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CASE REPORT

Malignant Peripheral Nerve Sheath Tumor in Neurofibromatosis Type 1 Mimicking an Infected Wound: A Case Report

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Abstract

Introduction: Malignant peripheral nerve sheath tumors (MPNSTs) are rare, aggressive soft-tissue sarcomas that may arise sporadically or in association with neurofibromatosis type 1 (NF1). NF1-associated MPNSTs are associated with substantial morbidity and mortality, particularly when diagnosis is delayed or metastatic disease is present. Rapid tumor growth, pain, neurological symptoms, or changes in pre-existing neurofibromas should raise clinical suspicion for malignant transformation. **Case Presentation:** A 64-year-old woman with NF1 presented with a 5-month history of a progressively enlarging mass over the anterior aspect of the right knee and a 1-week history of fever and wound discharge. A 13 × 13 cm lobulated mass was identified clinically, along with multiple superficial cutaneous nodules consistent with NF1. She was initially treated for a presumed infected wound. Biopsy subsequently demonstrated a high-grade MPNST. Magnetic resonance imaging revealed a heterogeneous 7.4 × 11.8 × 13.2 cm mass with restricted diffusion and cystic components involving the anterior knee region. Staging investigations identified multiple bilateral pulmonary nodules and enlarged right inguinal lymph nodes suspicious for metastatic disease. The patient developed severe sepsis with uncontrolled local infection. Because of extensive involvement of critical structures and the inability to achieve adequate limb-sparing margins, above-knee amputation was performed. Histopathological examination confirmed a 13.5 cm high-grade MPNST with involvement of the deep and subcutaneous soft tissues and negative surgical margins. Anthracycline-based systemic chemotherapy was planned; however, the patient developed acute pulmonary edema and cardiac arrest five days after discharge and died. **Conclusion:** This case illustrates the aggressive clinical course of NF1-associated MPNST and the diagnostic challenges that may arise when malignant transformation initially presents with infection-like features. Rapid enlargement of a mass in a patient with NF1, particularly when accompanied by ulceration, pain, or neurological symptoms, should prompt timely imaging and tissue diagnosis. Early recognition and multidisciplinary management are essential, although prognosis remains poor in patients with large, high-grade, or metastatic tumors.

Keywords: Malignant peripheral nerve sheath tumor, neurofibromatosis type 1, NF1, soft-tissue sarcoma, sarcoma

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Introduction

Neurofibromatosis type 1 (NF1) is an autosomal dominant genetic disorder characterized by café-au-lait macules, neurofibromas, and other multisystem manifestations. Individuals with NF1 have an increased risk of developing several neoplasms, including malignant peripheral nerve sheath tumors (MPNSTs), which represent one of the most serious malignant complications of the disease.

MPNSTs are rare and aggressive soft-tissue sarcomas that may arise de novo, develop from pre-existing peripheral nerve sheath tumors, or occur in association with NF1. They most commonly involve the proximal extremities and trunk but may arise at various anatomical sites. Clinical manifestations depend on tumor location and may include a rapidly enlarging mass, pain, sensory disturbances, weakness, or neurological deficits. However, malignant transformation may initially be difficult to recognize, particularly when symptoms are attributed to infection, trauma, or benign neurofibromas.

The diagnosis of MPNST relies on integration of clinical findings, imaging characteristics, histopathological examination, and, when necessary, immunohistochemical and molecular investigations. Magnetic resonance imaging is particularly important for local assessment,

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Figure 1. Lobulated 13x13cm on the Cutaneous Region of the Anterior Aspect of the Right Knee.



Figure 2. Circumscribed, Superficial, Soft Button-like skin-colored Nodules in the Face, and Lower Bilateral Extremities

while systemic staging is necessary to evaluate for metastatic disease. Complete surgical resection with negative margins remains the principal potentially curative treatment for localized disease. However, large tumors, involvement of critical anatomical structures, and metastatic disease can substantially limit therapeutic options and adversely affect prognosis.

We report a case of a 64-year-old woman with NF1 who developed a large, high-grade MPNST of the right knee (Figure 1) that initially presented as an infected mass. The case highlights the importance of recognizing clinical features suggestive of malignant transformation in patients with NF1 and demonstrates the challenges of managing advanced MPNST complicated by severe local infection and suspected metastatic disease.

Discussion

Malignant peripheral nerve sheath tumors (MPNSTs) are rare and aggressive soft-tissue sarcomas characterized by Schwannian or peripheral nerve sheath differentiation. They may occur sporadically or in association with neurofibromatosis type 1 (NF1), with NF1 being one of the most important recognized risk factors. MPNSTs can arise at various anatomical sites but commonly involve the proximal extremities, trunk, and head and neck. Clinical manifestations are variable and may include a rapidly enlarging mass, pain, neurological symptoms, or sensory disturbances. Because these features can overlap with those of benign neurofibromas and other soft-tissue lesions, early recognition of malignant transformation can be challenging [1, 2].

NF1 is an autosomal dominant tumor-predisposition syndrome characterized by café-au-lait macules, axillary or inguinal freckling, neurofibromas (Figure 2), and other multisystem manifestations. Individuals with NF1 have an increased lifetime risk of developing malignant neoplasms, including MPNST, as well as several other tumor types [3]. MPNST represents one of the most clinically significant malignant complications of NF1. The risk of MPNST is substantially higher among individuals with NF1 than in the general population, and NF1-associated tumors may occur at a younger age and have a less favorable prognosis [4].

The present case illustrates several important clinical challenges. The patient was 64 years old and had longstanding NF1 with multiple cutaneous nodules. She presented with a rapidly enlarging 13-cm mass around the right knee accompanied by fever and wound discharge. The initial clinical impression was an infected wound, potentially delaying recognition of the underlying malignancy. Although infection was an important component of her presentation, the marked enlargement and large size of the lesion in a patient with NF1 should prompt consideration of malignant transformation. A biopsy subsequently established the diagnosis of high-grade MPNST (Figure 3), emphasizing the importance of obtaining tissue diagnosis when the clinical course is atypical or progressive.

Imaging plays an important role in the evaluation of suspected MPNST. Magnetic resonance imaging (MRI) (Figure 4, 5 and 6) provides detailed assessment of tumor extent, involvement of adjacent structures, and relationships with nerves, muscles, vessels, and other critical anatomical structures. In the present case, MRI demonstrated a large heterogeneous mass with restricted diffusion and cystic components involving the anterior aspect of the knee. The tumor involved critical structures, including the patellar tendon and medial collateral ligament, limiting the possibility of function-preserving limb-sparing surgery. Staging investigations also identified multiple bilateral pulmonary nodules and enlarged inguinal lymph nodes that were considered suspicious

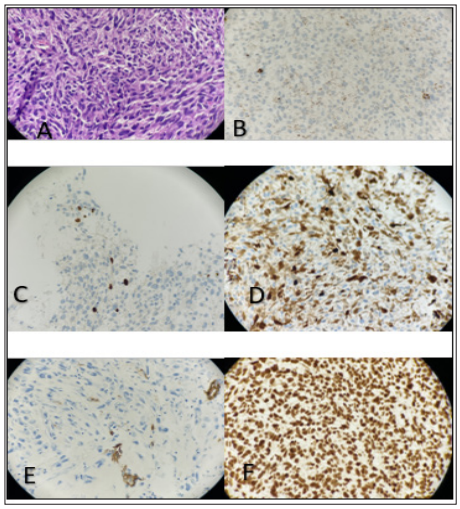


Figure 3. Histopathology and Immunostaining (A) HPF with Increased Mitotic Count (B) Negative EMA (C) Positive SOX10 (D) Focally Positive S100 (E) Negative CD34 (F) Intact Nuclear Expression for H3k27me3

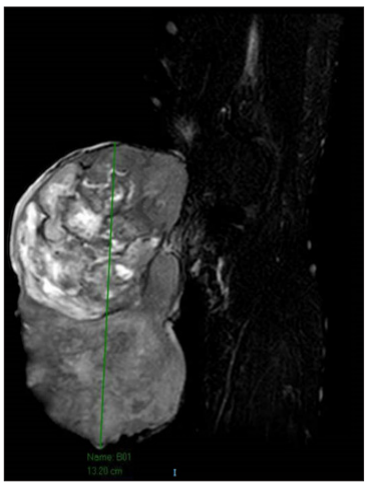


Figure 4. MRI of the Right Lower Extremity Revealing a Heterogenous Lobulated Mass on the Anterior Aspect of the Knee 7.4 x 11.8 x 13.2 cm (APxTxCC)

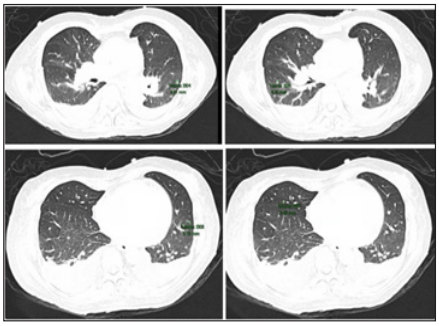


Figure 5. CT Scan of the Chest with Multiple Sub-centimeter Solid non-calcified Nodules in both Lungs

for metastatic disease. These findings indicated advanced disease and contributed to the complexity of treatment planning.

Complete surgical resection with negative margins remains the cornerstone of treatment for localized MPNST and is one of the most important determinants of outcome. Limb-sparing surgery is preferred when adequate oncological margins and acceptable function can be achieved. However, extensive involvement of major anatomical structures, infection, or inability to obtain adequate margins may necessitate amputation in selected patients. In this case, persistent infection and extensive involvement of critical structures prevented an adequate limb-sparing resection. The multidisciplinary sarcoma team therefore proceeded (Figure 7) with above-knee amputation to achieve local disease control and address the uncontrolled infection. Final histopathology demonstrated a 13.5-cm high-grade MPNST involving the deep and subcutaneous soft tissues, with negative surgical margins.

Prognosis in MPNST is influenced by multiple clinicopathological factors, including tumor size, depth, anatomical location, histological grade, metastatic disease, NF1 status, and completeness of surgical resection. Larger, deep-seated, high-grade, and metastatic tumors are generally associated with poorer outcomes [5]. The large tumor size, high-grade histology, suspected pulmonary metastases, and NF1 association in the present case therefore represented several unfavorable prognostic features. The rapid clinical deterioration and subsequent death shortly after discharge further illustrate the potentially aggressive course of advanced MPNST. However, because the patient died suddenly after discharge, the precise cause of death cannot be established from the available clinical information beyond the documented episode of acute pulmonary edema followed by cardiac arrest.

The role of systemic chemotherapy and radiotherapy in MPNST remains individualized. Surgery remains the primary potentially curative treatment for resectable localized disease, whereas systemic therapy may be considered for unresectable, metastatic, or high-risk disease. Anthracycline-based chemotherapy, often incorporating ifosfamide, is among the systemic treatment approaches used for advanced soft-tissue sarcomas, although the benefit of chemotherapy specifically for MPNST remains variable and should be determined by a multidisciplinary sarcoma team [5]. In the present case, anthracycline-based chemotherapy with doxorubicin and ifosfamide was planned because of the aggressive tumor characteristics and suspected metastatic disease. Unfortunately, the patient died before systemic treatment could be initiated.

Surveillance of patients with NF1 is essential because of their increased risk of multiple benign and malignant tumors. Current consensus recommendations emphasize regular clinical assessment, including careful history-taking and physical examination, rather than indiscriminate imaging-based screening for every patient. New, persistent, or rapidly enlarging lesions, particularly painful masses or changes in the character of a pre-existing neurofibroma, should prompt further evaluation. When malignant transformation is suspected, regional MRI is recommended, with additional functional imaging such as ^{18}F-FDG PET/CT or PET/MRI considered according

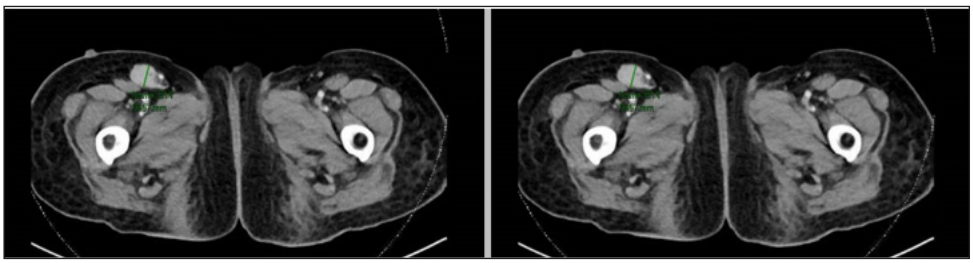


Figure 6. CT Scan of the Pelvic Area with Several Prominent and Enlarged Right Inguinal Lymph Nodes with the Largest Measuring 1.7 cm



Figure 7. Above the Knee Amputation Specimen with Adequate Surgical Margin

to the clinical context and local expertise [6, 7]. Thus, the management of NF1 should emphasize vigilant clinical surveillance and prompt investigation of suspicious changes rather than routine whole-body imaging in asymptomatic individuals.

The present case highlights the importance of educating patients with NF1 about warning signs of malignant transformation. Patients should be encouraged to report rapid growth of a pre-existing or new mass, persistent or unexplained pain, neurological symptoms, or changes in the consistency of a neurofibroma. Healthcare professionals should similarly maintain a high index of suspicion when evaluating new or changing soft-tissue lesions in patients with NF1. Early recognition may facilitate timely imaging, biopsy, referral to a specialist sarcoma team, and appropriate surgical planning.

This report has limitations inherent to its single-case design. The clinical course cannot be generalized to all patients with NF1-associated MPNST, and the pulmonary nodules were considered metastatic based on their radiological appearance and the overall clinical context without histological confirmation. Nevertheless, the case provides a clinically relevant example of an NF1-associated high-grade MPNST presenting with infection-like symptoms, extensive local disease, and suspected metastases. It underscores the importance of integrating clinical examination, imaging, histopathology, and multidisciplinary assessment in the management of these rare and aggressive tumors.

In conclusion, NF1-associated MPNST is an aggressive malignancy that may initially mimic benign or infectious conditions. Rapid enlargement of a soft-tissue mass, particularly when accompanied by pain, neurological symptoms, ulceration, or other changes in a patient with NF1, should prompt timely investigation for malignant transformation. Regular clinical surveillance and patient education are central to NF1 care, while MRI and functional imaging should be used when clinical findings raise suspicion for malignancy. Once MPNST is diagnosed, early referral to a multidisciplinary sarcoma team is essential for appropriate staging and treatment planning. In patients with large, high-grade, or metastatic tumors, prognosis remains poor despite aggressive multimodal management.

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Conflict of Interest

The authors declare that they have no conflicts of interest or financial relationships that could have influenced the work reported in this manuscript.

Consent For Publication

Written informed consent for publication of this case report and the accompanying clinical images was obtained from the patient's daughters.

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