

Case Report

Intrathoracic Malignant Peripheral Nerve Sheath Tumor: Histopathological and Immunohistochemical Features

Sunita Singh, Megha Ralli, Sonia Hasija, Renuka Verma

Department of Pathology, Post Graduate Institute of Medical Sciences, Rohtak, Haryana, India

ABSTRACT

Malignant peripheral nerve sheath tumor (MPNST) is a rare nerve sheath tumor derived from Schwann cells or pluripotent cells of neural crest. Neurogenic tumors make about 10-20% of all mediastinal tumors. Incidence of MPNST is 0.001% in general population and 0.16% in patients with neurofibromatosis I (NF I). We report a case of 60 year female presenting with progressive cough and breathlessness for 2 years. The CECT revealed multiple focal enhancing lesions along inferior mediastinal pleural surface and along lateral pleural surface. A thoracotomy and tumor excision was done and MPNST was diagnosed on microscopy and immunohistochemistry. This case highlights that this unusual tumor may involve lung parenchyma. So this possibility should be kept in mind in patients with intrathoracic mass.

Keywords: Peripheral Nerve Sheath Tumor, Mediastinum, Cancer, India

Introduction

MPNST is a rare and aggressive sarcoma, a malignant counterpart of benign tumors of neurogenic origin such as schwannoma and neurofibroma. It accounts for 5-10% of all soft tissue sarcomas. In the past, other terms like malignant schwannoma, malignant neurilemmoma, or neurogenic sarcoma were also used for MPNST(1). It arises from Schwann cells or pluripotent cells of neural crest with an incidence of 0.001% in general

population and 0.16% in patients with NF I (2). Large and medium-sized nerves are more often involved than small nerves. It is more commonly seen in extremities, head and neck. Intrathoracic MPNST is uncommon (3). It usually affects adult people aged 20-50 years and develops in deeper soft tissue. It is highly malignant with recurrence rate between 40-65% and metastasis rate between 40-68%. Both rates depend on tumor's degree of histological malignancy. The lungs are the most common site of metastasis (1).

Received: 03 October 2013

Accepted: 26 March 2014

Address Communications to : Dr. Megha Ralli, Department Of Pathology, Post Graduate Institute Of Medical Sciences, Rohtak, Haryana, India.

Email: drmegharalli@gmail.com

Case Report

A 60 yr old female presented with progressive cough and dyspnea sinetwo years ago. Physical examination revealed typical findings of neurofibromatosis including multiple cafe' au lait spots on the back (more than 6, 1–3 cm in diameter), freckling in the inguinal regions, and multiple 0.5–1 cm nodules all over the trunk. There was no evidence of finger clubbing. Auscultation re-

vealed decreased but coarse breathing sounds over the right lower chest. Chest X- ray revealed ill- defined areas of ground glass appearance with basal atelectasis of right lung (Fig. 1a). CECT showed multiple focal enhancing lesion of size 9×8cm along inferior mediastinal pleural surface, with two other large lesions of 8.8×5.8 cm and 6.8×3.8cm along lateral pleural surface (Fig. 1b).

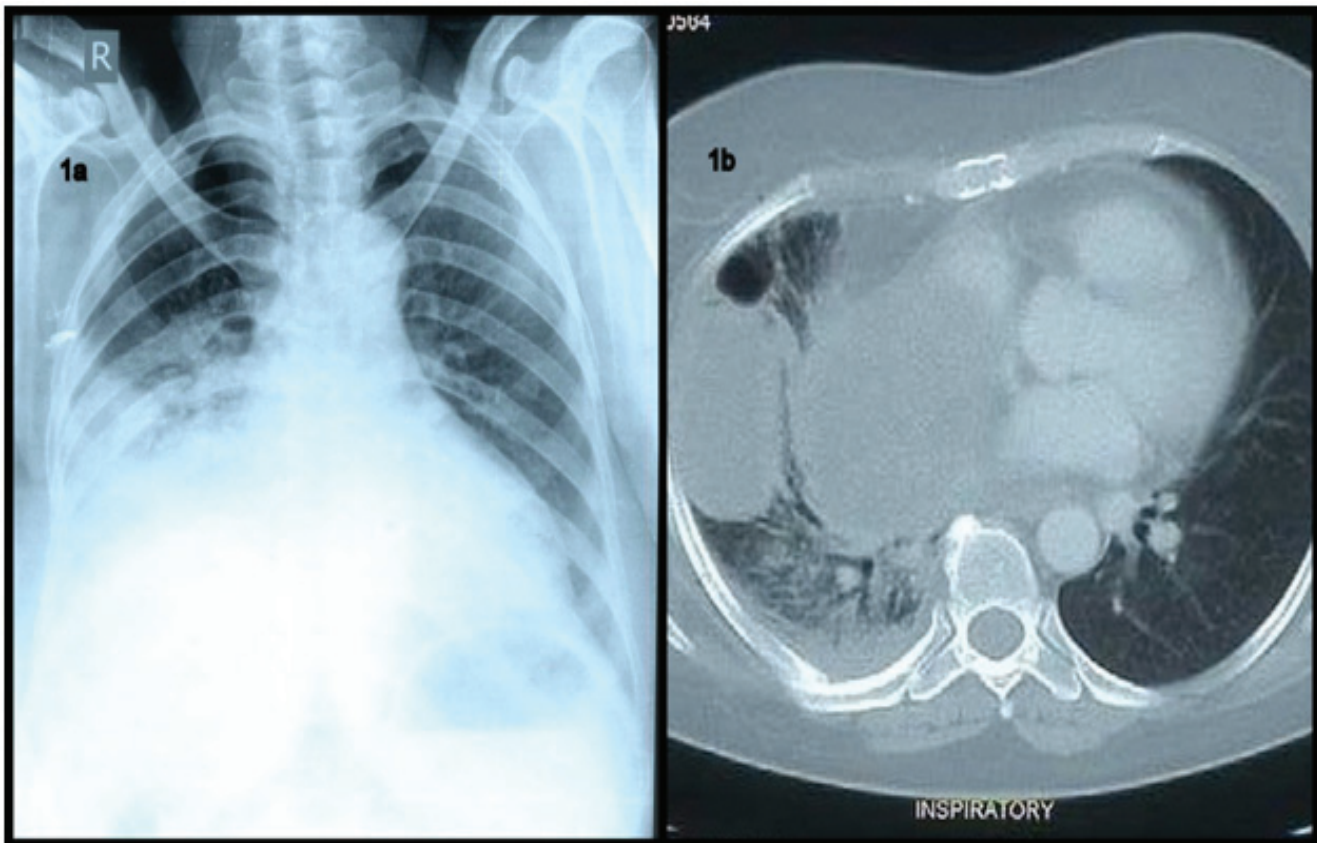


Fig. 1: a) X-ray shows ill defined ground glass appearance with basal atelectasis of right lung; **b)** CECT shows multiple focal lesions of size 9×8cm along inferior mediastinal surface and two other lesions of size 8.8×5.8cm and 6.8×3.8cm along lateral pleural surface

A thoracotomy and tumor excision procedure was done. On gross examination, a gray white encapsulated tumor measuring 10x8.5cm extending into lung parenchyma was identified. The cut surface revealed tumor nodule measuring 4×3×3cm inside lung parenchyma with surrounding lung showing consolidation (Fig.2a). Microscopically, the tumor showed oval to spin-

dle shaped cells with hyperchromatic and pleomorphic nuclei arranged in dense cellular fascicles admixed with matrix. The tumor showed high mitotic activity >10/10 hpf (Fig.2b). On immunohistochemistry, the tumor cells showed vimentin positivity (Fig. 2c); CD 34 positivity and focal positivity for S-100 (Fig. 2d) and so the diagnosis of MPNST was confirmed.

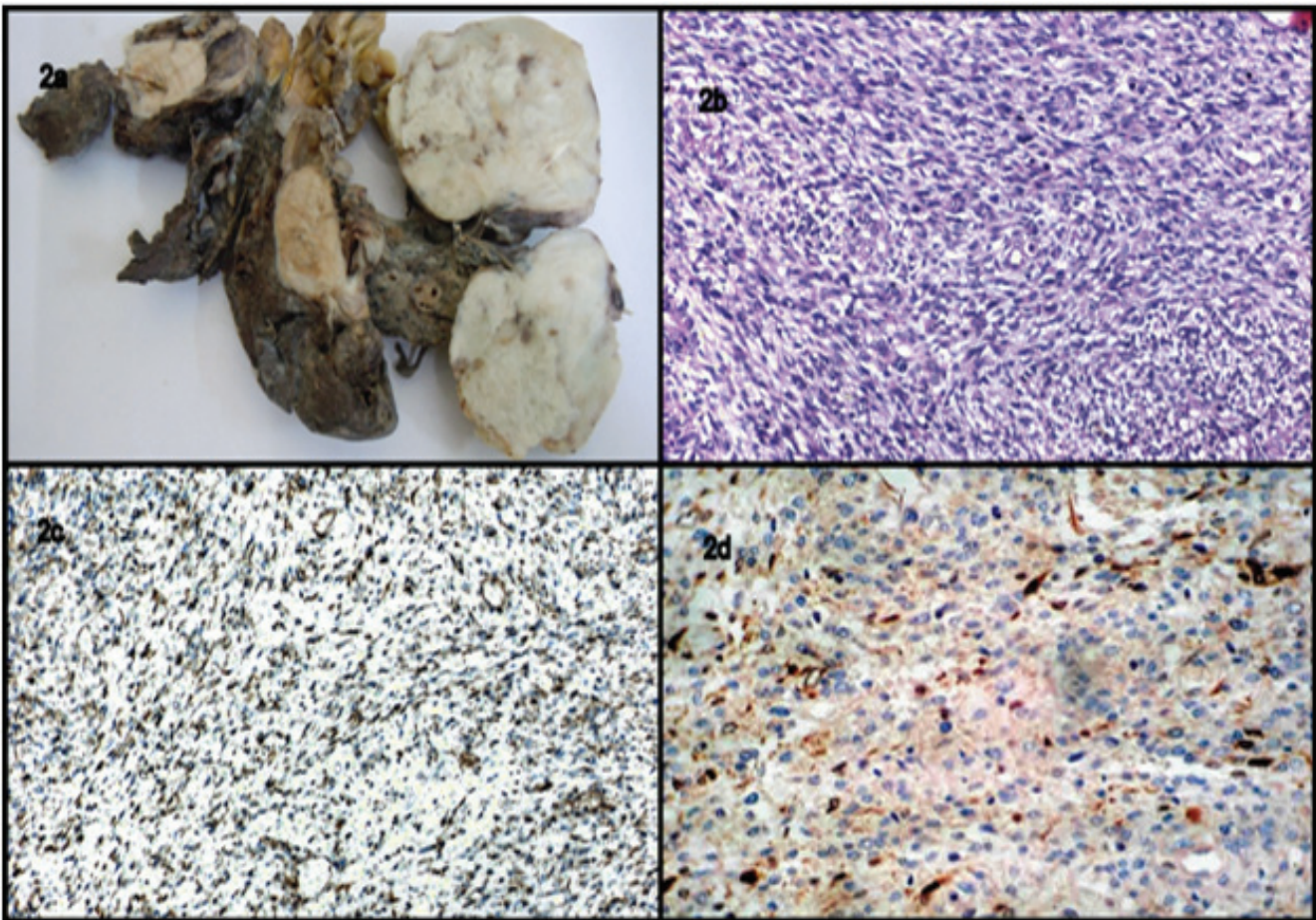


Fig. 2: **A)** Specimen shows gray white encapsulated tumor of size 10×8.5cm extending into lung parenchyma with tumor nodule in lung of size 4×3cm; **B)** Oval to spindle shaped cells with hyperchromatic and pleomorphic nuclei and tumor shows mitotic activity >10/10 hpf (H&E, ×200); **C)** Vimentin positivity in spindle cells consistent with MPNST (×100); **D)** S-100 focal nuclear and cytoplasmic positivity in spindle cells consistent with MPNST (×40)

Discussion

MPNST is a rare neoplasm and accounts for 5-10% of all soft tissue sarcomas. It is slow growing tumor and hence the patients are asymptomatic for long time and signs of disease such as pain and motor or sensory disturbances appear late as a result of tumor pressure on nerve (1). It is therefore usually detected in its advanced stage when it has already reached a considerable size. According to recent recommendations, a sarcoma is defined as MPNST when at least one of the following three criteria are met (4): (a) a tumor develops in a peripheral nerve, (b) a tumor develops from a pre-existing benign nerve sheath neoplasm, most frequently from neurofibroma, (c) a tumor shows a set of histologic features

consistent with Schwann cell differentiation.

Around 40-50% of MPNST cases appear in people suffering from Recklinghausen's disease (4-6). Neurofibromatosis I (NF I) is an autosomal dominant neurocutaneous disorder with estimated birth incidence of 1 in 2500 and prevalence of 1 in 5000 (2). The NF I gene mutation is on chromosome 17, and its product, neurofibromin, normally functions as a tumor suppressor to reduce cell proliferation by inactivating the proto-oncogene p21-ras. NF I patients, therefore, have an increased predilection for the development of both benign and malignant nerve sheath tumors (7).

MPNST are usually big, rubbery and cut surface is tan white in color with areas of necrosis and

hemorrhage. In classic forms microscopy shows presence of spindle cells arranged in dense cellular fascicles that resemble fibrosarcoma and therefore they are included in spindle cell neoplasms. The tumor cells have slender nuclei of wavy contour and indistinct cytoplasm. Cells are arranged in sweeping fascicles pattern. S-100 positivity is seen in 50-90% of cases but staining is usually focal (4). The tumor cells show diffuse positivity for vimentin. These findings are consistent with our case.

MPNST is known to occur in many differentiation patterns. In about 15% cases, epithelioid or heterologous differentiation is seen; the latter includes rhabdomyoblasts, smooth muscles, bone, cartilage and neuroendocrine component. The most common heterologous component is rhabdomyoblast differentiation, first reported by Masson in 1932 and named as 'malignant triton tumor' by Woodruff. In a case reported by Guo *et al* six kinds of differentiation, including rhabdomyosarcomatous, chondral, glandular, neuroendocrine, gangliocytic and liposarcomatous components were observed in a background of a classical MPNST (5). The diagnosis of MPNST with multiple mesenchymal differentiations is difficult and should be differentiated from rhabdomyosarcoma, osteosarcoma, chondrosarcoma or liposarcoma. Other differential diagnosis includes schwannomas, neurofibromas, fibrosarcoma, leiomyosarcoma, synovial sarcoma (CK7 positive) and other spindle cell tumors. Focal S-100 positivity favors MPNST rather than schwannomas which show diffuse S-100 positivity. Fibrosarcoma, monophasic synovial sarcoma and leiomyosarcoma show spindle cells with focal fascicular arrangement. A combination of S-100 and cytokeratin (CK) staining with smooth muscle antigen (SMA) is important in distinguishing them from MPNST. Thirty percent cases of synovial sarcoma are S-100 positive. Leiomyosarcoma show positivity with SMA and morphologically the nuclei in leiomyosarcoma

have more blunted ends. The epithelioid variant of MPNST has malignant epithelioid cells with polygonal configuration with abundant eosinophilic cytoplasm and prominent nucleoli. Such very prominent nucleolisation may be confused with malignant melanoma. In such cases HMB-45 or Melan-A negativity in these cells helps in diagnoses of MPNST.

The treatment of choice is surgery, regardless of tumor being a primary or recurrent one (1). The method of surgery depends on size, affected area, risk of nerve injury, degree of malignancy and distance from lungs and pelvis and also on tumor character (primary or recurrent) (8). The surgery is radical with excision of tumor with adjacent vessels, nerves, muscles and bone (6,9). In patients with unresectable tumor chemotherapy and radiotherapy are modality of treatment. Radiotherapy may delay recurrence but has little effect on long-term survival. Standard chemotherapy for advanced soft tissue sarcoma in adults involves single-agent doxorubicin and has a poor response rate of 12% (2); furthermore, neurofibromatosis I is one of the most significant prognostic factors indicating poor outcome with chemotherapy against MPNST (10,11). Radiotherapy and chemotherapy can be used as palliative treatment to prevent micrometastasis and to reduce symptoms (1). The prognosis is worse when MPNST appears in patients with NF I (five year survival rate 16-23% in comparison to 47-53% in patients without NF I) (8).

In our patient, complete resection of tumor was done. The margins were negative for tumor infiltration. The isolated lymph nodes submitted were also free from tumor metastasis. The patient was discharged within 10 days and is on every 3 months follow up.

To conclude, this case highlights that MPNST may involve lung parenchyma. So this possibility should be kept in mind in patients with intrathoracic mass.

Acknowledgements

The authors declare that there is no conflict of interest.

References

1. Gryglicka B, Szkutnik IW, Milanowski J, Mandziuk S, Szatkowska LG, Surdyka D, *et al.* Malignant peripheral nerve sheath tumor associated with clear cell carcinoma- case report. *PneumonolAlgerol Pol* 2012;80(3):269-74.
2. Chao BH, Stogner- Underwood KA, Kiev J, Smith TJ. Intrathoracic malignant peripheral nerve sheath tumor in neurofibromatosis I. *J ClinOncol* 2008;26(13):2216-8.
3. Kolarov V, Stanic J, Eri Z, Zvezdin B, Kojicic M, Hromis S. Intrathoracic malignant peripheral nerve sheath tumor with poor outcome: a case report. *Bosnian JBas Med Sci*2010;10(4):328-30.
4. Enzinger F., Weiss S. Enzinger& Weiss.: Soft tissue tumors. New York: Mosby; 2008.
5. Guo A, Liu A, Wei L, Song X. Malignant peripheral nerve sheath tumors: Differentiation patterns and immunohistochemical features - A mini-review and our new findings. *J Cancer* 2012;3:303-9.
6. Kar M, Deo SVS, Shukla NK, Malik A, DattaGupta S, Mohanti BK, *et al.* Malignant peripheral nerve sheath tumors (MPNST): Clinicopathological study and treatment outcome of twenty four cases. *World J SurgOncol* 2006;4:55.
7. Patel VS, Louis JD, Oduntan O, Landolfo KP. Intrathoracic peripheral nerve sheath tumor in patients with neurofibromatosis type I (von Recklinghausen disease). *J ThoracCardiovascSurg* 2006;131(3):736-7.
8. Gosk J, Zimmer K, Rutowski R. Peripheral nerve tumours: diagnostic and therapeutical basics. *Folia Neuropathol* 2004;42(1):31-5.
9. Ariel IM. Tumors of the peripheral nervous system. *CA Cancer J Clin* 1983;33(5):282-99.
10. Carli M, Ferrari A, Mattke A, Zanetti I, Casanova M, Bisogno G, *et al.* Pediatric malignant peripheral nerve sheath tumor: The Italian and German Soft Tissue Sarcoma Cooperative Group. *J ClinOncol* 2005;23(33):8422-30.
11. Hagel C, Zils U, Peiper M, Kluwe L, Gotthard S, Friedrich RE, *et al.* Histopathology and clinical outcome of NF1-associated vs. sporadic malignant peripheral nerve sheath tumors. *J Neurooncol* 2007; 82(2):187-92.