



## Introduction

Malignant peripheral nerve sheath tumor (MPNST) is a rare nerve sheath tumor. Which is derived from Schwann cells or pluripotent cells of neural crest. MPNST is usually occurred in association with neurofibromatosis type 1, also known as von Recklinghausen's neurofibromatosis. The incidence of this occurrence is 2%-16%<sup>1</sup>. Neurogenic tumors are found approximately 10-20% of all mediastinal tumors. The incidence of MPNST is 0.001% in general and 0.16% in patients with neurofibromatosis I (NF I). Neurogenic tumors possibly originate from either peripheral nerves, nerve sheaths, or sympathetic ganglions. In varying proportions, neurogenic tumors can be malignant. These tumors are variously recognized such as malignant schwannoma, neurogenic sarcoma, or neurofibrosarcoma, however MPNST is generally known. The majority of MPNSTs<sup>2,3</sup> are derived from neurofibroma or arise *de novo* in normal peripheral nerves. Large and medium size of nerves are commonly involved compared to small nerves. Schwannoma is the most common nerve sheath tumor in the posterior mediastinum whereas intrathoracic MPNST is rare.

MPNSTs are aggressive tumor with a high rate of local recurrence and distant metastasis. They are commonly found in extremities and head and neck. Intrathoracic MPNST is uncommon<sup>4</sup>. It is usually occurred in adult aging 20-50 years and it normally develops in deeper soft tissue. It is highly malignant and has 40-65% recurrence rate and 40-68% of metastasis rate. The degree of histological malignancy has strong influence on the rate of recurrence and metastasis. Lungs are the most common site of metastasis<sup>5</sup>. The major principle treatment of MPNST is surgical resection. The role of adjuvant treatment in MPNST is controversy. The patient with a huge mass of MPNST of posterior mediastinum is presented in this article.

## Case Report

A 40-years old woman with neurofibromatosis type 1 (NF 1) was admitted after presenting with 2 months history of dyspnea. She had no familial history of NF 1. A chest x-ray showed huge mass in the left thorax (Fig.1)

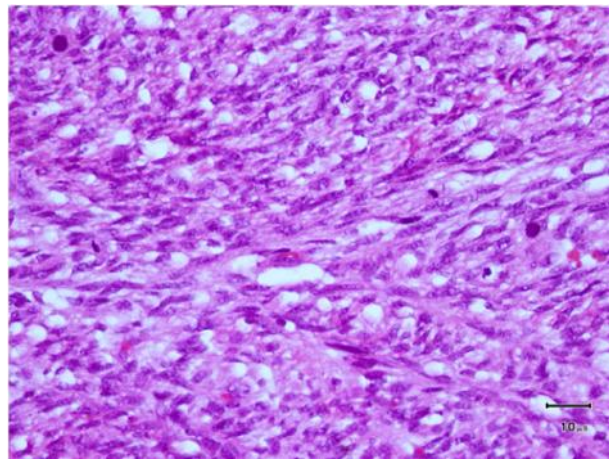
and CT of chest revealed a tumor, 8.6 x 8.6 cm in size, occupying in the left thorax with erosion posterior left 4<sup>th</sup> rib (Fig.2). We performed surgical resection with the aim of debulking, to inflate the collapsed lung. A left thoracotomy revealed an encapsulate round-shaped tumor originate from intercostal nerve. Tumor was adherent to left lung parenchyma and displaced left lung to inferomedial aspect. On gross examination, a gray brown encapsulated tumor measuring 10 x 9 x 7 cm extending close to lung parenchyma was identified. The cut surface revealed homogeneous whitish pale yellow with hemorrhage area. Microscopically, the tumor showed oval to spindle shaped cells with hyperchromatic and pleomorphic nuclei arranged in dense cellular fascicles admixed with matrix. The tumor showed high mitotic activity (Fig.3). On immunohistochemistry, the tumor cells showed Vimentin positivity, CD34 positivity and focal positivity for S-100. Therefore the final diagnosis of MPNST was confirmed. The patient received post-operative radiotherapy. After that 4 months, this patient had pancreatic mass and loss follow up.



**Figure 1** Chest x-ray shows a giant mass in the left upper thorax. Numerous small nodules representing neurofibromas of the skin can also be seen.



**Figure 2** Computed tomography shows a giant tumor occupying the left upper thorax with erosion posterior left 4<sup>th</sup> rib.



**Figure 3** Microscopic findings of the resected specimen. The tumor cells were composed of spindle cells with oval to long oval nuclei, arranged in sweeping fascicles. Mitosis was observed frequently.

## Discussion

MPNSTs, which are also known as malignant schwannomas, neurofibrosarcomas and neurogenic sarcomas, develop in 2%-16% of patients with NF1<sup>1</sup>. Neurogenic tumors account for about 10-20% of primary mediastinal mass in adult and 30-50% in children. They are almost exclusively located in the posterior mediastinum<sup>6</sup>. The tumors may arise from peripheral nerves, or nerve sheaths, including neurofibroma, neurilemmoma (schwannoma), and malignant nerve sheath tumors (neurogenic sarcoma) or from sympathetic ganglions, such as ganglioneuroma, ganglioneuroblastoma, or neuroblastoma. Nearly 85% of tumors in children are ganglion in origin<sup>7</sup>, while, in adults, more than 75% are nerve sheath tumors. Schwannoma is the most common nerve sheath tumor in the posterior mediastinum, and the vast majority arise from one of the intercostal nerves.

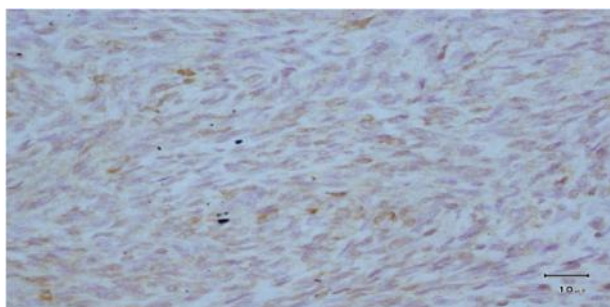
Clinically, peripheral nerve sheath tumors usually do not cause symptoms and are discovered on a screening chest roentgenogram<sup>6</sup>. In a minority of patients, compression of the intercostal nerves or major airways gives rise to pain or dyspnea. On plain radiographs, nerve sheath tumors typically appear as sharply margined round, elliptical, or lobulated paraspinal masses. Erosion of the ribs and vertebral bodies sometimes is evident. On CT scan, Schwannoma

has been shown to have a mixed attenuation, attributable to a confluent area of hypocellularity adjacent to dense cellularity, or xanthogranulomatous change, or regions of cystic degeneration<sup>8</sup>. Calcification (about 5-10%) may be present with either benign or malignant tumors<sup>9</sup>, but is not reliable sign of benignancy.

According to recent recommendations, a sarcoma is defined as MPNST when at least one of the following three criteria are met<sup>10</sup>: (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 Von Recklinghausen's disease<sup>10-12</sup>. 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. Histologically, MPNSTs are usually more hypercellular with spindle cell

proliferation. The tumor cells often show hyperchromatic nuclei and are mitotically active<sup>13</sup>. S-100 positivity is seen in 50-90% of cases but staining is usually focal<sup>10</sup> (Fig.4). The tumor cells show diffuse positivity for vimentin (Fig.5). These findings are consistent with our case. Focal S-100 positivity favors MPNST rather than schwannomas which show diffuse S-100 positivity.

Clinically, MPNSTs affect young to middle-aged adults, with a slight female predominance. Neurofibromatosis type 1 (NF 1) predispose to the development of MPNSTs. In addition to hereditary factors, exposure to ionizing radiation may also play a role in the development of MPNSTs<sup>14</sup>. These tumors are aggressive, locally invasive, and highly metastatic, and cause a variety of symptoms depending on their location and size. Hemothorax is a common complication of MPNSTs because of the characteristic



**Figure 4** Microscopic findings of the resected specimen. The tumor cells show S-100 positivity staining is usually focal.



**Figure 5** Microscopic findings of the resected specimen. The tumor cells show diffuse positivity for vimentin.

feature of intratumoral hemorrhage and necrosis<sup>15,16</sup>.

Complete surgical removal of the tumor is the optimal treatment goal, with adjuvant radiotherapy for invasive and large tumors, as our case. Wide en bloc is the treatment of choice for tumors involving soft tissue<sup>3</sup>. Local recurrence rate varied from 40% to 68%<sup>2,3,17</sup>. Postoperative radiation therapy of MPNST has led to a significant reduction of local recurrence<sup>18</sup>. Combination chemotherapy is recommended for unresectable tumors<sup>19</sup>.

The prognosis of patients with MPNST is unfavorable. In 2 major studies with long term follow-up, reported overall 5-year survival rates were 34-52%<sup>2,3</sup>. The factors that appear to affect the prognosis of patients with MPNST are tumor location, size, histologic subtype, Tumor grade, molecular genetics, completeness of resection, recurrence, metastasis and presence of NF1. Reported mean and median ages at death for patients with NF1 are 54.1 and 59 years, respectively, compared with 70.1 and 74 years for the general population. People with NF1 are prone to the development of other disease, and 1.2 times more likely to have malignant neoplasm at the time of death than people without NF1<sup>1,20</sup>. Thus, a careful follow up plan should be in place for patients with NF1 to allow for the early diagnosis of MPNST and other neoplasms. A large tumor (> 5 cm), association with NF1, and incomplete resection have been reported as poor prognostic factors<sup>2</sup>.

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