[8]. Our patient was referred to neurosurgery for further management, including surgical resection.

## CONCLUSION

This case illustrates the challenges of diagnosing MPNST in NF-1 patients and the importance of considering malignant causes when the patient presents with sciatica-like symptoms. MRI played an important role in diagnosing MPNST in this patient and we argue for early use in at-risk patients or patients with new or worsening pain symptoms. Screening with MRI could lead to early detection of MPNSTs, potentially improving survival outcomes in patients with this rare and aggressive malignancy.

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