Retroperitoneal Malignant Peripheral Nerve Sheath Tumour Associated with Vertebral Involvement and Spinal Cord Compression

E Yeap, D Singh, A Hussain, T Ramanujam, N Sithasanan

Citation

E Yeap, D Singh, A Hussain, T Ramanujam, N Sithasanan. *Retroperitoneal Malignant Peripheral Nerve Sheath Tumour Associated with Vertebral Involvement and Spinal Cord Compression*. The Internet Journal of Orthopedic Surgery. 2009 Volume 16 Number 1.

Abstract

Malignant peripheral nerve sheath tumour (MPNST) is usually seen in soft tissue. Intraosseous MPNST is rare, and so is secondary extension. Skeletal involvement usually involves the mandible and other long bones. Vertebral involvement is usually metastatic in nature. Here we report a case of a large retroperitoneal MPNST involving the L1 vertebra and producing spinal cord compression in a patient with neurofibromatosis (NF).

INTRODUCTION

Benign peripheral nerve sheath tumours include schwannomas and neurofibromas. Malignant peripheral nerve sheath tumours (MPNST) can arise de novo or from malignant transformation of benign nerve sheath tumours.[1] They represent 5% of all sarcomas and are associated with NF in up to 70% of cases.[2] There is also association with previous irradiation.[3] Diagnosis in these cases is difficult due to the admixture of benign and malignant histological components.[4]

We report a case of retroperitoneal MPNST with vertebral involvement and spinal cord compression occurring in an 11-year-old girl with undiagnosed NF, and include her clinical course, radiological and histological features, and treatment.

CASE REPORT

An 11 year old Malay girl presented with a 6 week history of low back pain. The pain started insidiously after exercise. The pain was associated with back swelling and there was radiation to the left thigh. However she was able to walk. The pain was not related to activity or posture. She was able to sleep at night and there was no loss of appetite, weight or fever. Bowel movement and micturation was normal.

There was no history of precipitating trauma. There was also no significant past medical or family history. She is the 2 nd child in a family of 6, and is a primary school student.

On physical examination, she was noted to be a slim well nourished girl. There were multiple caf□-au-lait patches over her face, body and legs. There was loss of lumbar lordosis with a slight kyphus deformity of her spine. Examination of the lower limbs revealed power Grade 4 over her left hip and knee. There was no sensory loss and reflexes were normal with the Babinski reflex down-going. Anal tone was normal. An abdominal examination revealed a firm to hard mass measuring 15 X 12 cm extending from the left subchondral region to the umbilical region. The margins were ill defined and the mass was ballotable.

Her laboratory investigations were unremarkable. Roentgenographic analysis showed collapse of the L1 vertebra. (Fig. 1) A CT and MRI scan showed a para-vertebral soft tissue mass adjacent to and involving the L1 vertebra, more on the left side infiltrating the left kidney and compressing the spinal cord. The left kidney was also enlarged. (Fig. 2 & 3)

Figure 1

Figure 1. Thoraco-lumbar x-rays at presentation

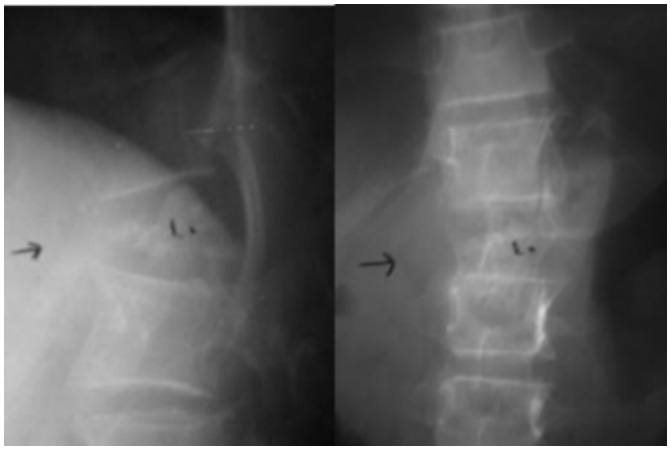


Figure 2

Figure 2. Axial CT cut through L1 vertebra

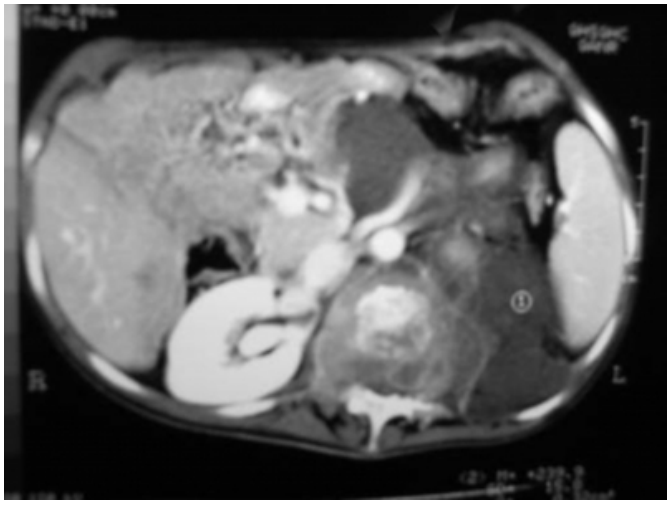
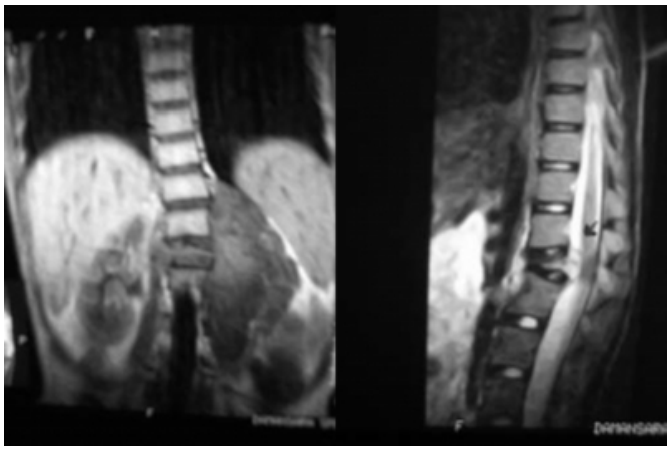


Figure 3

Figure 3. Coronal and sagittal MRI cuts

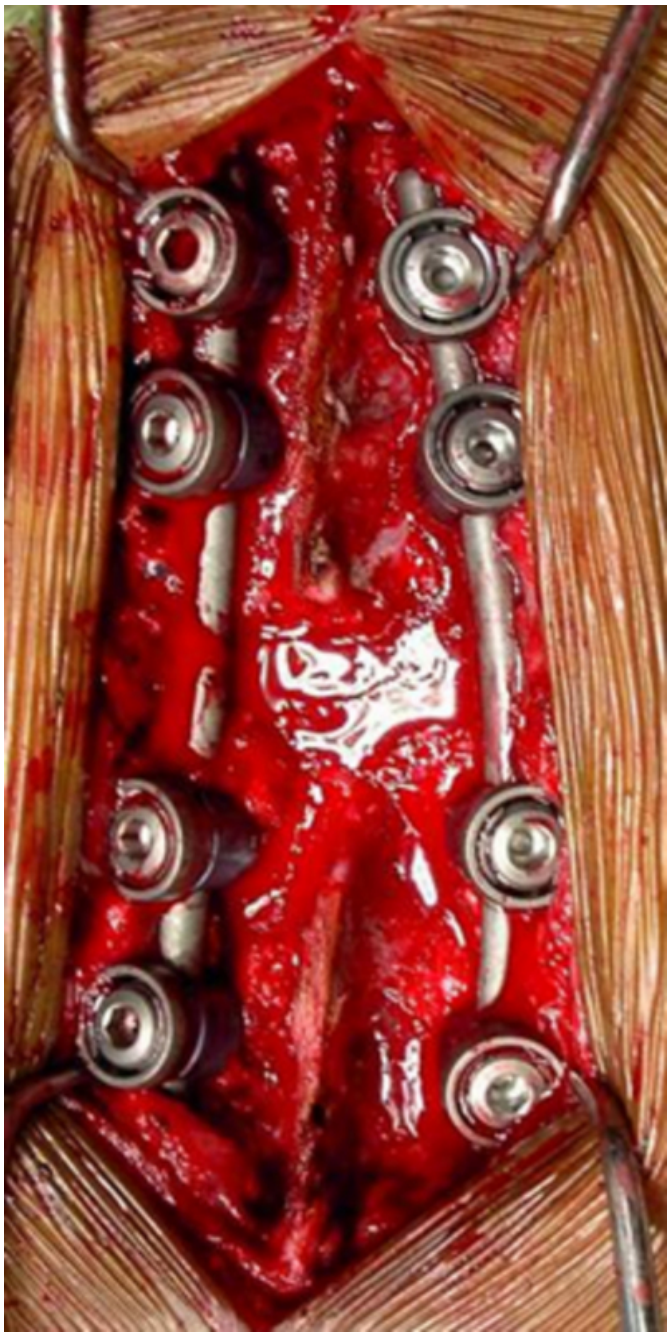


She was started on IV Dexamethasone 8mg tds. She was advised for rest in bed with a Type 2 thoraco-lumbar jacket. She subsequently developed hypertensive encephalopathy and was treated with anti-hypertensives.

Posterior decompression, instrumentation and fusion were performed. (Fig. 4) Both pedicles were infiltrated with tumour tissue, from which a biopsy was sent. It showed fragments of tumour tissue composed of spindle shaped cells in sheets and interlacing bundles. The tumour cells had pleomorphic hyperchromatic nuclei, some with coarse chromatin. The nucleoli were prominent. Aberrant mitotic figures and numerous apoptotic bodies were seen. In focal areas, the tumour cells had dense eosinophilic cytoplasm and eccentric nuclei. The tumour cells strongly express vimentin and focally express desmin, MNF 116, equivocal expression of mic 2 was noted but LCA, NSE, chromogranin, synaptophysin, NB849, actin and S100 were all negative. There was no mucin or glycogen. The overall features indicated a spindle cell sarcoma, in favour of Wilm's tumour.

Figure 4

Figure 4. Posterior decompression and fusion

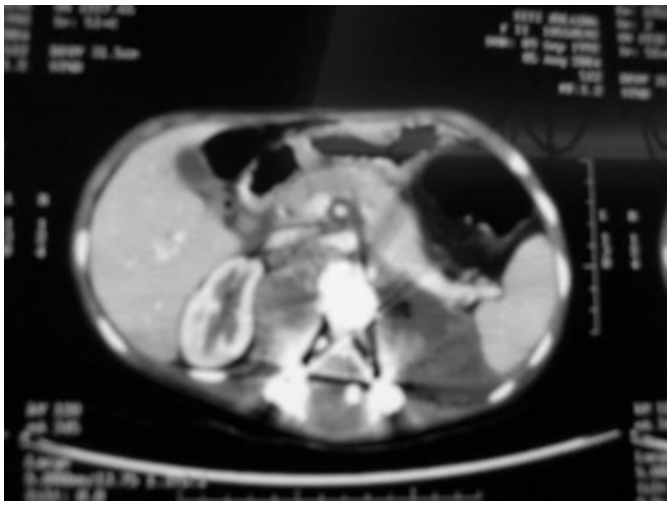


A repeat open wedge and trucut biopsy was done which revealed normal renal corticomedullary tissue. Subsequently, she underwent laparotomy, excision of the abdominal component, left nephrectomy, debulking of the chest component and L1 corpectomy with cage and iliac crest bone graft insertion. The tumour involved the left kidney, middle and lower poles. There was contiguous spread into para-vertebral tissue, para-aortic and left posterior mediastinum under the left crus of diaphragm and into the body of the L1 vertebra, left psoas, quadratus lumborum and inter-spinous spaces with involvement of the left sympathetic chain. Concurrent discectomy of D12/L1 and L1/L2 was done. Due to the immense size of the growth, the unresectable parts of the tumour was left in the quadratus, para-spinal and mediastinal areas.

The post operative period was uneventful. On review 3 weeks later, her wounds had healed but she had reduced sensation over the L1 dermatome on the right and S2 dermatome on the left. Her power was Grade 2 in the hips bilaterally. A CT scan showed residual malignant tumour with post-surgical collection. (Fig. 5) Radiotherapy was instituted at 50 Gy in 25 fractions over the L1 to the S2 vertebra. Chemotherapy was administered later with ifosfomide, etoposide, adriamycin and vincristine. However, 6 months after her initial presentation, CT scan revealed multiple lung, lymph node, splenic and pelvic metastases. She was then referred to Hospis for palliative care. She passed away peacefully at home 3 months after the last surgery.

Figure 5

Figure 5. Post operative CT scan



The specimen sent intra-operatively was divided into the left kidney with tumour, infra-diaphragmatic component, para-spinal component and L1 vertebral component. The left kidney was abnormally enlarged, weighing 449 g and measuring 13 x 11 x 6 cm with irregular tissues attached. The outer surfaces were nodular and these nodules were contained in perinephric fat. Bissection showed a firm homogenous fibrotic, whitish main tumour mass, well-circumscribed, measuring 6 x 5 x 4 cm, which tended to self-enucleate on sectioning. The tumour was located centrally and had compressed and effaced most of the pelvicalyceal

architecture leaving only a thin rim of normal kidney tissue. Smaller nodule were noted all around the main tumour, some in continuity with it (satellite nodules) so that the peripheral portions of the main tumour also appeared myxoid, similar to the peripheral nodules which were firm, greyish, translucent and myxoid - measuring between 0.5 to 5 cm in largest diameter. Focal areas of the tumour were bony hard. The infra-diaphragmatic component consisted of fibromyxoid pinkish to tan coloured nodules similar to the satellite nodules weighing 24 g and measuring 7 x 4 x 3 cm. Cut sections showed a homogenous surface. The paraspinal component consisted of multi-nodular fibrofatty tissue weighing 130 g measuring 8 x 6 x 4 cm with similar nodules. The vertebral fragment measured 4 cm in diameter.

Histologically, multiple sections of the various parenchymal and perinephric nodules showed similar features. The main tumour was composed of a fairly uniform population of cells disposed in swirling and intersecting fascicles composed of spindled cells exhibiting elongated plump but tapering enlarged hyperchromatic nuclei which exhibited moderate pleomorphism and brisk mitotic activity ranging from 0 to 5 to >20/10 hpf in numerous 10 hpf scrutinized. Hypocellular myxoid areas alternated with hypercellular areas. A large portion also exhibited metaplastic osteoid/bone directly arising from the ‘fibrosarcomatous stromal cells. Vague ‘verocays and Wagner Meissner bodies were also noted focally. In occasional foci, transition from benign neurofibromatous tissue to a sarcoma was apparent. Sections of the various other renal and perinephric nodules showed circumscribed lesions of varying sizes, some appearing to be evolving, composed of benign proliferations of spindle cells displaying wavy nuclei interdigitating with thick and short wavy collagen fibrils against a myxoid sarcoma.

Sections of the infradiaphramatic component revealed features similar to the corresponding benign lesions in the kidney and the perinephric fat. The paraspinal component contained diffuse and discrete nodular fibromyxoid neurofibromas contiguous with areas which exhibited sarcomatous features similar to the kidney. The vertebral component showed similar sarcomatous tumour infiltrating the marrow spaces. The tumour here appeared more pleomorphic and anaplastic but interesting fascicles and large areas of serpiginious necrosis were evident.

The vertebral and para-spinal components showed S100 reactivity in the benign components and some focal expression of cytokeratin (MNF 116) with desmin negative. Final histological diagnosis of the kidney tumour was neurofibroma with neurofibrosarcoma exhibiting osteosarcoma, infradiaphragmatic component was neurofibroma, para-spinal component was neurofibroma with neurofibrosarcoma and the vertebral component was neurofibrosarcoma.

DISCUSSION

This patient presented to us with a short history and abundant clinical findings. It is a rare example of spinal cord compression resulting from a retroperitoneal MPNST in a patient with NF. The incidence of MPNST patients suffering from NF ranges from 50-70%.[5] The incidence of NF patients developing MPNST has been reported as from 2-29% in various studies reported in literature.[6] As such, malignant change in a patient with NF favours MPNST. MPNST may develop de novo or by malignant transformation in a pre-existing neurofibroma.[6] MPNST usually occurs in the subcutaneous or deep tissues of the trunk (50%), limbs (30%), head and neck (20%).[1] MPNST comprises 5% of all sarcomas.[2,3,4] It usually affects those in the age group of 20-50.[7]

The previous terms synonymous with MPNST include malignant schwannoma, malignant neurilemmoma, neurofibrosarcoma and neurogenic sarcoma, but none are appropriate. It has been defined as any malignant tumour arising from or differentiating toward cells of the peripheral nerve sheath. Normal nerve sheath consists of Schwann cells, perineurial cells, and mesenchymal cells such as fibroblasts, endothelial cells, pericytes, and epineurial lipocytes.[8]

The nerves affected which can be identified in order of decreasing frequency are the sciatic, brachial plexus, spinal roots, vagus, femoral, median, popliteal and ulnar.[1] Intraosseous origin of MPNST is rare as there is a low density of sensory nerve fibres in bone and tumours of this origin are usually benign.[9] It is of intraosseous origin when the dura and spinal roots are not attachedand it can arise from the nerve roots accompanying nutrient artery.[10]

Primary MPNST arising from bone is most common from the mandible.[6,11,13] There have been a few cases of vertebral origin with one causing spinal cord compression.[11] Theoretically secondary erosion arising from an intraforaminal nerve or congenital nest of cells of neural crest origin within bone is possible, but we do not know of any retroperitoneal MPNST causing compression fracture

and affecting the spinal cord.[12] Mirra described 3 ways MPNST could involve bone:-

Secondary erosion by extraosseous or periosteal route.

Arising from nerve passing through a bony foramen, e.g. mandible.

Abnormal congenital nest of cells of neural origin from bone.[10]

In our case, from the final excision sent for histopathological analysis, we were unable to ascertain the origin of the tumour. We theorise that it most probably started as a retroperitoneal tumour, gradually enlarging in size asymptomatically until it eroded into the bone.

In children, MPNST are among the more common non-rhabdomyosarcomatous soft tissue tumours in the paediatric age group. The clinical presentation is usually a painful or enlarging mass.[13] Patients with NF usually develop MPNSTs at a much younger age, around 30.[1, 2] MPNSTs associated with NF tend to be centrally located.[14] MPNSTs of NF patients tend to be larger and higher grade.[15] They are also prone to develop multiple primary MPNSTs and other malignancies, including central nervous system tumours, phaeochromocytoma, neuroblastoma, Wilm's tumour, rhabdomyosarcoma and leukaemia. Heterologous differentiation, in the form of rhabdomyoblasts, osteoid or cartilage can occur in MPNST and are more common in patients with NF.[1, 22, 23]

We feel the first biopsy represented a mixed picture. Histologically, spindle shaped cells in sheets and interlacing bundles were identified in our case. Hruban et al reported 86% of MPNST cases in their series demonstrated that pattern.[23] It is a diagnostic challenge. S100 antibody was negative and desmin was positive indicating overlap between the immunocytochemical attributes of MPNST to other soft tissue sarcomas.[16] Immunoreactivity for S100 protein is usually found in 50-70% of MPNST.[8] Therefore, the initial diagnosis was of a Wilm's tumour in view of the clinical findings and histopathological examination.

Retroperitoneal prognosis is abysmal. It is locally invasive but grows undetected until a late stage. Surgery is the mainstay but gross excision is not feasible.[2] Chemotherapy and radiotherapy does not improve survival but radiotherapy is encouraging in local control.[2] High dose radiation at 70 Gy utilizing a saline filled tissue expander to protect the bowel has been reported.[17]

Most patients die of systemic metastasis. Recurrence rate is 75% with a 5 year survival rate of 16-53%.[1, 12, 21] Poorer survival is associated with tumour > 5cm, subtotal resection, pre-existing NF and younger age at diagnosis.[1, 12]

In conclusion, we describe a rare case of retroperitoneal MPNST involving the L1 vertebra and producing spinal cord compression.

References

1. Wanebo J, Malik J, Vanden Berg S, Wanebo H, Driesen N, Persing J (1993) Malignant peripheral nerve sheath tumors. Cancer 71: 1247–1253
2. Wick M, Swanson P, Scheithauer B, Manivel J (1987) Malignant peripheral nerve sheath tumor. Am J Clin Pathol 87: 425–433
3. Gnanalingham K, Bhattacharjee S, O'Neill K (2004) Intraosseous Malignant Peripheral Nerve Sheath Tumor (MPNST) ot the Thoracic Spine. Spine 29: E402-E405.
4. Hajdu SI. Peripheral nerve sheath tumors: histogenesis, classification, and prognosis. Cancer 1993; 72:3549–3552.
5. Stark AM, Buhl R, Hugo HH, et al. Malignant peripheral nerve sheath tumours—report of 8 cases and review of the literature. Acta Neurochir (Wien) 2001;143:357–64.
6. Mirra JM. Bone tumors: clinical, radiologic and pathologic correlations. Beckenham Kent Philadelphia: Lea and Febiger, 1989: 855–867.
7. Kendi TK, Erakar A, Yildiz HY, Saglik Y, Erekul S. Intraosseuos malignant peripheral nerve sheath tumor with local recurrence, lung metastases and death. Skeletal Radiol (2004) 33:223-225
8. Wong WW, Hirose T, Scheithauer BW, et al. Malignant peripheral nerve sheath tumour: analysis of treatment outcome. Int J Radiat Oncol Biol Phys 1998;42:351–60.
9. Dunnick NR. Image interpretation session: 1999. Intraosseous malignant peripheral nerve sheath tumor (malignant schwannoma) in a patient with neurofibromatosis. Radiographics 2000; 20:271–273.
10. Polkey CE. Intraosseous neurilemmoma of the cervical spine causing paraparesis and treated by resection and grafting. J Neurol Neurosurg Psychiatry 1975;38:776–81.
11. Preston FW, Walsh WS, Clarke TH. Cutaneous neurofibromatosis (von Recklinghausen's disease). Arch Surg 1962;64:813–27.
12. Terry DG, Sauser DD, Gordon MD. Intraosseous malignant nerve sheath tumor in a patient with neurofibromatosis. Skeletal Radiol (1998) 27:346-349.
13. Casanova M, Ferrari A, Spreafico F, et al. Malignant peripheral nerve sheath tumours in children: a single institution twenty year experience. J Paediatr Haematol Oncol 1999;21:509–13.
14. Ramanathan RC, Thomas JM. Malignant peripheral nerve sheath tumors associated with von Recklinghausen's neurofibromatosis. Eur J Surg Oncol 1999;25:190–3.
15. Hruban RH, Shiu MH, Senie RT, et al. Malignant peripheral nerve sheath tumors of the buttock and lower extremity: A study of 43 cases.Cancer 1990; 66:1253–1265.
16. Wick MR, Swanson PE, Scheithauer BW, et al. Malignant peripheral nerve sheath tumour: an immunohistochemical study of 62 cases. Am J Clin Pathol 1987;87:425–33.

17. Ogose A, Hotta T, Uchiyama S, Matsumoto Y, Hasegawa K, Takahashi HE. Retroperitoneal malignant peripheral nerve sheath tumor associated with scoliosis in neurofibromatosis. Journal of Spinal Disorders 2001;14(3):260-263.

Author Information

Ewe Juan Yeap, MS(Ortho)
Tuanku Fauziah Hospital

Deepak Ajit Singh, FRCS(Ed)
Prince Court Medical Centre

Abdul Malik Mohamed Hussain, FRCS(Glasgow)
Damansara Specialist Centre

TM Ramanujam, FRACS(Paed Surg)
University Malaya Medical Centre

NN Sithasanan, FRCS(Paed Surg)
Gleneagles Medical Centre