Perineum Spindle Cell Sarcoma in Neurofibromatosis Type 1

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Abstract

Soft tissue neoplasm is common among patients with neurofibromatosis type 1 (NF-1). We present a case of a middle-aged NF-1 lady who presented with a painless, insidiously increasing perineal mass for the past eight months. She underwent colonoscopy, CT staging, MRI pelvis, core-needle biopsy and subsequently wide local excision of left perineum swelling. The histopathology examination showed high-grade spindle cell sarcoma, which is a rare association among the NF-1. Spindle cell sarcoma is a group of malignant soft tissue tumours with locally destructive growth with spindle-shaped neoplastic cells. The solitary spindle cell sarcoma of the perineum is rare, and wide local resection with a clear margin is the only treatment at present—the scarcely available evidence limiting the use of adjuvant chemotherapy, immunotherapy, and radiotherapy.

Keywords: *Neurofibromatosis 1, sarcoma, spindle cell, soft tissue neoplasms, perineum*

Introduction

Neurofibromatosis type 1 (NF-1), also known as von Recklinghausen disease, results from mutation of the NF-1 gene inherited via an autosomal dominant Mendelian pattern. NF-1 is the most common subtype of neurofibromatosis diagnosed in the first decade of life (1). NF-1 is characterized by developing multiple non-cancerous nerve and skin tumours (neurofibromas), Lisch nodules, café-au-lait, axillary and inguinal freckling (2,3).

NF-1 mutation has 34 times at risk more common to develop sarcoma compared to the general population (4). Neurosarcoma is another common malignant transformation encounter among NF-1 (4).

Spindle cell sarcoma is a malignant soft tissue tumour identified by the presence of spindle shape neoplastic cells. They could be locally infiltrative with metastatic potential, and the recurrences commonly occurred within 24 months from the index resection (5). They are subtyped via genetics, immunophenotype, morphology and degree of differentiation and broadly divided into differentiated types (leiomyosarcoma, fibrosarcoma and myofibroblastic sarcoma) and uncertain differentiation type (synovial sarcoma) (6). The incidence of spindle cell sarcoma in the perineum with a background of NF-1 is rare, with less than 1% of all soft tissue sarcoma (5). We report a case of solitary spindle cell sarcoma presented at the perineum of a lady with NF-1.

Case Report

A 47-year-old lady with a background of NF-1 presented to our surgical department with eight months history of rapidly increasing left perineal swelling and pain upon sitting. The swelling was

initially small, 2 x 1 cm; however, it rapidly grew to 10 x 12 cm over the past eight months. In addition, her mother and younger brother were also diagnosed with NF-1.

On examination, there was a mass located from one to six o'clock position, 4 cm away from the anal verge (Fig. 1).

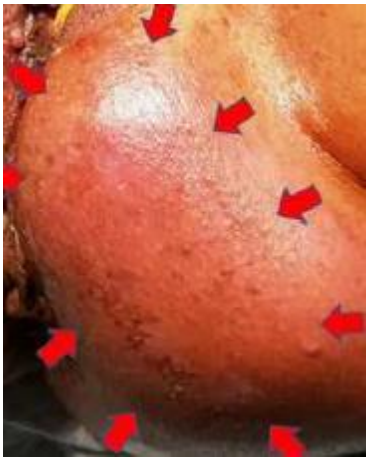

Figure 1: Perineal mass measuring 10 x 12 cm from one to six o'clock position around the perineum (outlined by red arrows)

Colonoscopy was normal until caecum with no intraluminal mucosal lesion seen. The rapid growing mass was highly suspicious of malignancy; hence, the contrast-enhanced computed tomography (CECT) of the thorax, abdomen and pelvis was performed and confirmed no distant metastases. The magnetic resonance imaging (MRI) of the pelvis reported a soft tissue mass measuring approximately 5.2 x 10.2 x 5.2 cm (AP x WT x CC), displacing the vagina and anus to the right with no direct local infiltration to the adjacent organs. It appeared to be a tumour of mesenchymal origin with the differentials of liposarcoma (Fig. 2).

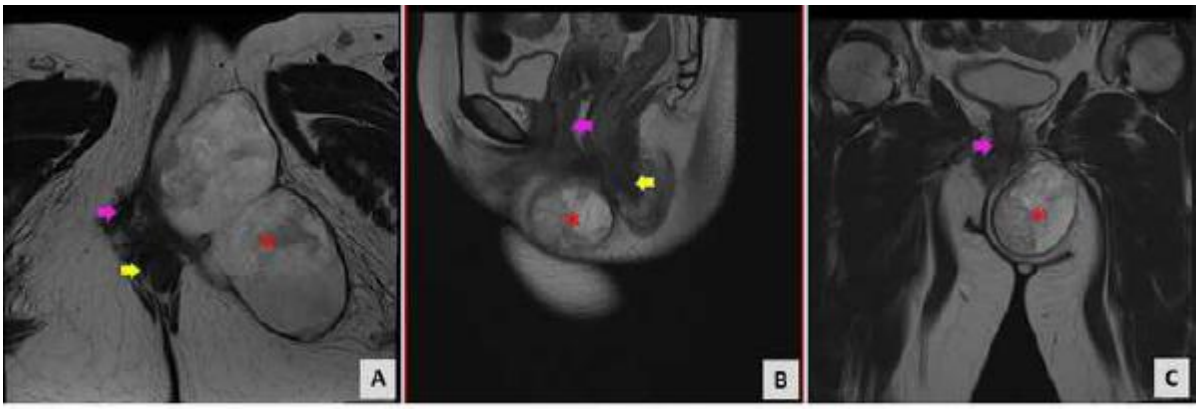

Figure 2: MRI pelvis T2-weighted images in Axial (A), Sagittal (B), Coronal (C) demonstrating the perineal mass (red asterisk) compress and displacing the vagina (pink arrow) and anus (yellow arrow).

Ultrasound-guided core-needle biopsy confirmed a spindle cell lesion. She underwent wide local excision of the left perineal mass. The intraoperative finding was 10 cm x 12 cm irregular border soft-tissue mass at the left perineal area with attachment to the overlying skin but no infiltration to adjacent bone and external anal sphincter (Figure 3). The elliptical skin incision was closed without tension and did not require further reconstruction. She was discharged well on the next day after the operation.

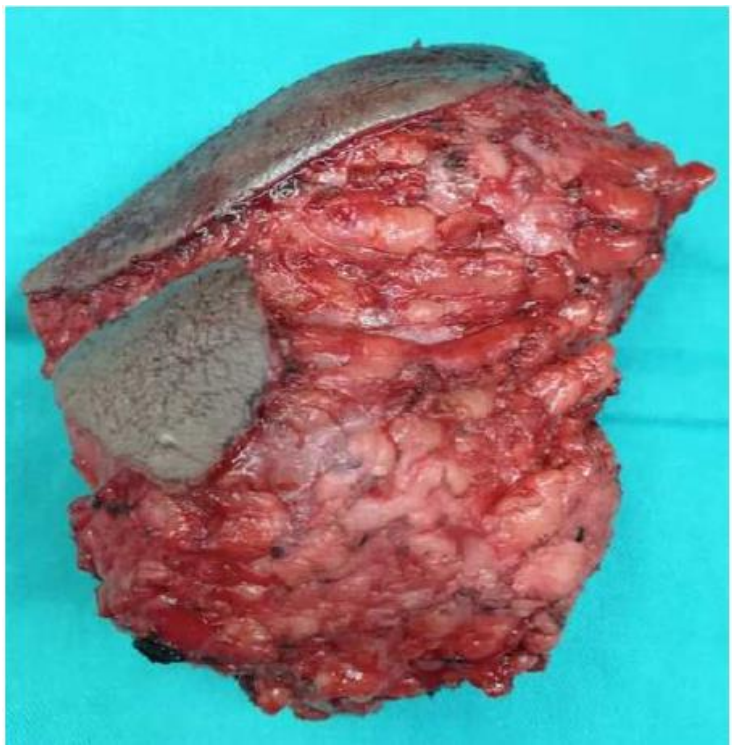

Figure 3: A 10 cm x 12 cm irregular shaped tumour removed from left perineum with attachment to the skin but no local infiltration to bone and anal sphincter.

The histopathological examination revealed a malignant spindle cell tumour with a clear 30 mm surgical margin and high-grade sarcoma (Fig. 4). At one month follow-up, her left perineal scar was well-healed. She was also referred to the radiation-oncology team for radiotherapy. She visited us in the third and sixth months with no evidence of local recurrence on surveillance CECT of thorax, abdomen and pelvis.

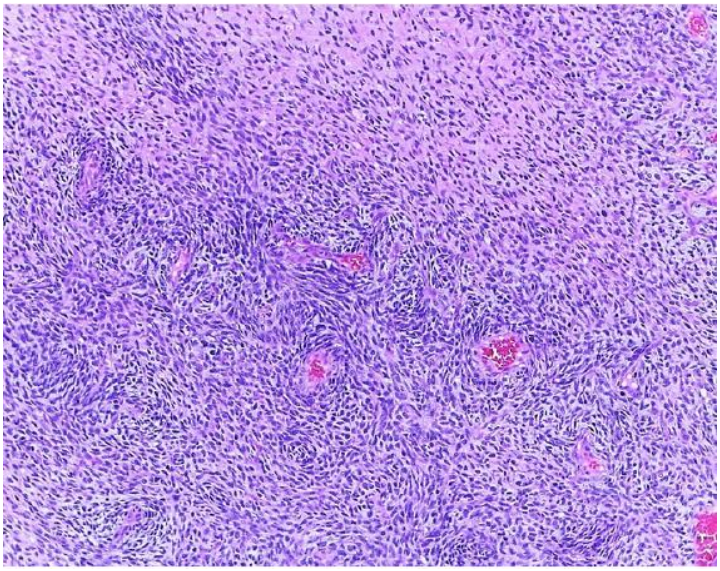

Figure 4: Fascicles of spindle-shaped cells with varying cellularity and perivascular accentuation (H&E Stain; Magnification x 100).

Discussion

NF-1 are at higher risk of developing malignant soft tissue tumour and, this incidence rises with advancing age, 2% for an individual below 21-year-old and 4.2% for an individual above 21-year-old (7). Soft tissue sarcomas such as angiosarcoma, chondrosarcoma, rhabdosarcoma, leiomyosarcoma and undifferentiated pleomorphic sarcoma were more common among NF-1 patients at their sixth and seventh decades of life; in contrast to their younger counterpart, malignant peripheral nerve tumour was a more common occurrence (8).

The predilection of tumour development to either benign or malignant variant in NF-1 imposed a significant diagnostic challenge. This is crucial to prognosticate and treatment planning. Moreover, it gets more challenging to diagnose when the soft tissue tumour is presented at an unusual area

such as the perineum—nevertheless, past reports of these tumours presented at the female genitalia and genitourinary system (9,10).

Soft tissue sarcoma of spindle cell variant was classified into two types; clear differentiation lineage type such as leiomyosarcoma and fibrosarcoma, and the uncertain lineage type (11,12). Perineum spindle cell sarcoma was rare, and due to its heterogenicity, it imposed a significant diagnostic challenge.

A multidisciplinary approach to spindle cell sarcoma remains a challenging endeavour despite the advances in cytogenetics and immunohistochemistry. The MRI remains the imaging of choice for soft tissue tumours and is essential for surgical planning and staging. Biopsy has a limited role as most of these tumours eventually requires resection. The biopsy is reserved for the tumour that is potentially responding to preoperative radiotherapy or chemotherapy.

Wide local surgical excision with clear margin is still the gold-standard treatment for soft tissue sarcoma. The close or unclear margins have a proportional relationship to the recurrence rate and poorer prognosis (13). The soft tissue tumour management strategy revolutionized as we researched and explored in-depth its molecular biology and immuno-profiling. Most of these soft tissue sarcoma were angiogenesis dependent tumours. Anti-angiogenesis therapy such as pazopanib, sorafenib and sunitinib was recommended in the latest NCCN guidelines as targeted therapy for advanced or metastatic soft tissue sarcoma (1,7,13). On-going studies exploring the role of immunotherapy in soft tissue sarcoma produced promising results but were heterogeneous. The immune-profiling and identification of immune biomarkers like the immune checkpoint inhibitors (ICIs) in soft tissue sarcoma were challenging due to its rare and heterogeneous disease (14).

Learning Points

1. Tissue biopsy has a limited role in the management of soft tissue tumours. However, in NF-1 patients, attaining information regarding benign or malignant nature facilitate planning to the extent of resection.

2. Molecular testing on angiogenesis-dependent factors may help us decide which patient should be subjected to adjuvant immunotherapy selectively.

3. Adjuvant radiotherapy is currently the most advocated preventive strategy towards recurrence.

Conclusion

A malignant spindle cell tumour at the perineum is a rare variant of high-grade sarcoma. Soft tissue neoplasms in NF-1 imposes a diagnostic challenge in discriminating those with malignant potential. Therefore, wide local excision complimented with adjuvant radiation therapy is the best strategy to reduce recurrence. In addition, there were emerging promising evidence from adjuvant chemotherapy and targeted therapy depending on the variant of the soft tissue sarcoma.

Conflict of Interest

All authors declare no conflicts of interest in the production of this report.

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