Rare Presentation of Malignant Peripheral Nerve Sheath Tumor of the Femur in Neurofibromatosis-1

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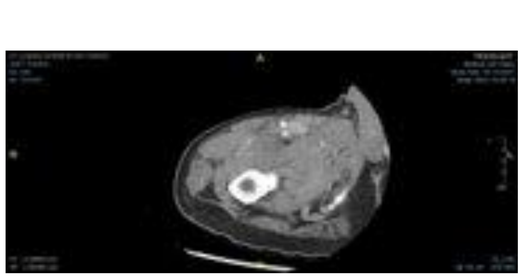
Abstract

Malignant peripheral nerve sheath tumors (MPNSTs) are rare sarcomas, most commonly seen in patients with Neurofibromatosis type 1 (NF1), that are characterized as aggressive with high rate of local recurrence. Among NF1 patients, the risk of developing MNPSTs is approximately 8-13% over a lifetime. Primary MPNST is exceedingly rare, of which the vast majority are concentrated in the head and neck region. Here, we present a case of a 40-year-old male with NF1 who presented with a giant MPNST that originated in the right proximal femur. The mass was treated with complete surgical resection with right hip disarticulation. In a matter of 4 months, the patient had a rapid progression with metastatic disease to the brain and lungs. Current guidelines only indicate a thorough yearly physical with active monitoring of new neurofibromas. Once found, surgical resection and post-operative radiotherapy are the main stay of treatment. The aim of this case is to highlight the need to further expand on disease surveillance especially on those individuals that carry a higher tumor burden.



- (Above) Axial view of CT imaging of the large heterogeneously enhancing mass of the right thigh measuring 11.9 x 11.6 cm transaxially over a distance of 15 cm.
- (Below) Coronal view of MRI 12.7 cm aggressive osseous lesion centered in the proximal femoral diaphysis with extraosseous extension into the surrounding musculature and extending superiorly along the femoral neck

Case Presentation

- Patient is 40-year male with a past medical history of Neurofibromatosis type 1, scoliosis, and hyperlipidemia presented to the hospital for increasing right thigh pain for the past 3 months with an associated large thigh mass that has grown progressively.
- MRI imaging of the extremity revealed a 12.7 cm aggressive osseous lesion centered in the proximal femoral diaphysis with extension into the surrounding musculature and extending superiorly along the femoral neck & hip joint. Biopsy was performed of the mass and returned positive for high-grade sarcoma.
- The final biopsy report was positive for pleomorphic spindle cell sarcoma consistent with MPNST of high-grade. The various treatment options were discussed, and the patient ultimately decided to pursue a complete right hip disarticulation.
- The pathology of the amputated limb exhibited a soft tissue mass of 25.0 x 23.0 x 13.0 cm located above the knee. The mass grossly appeared to have originated from the cortical bone at the femoral shaft. The surgical margins were reported to be negative.
- 5 months later, the patient returned to a different facility for symptoms of new onset left sided weakness. Initial head CT imaging finds showed a 5.9 x 3.7 x 4.7 cm right posterior frontal intraparenchymal hematoma with mild surrounding edema with 3 mm right to left midline shift. MRI done of the head showed findings concerning for an underlying metastatic lesion.
- In addition, chest CT exhibited bilateral large lung masses compatible with metastatic disease as well as a persistent large mass seen in the right paraspinal region with chronic changes involving the lumbar spine.
- Treatment options were discussed with the patient. The patient refused any immunotherapy and ultimately elected for hospice care measures.

Discussion

- NF1 is an autosomal dominant disease that does not display a propensity to affect one particular race or gender specifically[1]. The disease affects the neurofibromin 1 gene that functions as a negative regulator of the RAS signaling transduction pathway. The clinical manifestations include café-au lait spots, Lisch nodules, optic gliomas, and cutaneous neurofibromas[2].
- MPNSTs are very high-grade sarcomas with a poor prognosis. MPNSTs comprise approximately 5-10% of all soft tissue sarcomas[3]. Majority of cases occur with association of NF1 but can also occur spontaneously. The risk of developing MPNSTs in NF1 is approximately 8-13% over a lifetime[4]. In patients with NF1, MPNSTs occur most commonly in the 20-40-year age group.
- Primary MPNST of bone is very rare and most cases report occurrences in the head and neck region[7-9]. A recent clinical review identified 36 cases of MPNST originated outside maxillofacial region of which only 5 cases arising in the femur[10]. Surprisingly, only two of those were associated with NF1[11,12].
- Despite adequate sectioning and/or aggressive chemo-regimen, majority of the patients did not survive shortly after initial treatment, highlighting the aggressiveness of the tumor. Among sarcomas, MPNST reoccurrence remains the highest[13].
- MPNST has a high probability rate of local recurrence and distant metastasis, with a poor prognosis. A local recurrence rate of 40–65% and a 5-year survival rate of 23–69% have been reported[14].
- Despite limp amputation, metastatic disease in MPNSTs remains a common phenomenon due to its aggressive features. The most common sites of metastasis that have been observed are lung, bone, liver, lymph nodes, and pleura[15].
- Given the high rate of recurrence, it is vital to understand the various prognostic factors that may affect disease progression. The most significant that have been established are NF1, tumor size above > 5cm, tumor depth, grade, and metastatic disease[16].
- Although the nature of disease presentation for this patient is rare, the increased risks of MPNST in NF1 patients highlights the need for more aggressive surveillance patterns.
- Currently, guidelines only indicate a thorough yearly physical with active monitoring of new neurofibromas[17]. Though some experts suggest regular MRI screenings in adults, the variable nature of MPNST presentation may complicate the cost-benefit ratio[19]. It may however be worthwhile to isolate and focus on those individuals who carry a higher degree of tumor burden[20].
- Recent technical advances in image guided therapy as well as improvements in biogenetics have provided more tools for clinicians to titrate their surveillance efforts[21,22]. Despite such improvements, there remains a need for more comprehensive studies to establish a better framework for monitoring disease progression.

Conclusion

Malignant peripheral nerve sheath tumor in NF1 remains a very challenging entity to diagnose and treat. Despite the rarity of the disease in comparison to the general population, the increased risk associated in individuals with NF1 emphasizes the need for an established guideline for frequent surveillance and monitoring. Our case highlights the rapidity and complexity that this disease may progress if left unchecked.

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