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Malignant peripheral nerve sheath tumor with extensive osteosarcomatous and chondrosarcomatous differentiation: A case report

Abdul-Wahed N. Meshikhes[a,*], Mohammed A. Duhaileb[a], Samir S. Amr[b]

[a] General and Minimally Invasive Surgery Section, King Fahad Specialist Hospital, Dammam 31444, Eastern Province, Saudi Arabia
[b] Department of Surgery and Department of Pathology and Laboratory Medicine, King Fahad Specialist Hospital, Dammam 31444, Eastern Province, Saudi Arabia

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ABSTRACT

BACKGROUND: Malignant peripheral nerve sheath tumor is an uncommon tumor of the peripheral nerves. The commonest presenting symptom is soft tissue mass and pain with local neurological findings. Imaging modalities are unhelpful in making a reliable diagnosis. Treatment is radical resection with adequate clear resection margins. Radiotherapy improves the local control, but the prognosis remains poor especially in those with divergent differentiation.

SUMMARY: A 23-year-old man with no history of neurofibromatosis presented with a swelling on the back which has been gradually increasing in size and causing him discomfort. The tumor was surgically excised and the histopathological examination revealed malignant peripheral nerve sheath tumor with extensive osseous and cartilaginous differentiation. He developed pulmonary metastases one year after the surgical resection. Pulmonary metastatectomy was therefore performed and the histopathology of the metastatectomy specimen revealed metastatic malignant peripheral nerve sheath tumor, but without any osseous or cartilaginous differentiation. He remained well with no recurrence or metastases at 9-month follow-up.

CONCLUSION: Malignant peripheral nerve sheath tumor is a malignant tumor that behaves aggressively despite adequate radical resection. This case also illustrates extensive osseous and cartilaginous divergent differentiation of the primary tumor which was surprisingly absent in the metastatic lesions. This finding warrants further research.

1. Introduction

Malignant peripheral nerve sheath tumor (MPNST) is an uncommon soft tissue sarcoma that arises from the peripheral nerves. It may originate from normal nerves or pre-existing plexiform neurofibromas and perineuriomas. The tumor is sporadic in the majority of the cases but it is associated with neurofibromatosis type 1 (NF1) in 20%–50% of the cases especially in younger patients [1,2]. MPNST commonly affects the trunk and extremities and less often the head and neck area [3]. The tumor is well known for its aggressiveness and tendency to metastasize to distant organs especially lung and bones. The local control of the tumor is best achieved by radical surgical resection and adjuvant radiotherapy. However, this does not prevent early development of distant metastases.

We report herein a case of MPNST of the trunk with bone and cartilage differentiation in a young man who had no clinical features of neurofibromatosis type 1 (NF-1) and who developed pulmonary metastases one year after surgical resection and adjuvant radiotherapy. Of interest is that the metastatic lesions in this case – unlike the primary tumor – did not exhibit any divergent osseous or cartilaginous differentiation.

2. Case report

A 23-year-old male presented to the surgical clinic with a swelling over the left side of his back. The swelling was noticed several years earlier, but was small and painless. He was examined at another facility and was advised to observe. The swelling became larger, harder and uncomfortable over the recent months and was therefore referred as a case of 'back lipoma'. There was no significant past surgical or medical history and he denied any family history of neurofibromatosis. Examination revealed a hard oval swelling (7 × 4 cm) just to the left of the upper lumbar spine which was partially mobile. Routine blood tests were within normal range

* Corresponding author.
E-mail addresses: Meshikhes@gmail.com, meshikhes@doctor.com (A.-W.N. Meshikhes).

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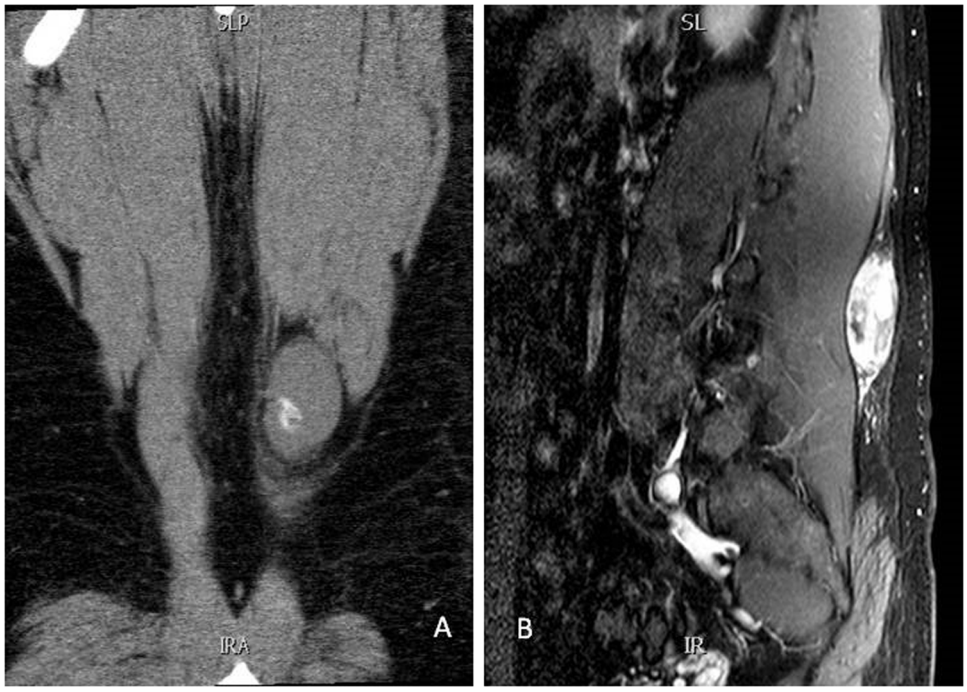

Fig. 1. Magnetic resonance imaging coronal view (panel A) and sagittal view (panel B) showing clearly the lesion with some calcification.

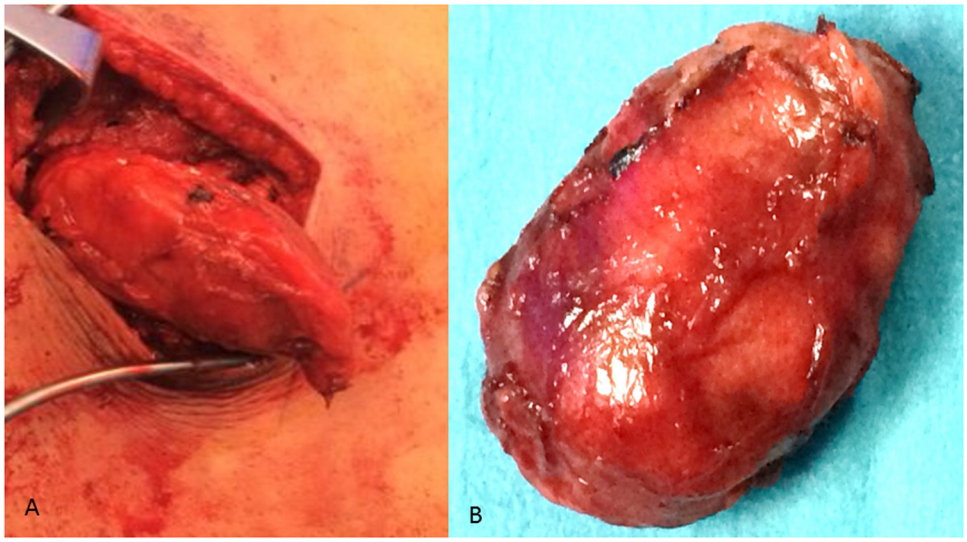

Fig. 2. An operative view showing the lesion as it was dissected from the surrounding structure (Panel A). Panel B showing the excised mass which looked well encapsulated with a smooth surface.

and review of the computed tomography (CT) and magnetic resonance imaging (MRI) scans which were done outside confirmed the presence of a soft tissue mass which was unlikely to be a lipoma (Fig. 1). Fine needle aspiration cytology (FNAC) was offered, but refused by the patient and hence surgical resection of what appeared to be an encanpsulated mass (Fig. 2) was carried out.

Pathological examination revealed a soft tissue mass measuring $7 \times 4 \times 2.5$ cm, with soft myxoid areas and firm hard areas. Histologically, the tumor exhibited areas of malignant spindly mesenchymal cells with brisk mitotic activity within loose myxoid stroma and foci of tumor necrosis. In addition, areas with marked osteosarcomatous and chondrosarcomatous differentiation were identified (Fig. 3A–D). However, no rhabdomyosarcomatous or glandular differentiation was noted. Immunohistochemical stains show focal nuclear staining of the malignant spindly cells for S100 protein but they were negative for smooth muscle actin, desmin and myogenin. These findings confirm the tumor as MPNST. Based on the pathological findings, CT scan of the chest, abdomen and pelvis was performed and this excluded presence of distant metastases. Also, neurosfibromatosis type I (NF1) gene sequencing was ordered at a referral laboratory and found to be negative.

The case was discussed in the multidisciplinary tumor board and adjuvant radiotherapy was recommended. After finishing all radiotherapy sessions, he remained well with no evidence of recurrence or metastases at 6- and 9-month follow-ups. However, at 12-month follow-up a body combined ^{18}F-fluorodeoxyglucose–positron-emission tomography and CT (FDG–PET–CT) scan showed a right lung metastatic nodule with avid FDG activity (SUV_{max} 6.8) (Fig. 4). Another smaller nodule was also noted in the anterior aspect of the left upper lobe. The patient underwent right mini-thoracotomy

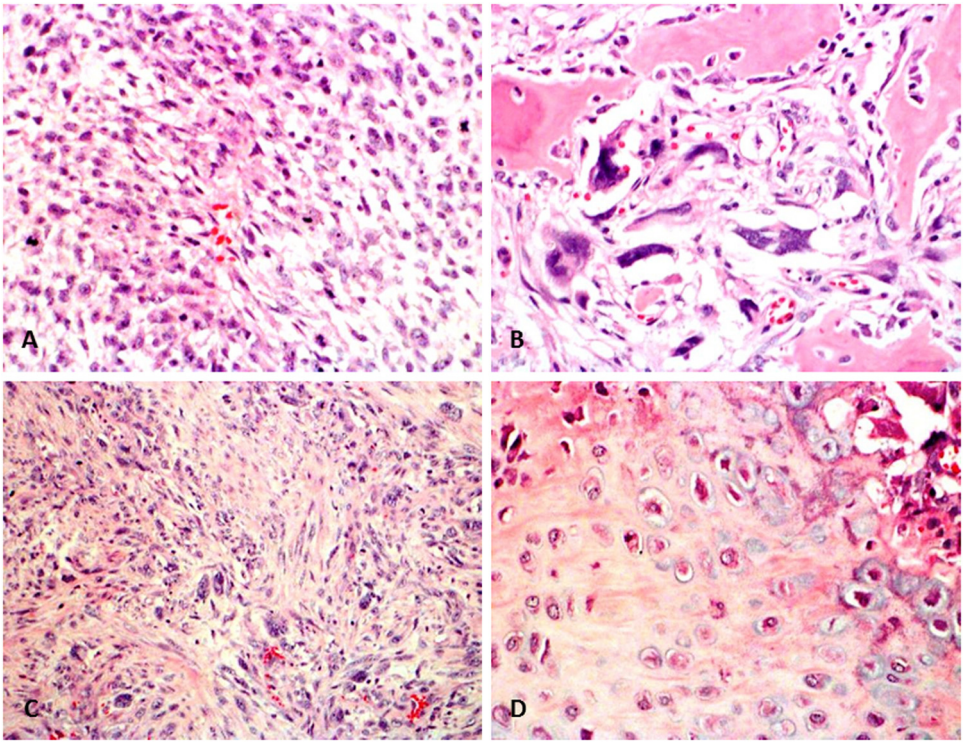

Fig. 3. Micrograph of the resected lesion showing an area of the tumor featuring spindle cells within loose stroma with associated nuclear atypia and scattered mitotic figures (panel A; H&E stain. ×200). The microscopic field in panel B shows the presence of bony trabeculae surrounded by large malignant hyperchromatic, multinucleated bizarre cells (H&E stain ×200). Panel C shows the tumor acquiring a pleomorphic undifferentiated (malignant fibrous histiocytoma-like) pattern (H&E stain ×200). Panel D shows an area with chondrosarcomatous differentiation (H&E stain ×200).

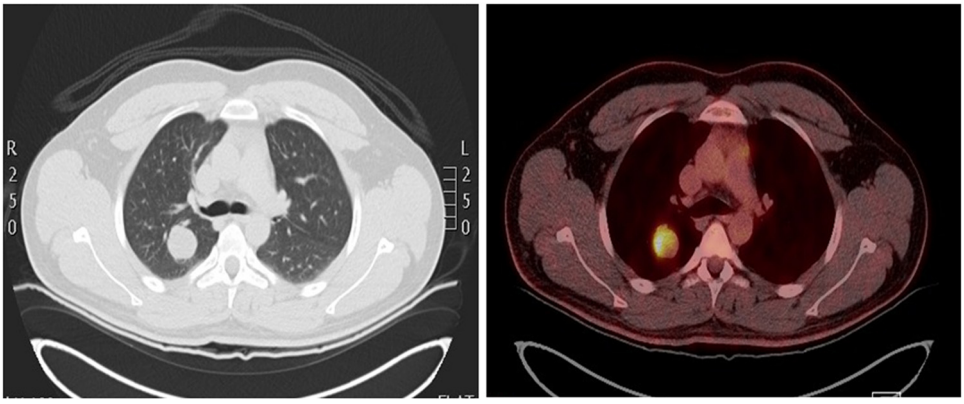

Fig. 4. The metastatic lesion in the right lung as it appeared on CT scan (left panel) and PET scan (right panel) with an avid uptake (SUV_{max} 6.8).

and upper lobe lung metastesectomy and after 2 months left mini-thoracotomy and lung metastatectomy was also performed. The histology of both metastatectomies confirmed metastatic MPNST with a pure spindle cell sarcomatous pattern but without osseous or cartilaginous elements. He remained well after the metastatectomy with no evidence of further metastases at 9–month follow up.

3. Discussion

Malignant peripheral nerve sheath tumor (MPNST) accounts for about 5% of all soft tissue sarcomas. The tumor is associated with neurofibromatosis type 1 (NF1) especially in younger patients [1,2]. However, this was not the case in this patient as he exhibited no features of neurofibromatosis and screening for NF1 gene sequencing was negative.

The presenting symptoms are often non-specific and arise as a result of direct nerve invasion or pressure effect on the surrounding tissues. The commonest presentation is soft tissue mass, followed by pain and local neurological findings [2]. Unfortunately, more than 15% of cases have distant metastases at the time of presentation [1]. It has been suggested that sudden change in tumor size and increase in pain intensity indicate malignancy [4].

Imaging studies are usually not helpful in making a reliable diagnosis but large tumor size (>5 cm) with ill-defined margins, fat plane invasion and surrounding edema may suggest MPNST [5]. Nevertheless, definitive diagnosis can only be made after excisional biopsy [1]. PET-CT scan can distinguish between MPNST and neurofibroma and it is also – as in the present case – helpful in identifying distant metastases during follow-up.

On gross examination, MPNST tend to be firm (Fig. 2) and microscopically it is highly cellular and comprised of spindle

mitotically-active cells which are weakly S100 positive. This weak positivity is consistent with dedifferentiation from Schwann cells. MPNSTs have the capacity in about 15% of cases to exhibit divergent differentiation to various elements other than Schawanian or fibroblastic differentiations [6]. Such heterotopic elements include osteosarcoma, chondrosarcoma, angiomsarcoma and rhabdomyosarcoma. It is rare to have divergent differentiation of two or more components in a single MPNST. However, MPNST cases with 4 and even 6 differentiation patterns have been reported [7,8]. By far bone and cartilage are the most common elements [9–11] as exhibited in this case. Of great interest, there was no such divergent element detected in the pulmonary metastatic lesions. We can offer no explanation to this interesting pathological finding but it warrants future research and analysis. It is believed that this divergent differentiation may be associated with poor prognosis [11,12] as 65% of patients die of the tumor after a mean survival of 2 years only [6]. Other differentiations include malignant triton tumor (MPNST with rhabdomyosarcomatous differentiation); a highly malignant tumor containing embryonic striated muscle components, and is associated with very poor prognosis [13].

Treatment is better drawn by a multidisciplinary team and it involves radical surgical resection of the tumor with sufficient wide margins to achieve a potentially curative operation [13–15] For head and neck lesions wide excision may be hindered by the close proximity of vital organs. Adjuvant or neoadjuvant radiotherapy improves local control especially when wide excision alone is difficult. However, R0 resection can be achieved in 70% of cases only [14,15].

Prognosis is generally poor mainly due to high local recurrence and distant metastases. Some poor prognostic signs include truncal location, tumors larger than 5 cm in size, inability to achieve tumor-free margins, and higher tumor grade. Other poor prognostic factors are the association with NF1, older age, rhabdomyosarcomatous differentiation and distant metastases at the time of diagnosis. The 5-year survival remains poor ranging from 35 to 65% [1,2,13–16].

This case highlights the fact that MPNST is an aggressive tumor especially in younger age group even if there is no association with NF1 gene. Distant metastasis may appear within 1 year of radical R0 resection of the primary tumor and divergent differentiation is associated with poor prognosis. Moreover, metastatic lesions of MPNST may not exhibit divergent differentiation despite its presence in the primary lesion; the impact of this finding on the prognosis is yet to be determined.

Conflict of interest

The authors have no conflict of interest to declare.

Funding

None to declare.

Ethical approval

Hospital IRB was obtained.

Consent

Patient consent was obtained and is available upon request.

Author contribution

- A-W Meshikhes was the primary surgeon in charge of the case. He wrote the final draft.
- M Duhaileb searched the literature and wrote the case history.
- S. Amr read the pathology and participated in drafting the initial draft.

Guarantor

Abdul-Wahed N. Meshikhes is the corresponding author.

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