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Case Report

Plexiform neurofibromatosis with peripheral malignant nerve sheath tumor and scoliosis - more surveillance imaging needed?☆

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ABSTRACT

Malignant peripheral nerve sheath tumors (MPNSTs) are rare but aggressive neoplasms associated with neurofibromatosis type 1. Specifically, children with deep plexiform neurofibromas are 18 times more likely to develop MPNSTs compared to the general population. However, there is currently no standard surveillance imaging protocol for children diagnosed with deep plexiform neurofibromatosis. We present a case of a boy with neurofibromatosis type 1 and scoliosis, who later developed MPNST. This case highlights the need for more frequent surveillance imaging and the challenges of diagnosing MPNST in a patient with scoliosis. In order to facilitate early detection of malignant transformation, we suggest annual surveillance MR imaging for patients known to have deep plexiform neurofibromatosis.

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Abbreviations: NF-1, neurofibromatosis type 1; MPNST, malignant peripheral nerve sheath tumor.

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Introduction

Neurofibromatosis type 1 (NF-1) is an autosomal dominant disease affecting 1 in 3000 to 1 in 4000 people worldwide [1]. Patients with NF-1 have reduced life expectancy with malignant peripheral nerve sheath tumors (MPNSTs) being the leading cause of death in young adults [2,3]. Patients with NF-1 have an increased risk of developing MPNST in comparison with the normal population - a frequency of 0.001% in the normal population in comparison with 2%-5% in NF-1 patients [4]. Patients with NF-1 carry a lifetime risk of 8%-15% for developing MPNSTs [5]. Some patients with deletion of the entire NF-1 gene also carry a high risk of malignant degeneration, which translates to a lifetime risk of 16%-25% for developing MPNSTs [6].

One study found that the greatest risk for developing MPNST is the presence of a plexiform mass with subcutaneous and cutaneous neurofibromatosis [7]. Individuals with internal plexiform neurofibromas are 18 times more likely to develop MPNSTs than patients without internal neurofibromas [1]. Rapid growth and persistent pain in a previously stable plexiform neurofibroma should raise the suspicion of malignant transformation and are indications for surgical excision or biopsy [8]. As surgical excision is the primary treatment modality, early detection of malignant transformation is necessary for timely intervention [9].

Despite these risk factors, there is no standard imaging protocol to screen for internal plexiform neurofibromas in NF-1 patients, nor are there any guidelines for the surveillance of known plexiform neurofibromas in children.

This report discusses a case in which concomitant scoliosis masked the presence of a rapidly growing MPNST in a child with NF-1.

Case report

A 2-year-old indigenous Idahan boy was initially diagnosed with scoliosis at our center. He was under Orthopedics follow-up for his condition and was scheduled for corrective treatment later.

At the age of 3 years, several cafe-au-lait spots were detected on his body. This cutaneous manifestation led to the diagnosis of NF-1. He had no family history of neurofibromatosis. MR imaging showed spinal plexiform neurofibromas at the lumbar region as well as dermal neurofibromas (Fig. 1).

When the patient was 4 years old, serial applications of Risser casts were initiated to treat his scoliosis. Over the course of 2 years, he underwent Risser cast application every 3-4 months - a total of 6 applications. Radiographs during this period did not demonstrate any evidence of a suspicious intraabdominal or paraspinal mass (Fig. 2). The patient was followed-up with interval thoracolumbar radiographs to assess the progress and outcome of his treatment. When the boy was 6 years old, the Risser cast was exchanged for a corrective body brace which was worn throughout most of the day. The body brace was only removed for a short interval when bathing.

Approximately a year later, the now 7-year-old boy presented with a lower back swelling, which had been rapidly growing for approximately 4 months, accompanied by intermittent back pain, loss of appetite, and loss of weight. On physical examination, there was a huge solid mass occupying the entire right side of his back. The mass was firm, and non-tender with the overlying skin intact (Fig. 3).

Tissue biopsy of the mass showed features of malignant peripheral nerve sheath tumor with pre-existing neurofibroma.

To assess the extent of the enlarging back mass, MRI of the whole spine was performed. There was substantial tumoral extension into the lower thoracic cavity, intra- and retroperitoneal regions, and extensive involvement of the posterior cutaneo-muscular planes. The extent of the tumor precluded any curative surgical intervention (Fig. 4, Fig. 5).

A family conference was held and the patient's family decided to opt for palliative management.

Discussion

Individuals with deep plexiform neurofibromas are 18 times more likely to have malignant peripheral nerve sheath tumors than those without deep plexiform neurofibromas [1]. Once a suspicious lesion is detected, timely imaging and biopsy should be arranged to establish a diagnosis of malignant transformation.

In this case, the detection of the thoracolumbar mass was complicated by the presence of scoliosis and the long-term usage of body casts. This poses difficulties in detecting the lesion when the child was at home as most of the body surface was concealed for extended periods of time. Timely clinical evaluation was also delayed due to the ongoing COVID-19 pandemic at the time of presentation. In light of this, one way of improving the odds for early detection of malignant transformation is to schedule regular interval surveillance MR imaging studies. However, there is a lack of surveillance imaging guidelines for children with deep plexiform neurofibromatosis.

This patient's case highlights the importance of high clinical suspicion for malignant degeneration of plexiform neurofibromas in NF-1 patients. Also, more frequent surveillance imaging would be helpful for the early detection of malignant degeneration. As larger tumors with extensive adjacent structural involvement pose a greater challenge in attempting a gross total excision with a negative margin, it stands to reason that earlier detection of a MPNST could be linked to a better surgical outcome. We suggest annual MR surveillance imaging for patients with deep-seated plexiform neurofibromatosis to enable early detection of MPNST in this high-risk population.

Imaging modalities including CT and MRI may be used to evaluate and diagnose MPNSTs. MRI is usually the investigation of choice because it has superior tissue contrast in comparison to CT. One study identified several MRI findings that can best differentiate malignant peripheral sheath tumors from benign neurofibromas in NF-1 patients [10]. An increase in the largest dimension of the mass, presence of peripheral enhancement in post-Gadolinium T1-weighted images,

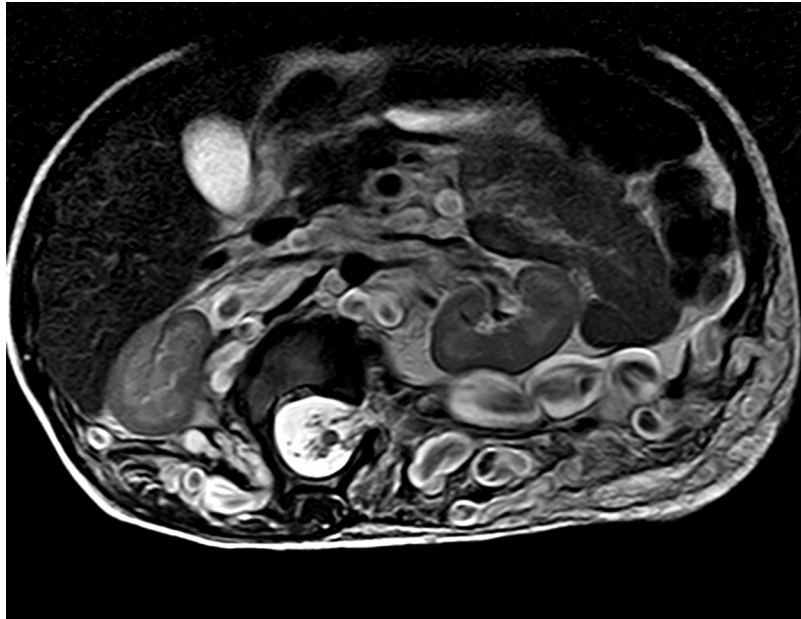


Fig. 1 – Axial T2-weighted image demonstrates multiple hyperintense target lesions representing the plexiform neurofibroma, with intraspinal extension. The patient was 3 years old.

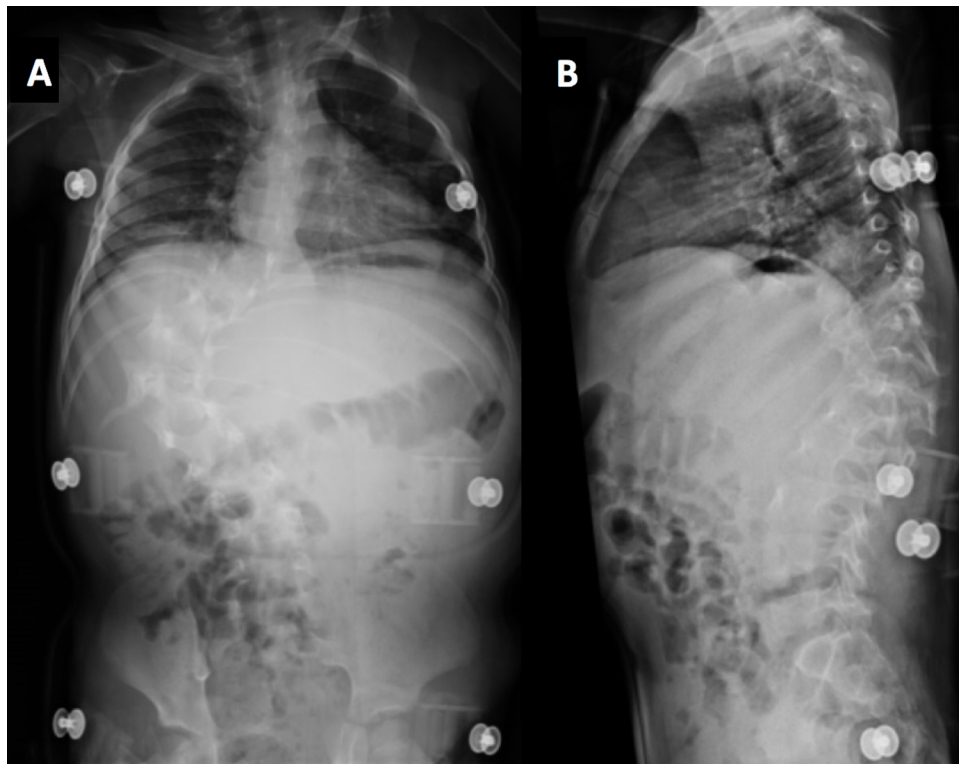


Fig. 2 – Spinal radiographs in anteroposterior (A) and lateral (B) projections taken when the patient was 5 years old with Risser cast in situ. The radiographs demonstrate scoliosis with apex at the level of T12 vertebra towards the right; Cobb's angle = 66°.



Fig. 3 – Photograph of the patient, at 7 years old, with a huge mass arising from the back.

presence of perilesional edema-like zones, and presence of intratumoral cystic-like lesions are MR findings that are suggestive of a MPNST. In NF-1 patients, the presence of intratumoral heterogeneity on T1-weighted images is another useful MRI finding to help distinguish malignant lesion from benign ones [11].

The central limitation of MRI is that when used alone, it cannot reliably distinguish between malignant and benign peripheral nerve sheath tumors, especially when the tumors

are inhomogeneous [12]. A biopsy is still required to secure a definite diagnosis. Once the diagnosis is established, tumoral size and systemic involvement are taken into consideration to plan viable treatment options for patients. The definitive treatment for a localized high-grade MPNSTs is surgical resection with a wide negative margins and adjuvant radiation. Treatment options for our patient were severely limited due to the extensive intrathoracic, intraabdominal and intra-thecal involvement.

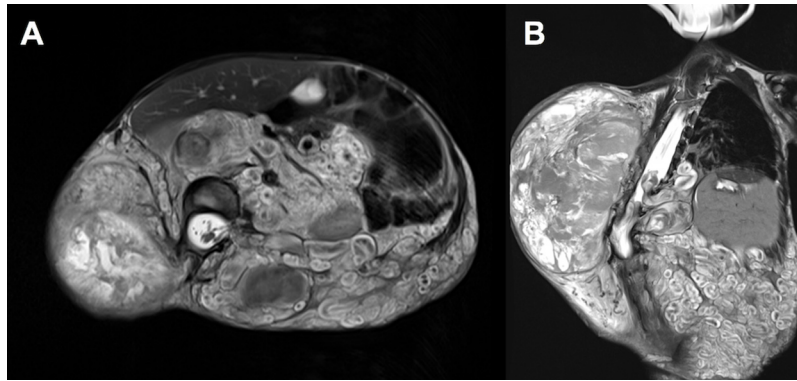


Fig. 4 – Axial (A) and sagittal (B) T2-weighted MR images demonstrate intraspinal extension of the tumor and intraabdominal involvement.

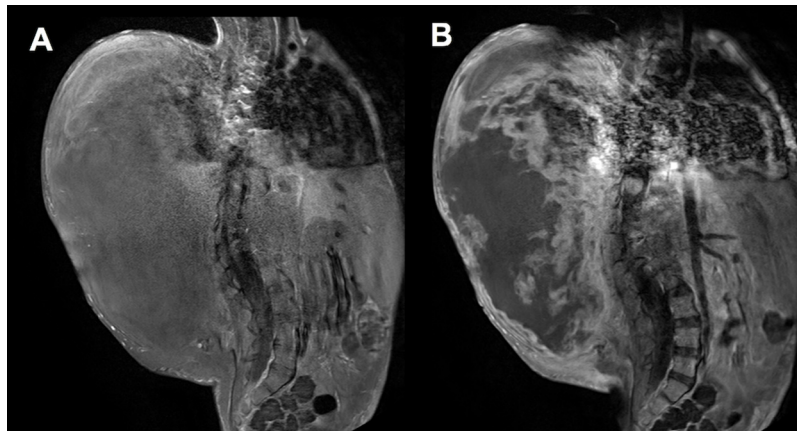


Fig. 5 – Pre-contrast (A) and post-contrast (B) T1-weighted sagittal MR images demonstrate heterogeneous enhancement of the thoracolumbar mass.

Conclusion

This case highlights the importance of high clinical suspicion for MPNSTs in NF-1 patients, especially with existing deep-seated plexiform neurofibromas. Surveillance MR imaging at regular intervals may help in the early detection of malignant degeneration. To date, no established protocol is available to help clinicians decide on how frequent surveillance MRI imaging should be carried out in NF-1 patients despite their predisposition to develop MPNST. We advocate annual surveillance MRI to enable early detection of MPNST in this high-risk population.

Patient consent

Consent has been given by the patient's parents for the publication of this case report.

Ethics approval

Ethical approval not required.

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