The Korean Journal of Internal Medicine
Vol. 16, No. 3, September, 2001

Intrathoracic Malignant Peripheral Nerve Sheath Tumor in von Recklinghausen's Disease

Ju-Hyung Park, M.D.*, Koang-Ho Choi, M.D.*, Heung-Bum Lee, M.D.*, Yang-Keun Rhee, M.D.*, Yong-Chul Lee, M.D.*‡ and Myung-Ja Chung, M.D†

Departments of Internal Medicine and Clinical Pathology †, Chonbuk National University, School of Medicine, Research Institute of Clinical Medicine‡, Chonju, Chonbuk, South Korea*

Malignant peripheral nerve sheath tumor (MPNST) is defined as any malignant tumor arising from or differentiating toward the cells of the peripheral nerve sheath. MPNST accounts for about 5-10% of all soft tissue tumors and is often associated with neurofibromatosis type I (NF-1, von Recklinghausen's disease). It is one of the malignant tumors associated with von Recklinghausen's disease. Its common site is the lower and upper extremities, trunk, head and neck. But intrathoracic manifestations are very rare. We report a case of a 40 year-old man with multiple neurofibromatosis who was presented with an intrathoracic malignant peripheral nerve sheath tumor.

Key Words : *Malignant peripheral nerve sheath tumor; Thoracic cavity; Von Recklinghausen's disease*

INTRODUCTION

Type I neurofibromatosis, also referred to as von Recklinghausen's disease, is an autosomal dominant disease characterized by neurofibromas and abnormal cutaneous pigmentation (cafe-au-lait spot). Its malignant transformation, that is malignant peripheral nerve sheath tumor (MPNST), accounts for about 5-10 percent of all soft tissue tumors[1, 2]. Common site of the origin for MPNST is the lower and upper extremities, trunk, head and neck. Its intrathoracic manifestations are very rare.

We have recently experienced a case of intrathoracic MPNST in a patient with von Recklinghausen's disease.

CASE REPORT

A 40-year-old man presented to Chonbuk National University Hospital, Chonju, Korea, due to one rapidly enlarging palpable mass in the right neck which was extended to the supraclavicular fossa. He complained of right side posterior neck pain and radiating pain with mild numbness. The motor weakness of his right upper extremity began 4 months ago. Physical examination showed a firm, non-tender and fixed mass associated with ptosis of right eyelid, engorgement of right neck vein, facial swelling and multiple cafe-au-lait spots and pigmented nodular skin lesions on the chest wall and both arms (Figure 1. (A)).

Chest radiography showed an increased homogeneous mass density at right upper lung field with well-demarcated margin and elevation of right side diaphragm (Figure 1. (B)). Magnetic resonance imaging (MRI) scan of the thorax revealed a homogeneous, well-enhanced and well-circumscribed mass measuring 12×10×8 cm. The central portion of the huge mass showed necrotic tissue which was high signal intensity in T-2 weighted image and low signal intensity in T-1 weighted image. The main mass was located in right upper hemithorax and was associated with multiple adjacent lymphadenopathy. The lesion compressed the trachea, esophagus, right carotid and subclavian artery, and encased the brachial plexus (Figure 1. (C)).

Address reprint requests to : Yong-Chul Lee, M.D., Department of Internal Medicine, Chonbuk National University Medical School, 634-18 Keumam-dong, Duckjin-ku, Chonju 561-712, Chonbuk, South Korea

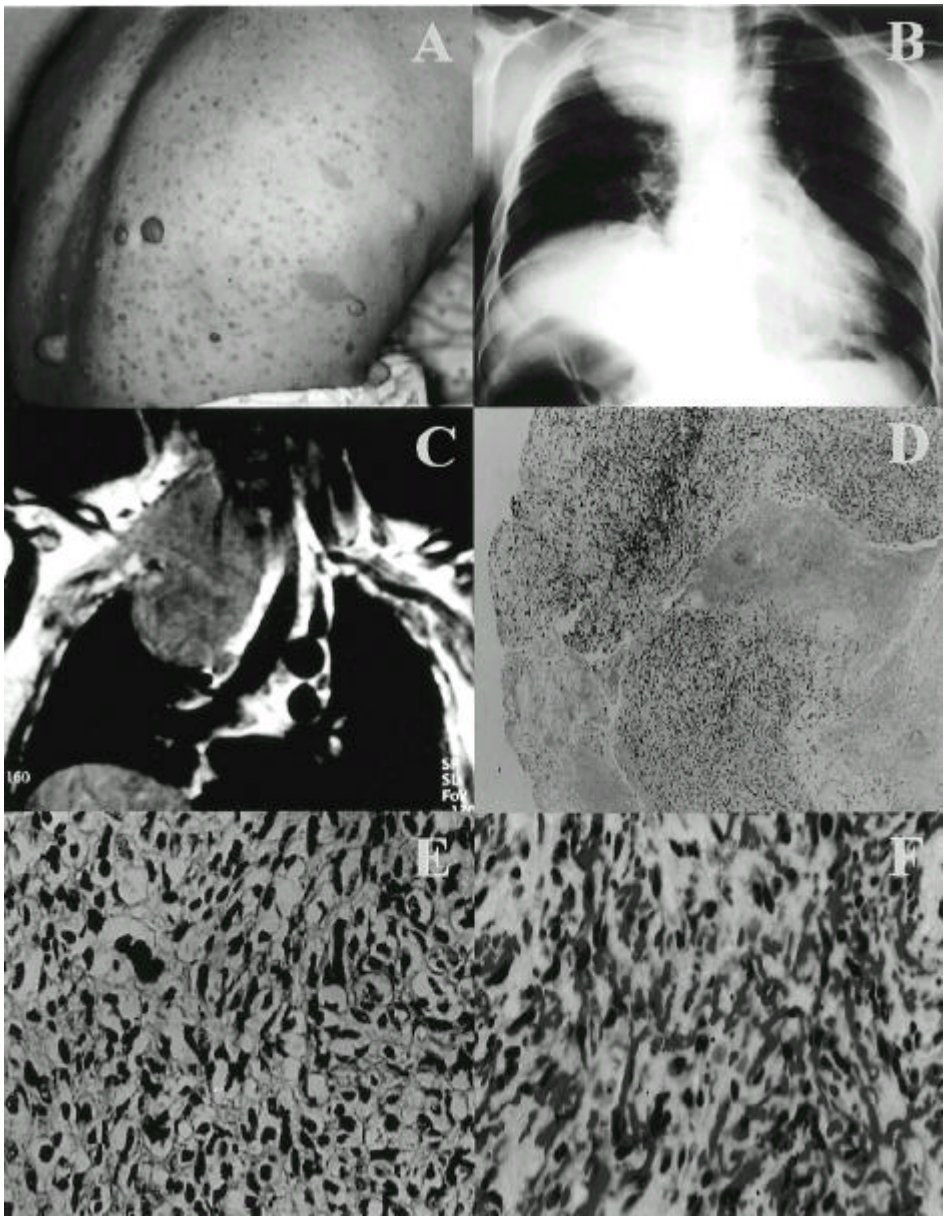

Figure 1. (A) Multiple variable sized cafe-au-lait spots and nodular skin lesions over the chest wall and both arms. **(B)** Chest PA shows a homogeneous mass density at right upper lung field with well demarcated margin and elevation of right side diaphragm. **(C)** Chest MRI shows a homogeneous, well-enhanced and well-circumscribed 12×10×8 cm mass involved in the mediastinum and right supraclavicular fossa with multiple adjacent lymphadenopathy. The lesion extrinsically compressed the trachea, esophagus, right carotid and subclavian artery, and encased the brachial plexus. **(D)** Lower power view of MPNST shows nodular growth pattern and conspicious necrosis (H&E stain, x100). **(E)** The tumor cells show pleomorphism and twisted and irregular-shaped nuclei in high power field (H&E stain, x400). **(F)** Immunohistochemical stain for S-100 stain shows positive reaction on tumor lesion (x100).

Transthoracic needle biopsy was done. In lower power view, it showed nodular growth pattern and conspicious necrosis in the tumor. Densely cellular fascicles alternated with hypocellular zones where the parallel orientation of the cell was lacking (Figure 1. (D)). In the high power view, the tumor cells had markedly irregular contours and high mitotic activity. The nuclei were wavy, buckled, irregular-shaped or occasionally comma-shaped, and the cytoplasm was lightly stained and usually indistinct (Figure 1. (E)). Immunohistochemical stain for s-100 protein showed positive reaction on the cytoplasm of tumor cells (Figure 1.(F)). But, actin and p53 stain were negative.

DISCUSSION

Von Recklinghausen's disease (neurofibromatosis type I) is an autosomal dominant disease with an incidence of about 1 in 3,000 live births. Both sexes and all races appear to be affected equally[1]. The clinical features of this disorder invariably include cafe-au-lait spots, multiple neurofibromas, lisch nodules or pigmented iris hamartomas[1, 3, 4]. The schwann cell most likely is the cell of origin, but some may originate from perineurium or endoneurium[5]. In our case, the patient showed multiple cafe-au-lait spots and pigmented nodular skin lesions over the chest wall and both arms.

MPNST is a kind of malignant tranformation of type I neurofibromatosis, with an incidence recently reported at about 5-10%[6]. Malignant transformation usually occurs in a neurofibroma, which has been present for an extended period of time. It is heralded by rapid growth of the tumor. The most common anatomic location for malignant schwanomas is the lower and upper extremities, trunk, head and neck, and miscellaneous sites in descending order[7]. But intrathoracic manifestations of MPNST in patients with neurofibromatosis are very rare [8, 9].

This presented case showed an increased homogeneous mass density at the right upper lung field, with well-demarcated margin and elevation of right hemidiaphragm on chest radiographies. Radiologic study revealed a homogeneous, well-enhanced and well-circumscribed mass measuring 12×10×8 cm. In our case, the mass was located in the thoracic cavity, extending toward the right supraclavicular fossa and associated with multiple adjacent lymphadenopathy. This lesion compressed the trachea, esophagus, right carotid and subclavian artery, and encased the brachial plexus that caused neurologic manifestation, such as radiating pain with mild numbness, motor weakness of right upper extremity and ptosis. In our case, the histologic examinations of the nodular skin lesion showed expansion of endoneurium by myxoid ground substance, such as neurofibroma. The histologic examinations of intrathoracic mass showed consistent with malignant peripheral nerve sheath tumor which was stained with s-100 protein.

Surgical management of intrathoracic neurogenic tumors, even if clinically benign, is advocated[10]. Our case was not accessible to operate due to the extension of the tumor to adjacent mediastinal structure, so we started radiofrequency ablation and doxorubicin-based chemotherapy.

We report a case of intrathoracic MPNST in a 40-year-old man with neurofibromatosis. Review of the literature showed that intrathoracic MPNST is very rare but shows highly aggressive manifestation of malignancy and poor prognosis. So, intrathoracic MPNST should be considered in the differential diagnosis of intrathoracic mass in young men with von Reckling-hausen's disease.

REFERENCES

1. Ducatman BS, Scheithauer BW, Piepgras DG: *Malignant peripheral nerve sheath tumors. A clinicopathologic study. Cancer 57:2006-2021, 1986*
2. Enzinger FM, Weiss SW. *Malignant tumor of peripheral nerve. In: Enzinger FM. Weise SW: Soft tissue tumors. St Louis, C.V. Mosby, 781-815, 1988*
3. Brasfield RD, Das Gupta, Tapas K: *Von Recklinghausen's disease: clinicopathological study. Ann Surg 175:86-104, 1972*
4. Knight WA, Murphy WK, Gottlieb JA: *Neurofibromatosis associated with malignant neurofibroma. Arch Dermatol 107:747-750, 1973*
5. Herra GA, de Moraes PH: *Neurogenic sarcoma in patients with neurofibromatosis (von Recklinghausen's disease), Virch Arch 403:361-368, 1984*
6. Ducatman BS, Scheithauer BW, Piepgras DG, Reiman HM, Ilstrup DM: *Malignant peripheral nerve sheath tumors: a clinicopathologic study of 120 cases. Cancer 46:605-610, 1980*
7. D'Agostoni AM, Soule EH, Miller RM: *Sarcoma of peripheral nerves and somatic soft tissues associated with multiple neurofibromatosis (von Recklinghausen's disease).*

Cancer 16:1015-1019, 1963

8. Inoue M, Mitsudomi T, Osaki T, Oyama T: *Malignant transformation of an intrathoracic neurofibroma in von Recklinhausen's disease. Scand Cardiovasc J 32(3): 173-175, 1998*
9. Suzuki H, Yamaguchi Y, Kimura H, Baba M, Hiroshima K: *Malignant mediastinal schwannama associated with von Recklinghausen's disease: a resected case. Nippon Kyobu Geka Gakkai Zasshi 44(6):864-868, 1996*
10. Ramanathan RC, Thomas JM: *Malignant peripheral nerve sheath tumors associated with von Recklinghausen's neurofibromatosis. Eur J Surg Oncol 25(2):190-193, 1999*