Malignant Transformation of Intrathoracic Ancient Neurilemmoma in a Patient without Von Recklinghausen's Disease

Malignant transformation of a neurilemmoma is an exceedingly rare event. We describe a case of intrathoracic ancient neurilemmoma undergoing a malignant change in a 39-yr-old man. The patient presented with right flank and chest pain for several months. Plain radiography and CT scan of the chest showed a soft tissue mass lesion at the extrapleural space with erosion of surrounding ribs at the right basal lung area. The excised mass was encapsulated and measured 4.5×3.5×2.3 cm. The cut surface showed grayish-white and glistening with a focal cystic change and hemorrhage. Necrosis was not seen. Histologically, the tumor showed the features of classic neurilemmoma composed of the Antoni type A and B areas with perivascular hyalinization. In addition, obviously histologically malignant foci manifested by presence of markedly increased cellularity with fascicular arrangement, active mitotic activity, hyperchromasia, and gradual loss of original neurilemmomatous feature were noted.

Key Words : *Neurilemmoma; Cell Transformation, Neoplastic; Neoplastic Processes*

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INTRODUCTION

Malignant transformation of a neurilemmoma is an exceedingly rare event. Review of the available literature revealed only a few other similar cases documenting malignant transformation of a solitary benign neurilemmoma in a patient without von Recklinghausen's disease (1-11). We report a case of intrathoracic ancient neurilemmoma undergoing a malignant change in a 39-yr-old man.

CASE REPORT

A 39-yr-old man presented with right flank and chest pain for several months. Plain radiography and CT scan of the chest showed a heterogeneous enhancing soft tissue mass at the extrapleural space with erosion of the surrounding ribs at the right basal lung area (Fig. 1). Laboratory findings were normal. The patient had no history of specific disease or irradiation. There were no stigmata of von Recklinghausen's disease. Operative findings showed extrapleural mass on the posterior aspect of the 8th and 9th ribs of the right thoracic cavity. The tumor was considered to arise from intercostal nerve but attached nerve was not found. Excisional biopsy was performed. The excised mass was encapsulated and measured 4.5×3.5×2.3 cm. The cut surface was grayish-white and glistening with a focal cystic change and hemorrhage. Necrosis was not seen (Fig. 2).

Histologically, the tumor revealed predominant Antoni A areas and focal B areas (Fig. 3). These two components blend imperceptibly. The Antoni A areas were composed of compact spindle cells that had twisted nuclei and indistinct cytoplasmic borders. They were arranged in short bundles. Nuclear palisading, whorling of the cells, and Verocay bodies were present. The hypocellular Antoni B areas showed a loosely textured matrix, microcystic change, delicate collagen fibers, and large irregularly spaced vessels with prominent perivascular hyalinization. A degenerative change with stromal hemosiderin deposition and enlarged pleomorphic nuclei were noted. In the cellular Antoni A areas, there were diffuse, ill defined, obviously malignant foci showing a markedly increased cellularity, long fascicular arrangement of hyperchromatic spindle cells, frequent mitotic figures, and loss of the original neurilemmomatous feature. The spindle cells were uniform in size and shape but became more plump. There were 5 mitotic figures per 1 high-power field at the most active hypercellular area (Fig. 4). Immunohistochemical finding for S-100 protein demonstrated diffuse strong positivity in benign neurilemmomatous areas (Fig. 5A) and very weak positivity in malignant foci (Fig. 6A). Immunohistochemical finding for MIB1 revealed a very low MIB1 index (less than 1%) in benign neurilemmomatous areas (Fig. 5B) and a very high MIB1 index (greater than 60%) in malignant foci (Fig. 6B). The malignant component comprised about two thirds of the tumor but remained encapsulated.

Fig. 1. CT scan of the chest shows a soft tissue mass lesion at the extrapleural space with erosion of the surrounding ribs at the right basal lung area.
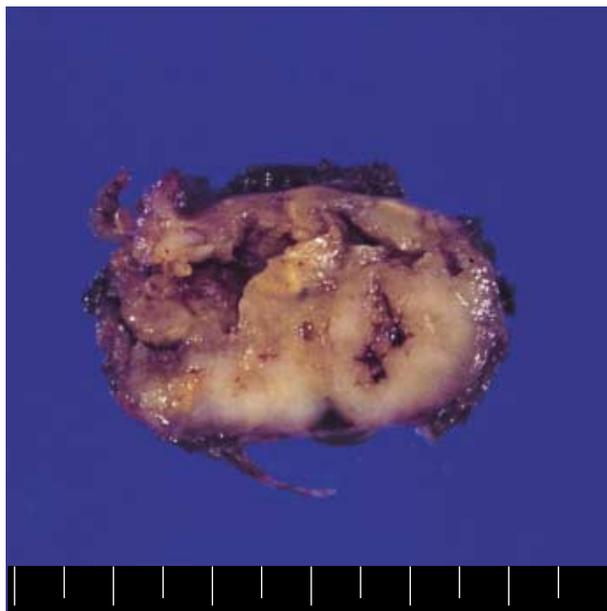
Fig. 2. The excised mass was encapsulated and measured 4.5 ×3.5×2.3 cm. The cut surface shows grayish-white and is glistening with a focal cystic change and hemorrhage. Necrosis is not seen.
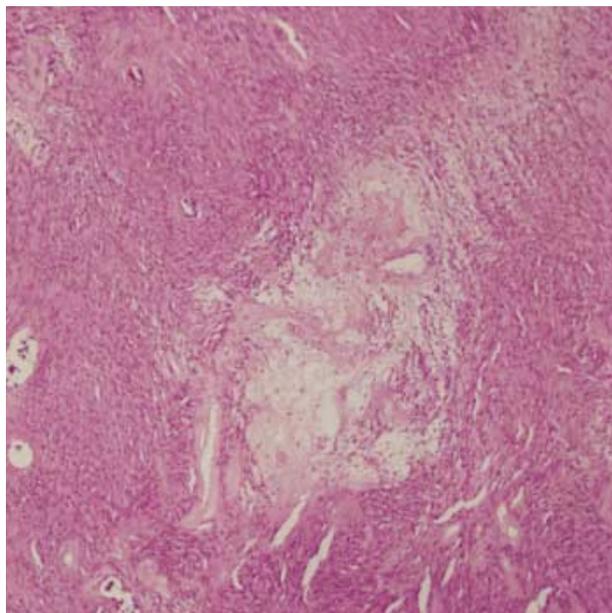
Fig. 3. The tumor shows the features of classic neurilemmoma composed of the Antoni type A and B areas with perivascular hyalinization (H&E, ×40).
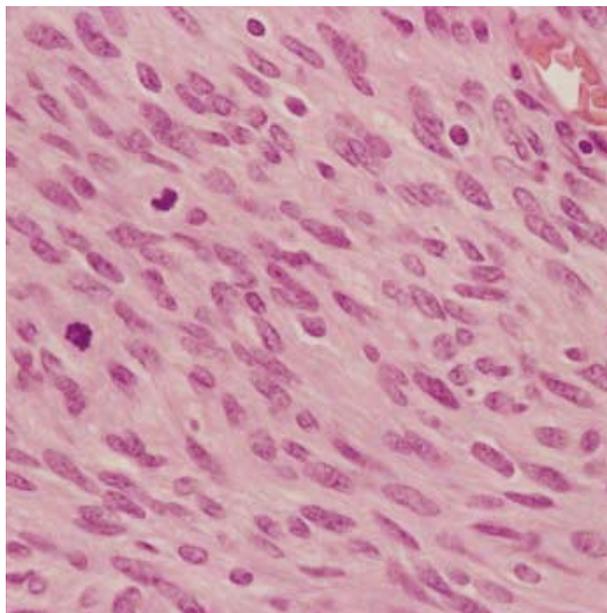
Fig. 4. The tumor cells shows spindle shaped nuclei, hyperchromasia, high mitotic activity, and loss of the original neurilemmomatous feature (H&E, ×400).

DISCUSSION

Neurilemmomas are encapsulated benign neoplasms of nerve sheath origin with a well defined histologic feature (12). Neurilemmomas comprise the most frequent lesion among various neurogenic tumors encountered within the thorax or mediastinum (13). Almost all of the neurilemmomas of

this anatomic location originate from the posterior mediastinum or paravertebral chest wall, and present as a slow growing, well-defined mass projecting into the thoracic cavity. Pain and neurologic symptoms are uncommon unless the tumor becomes large. Patients with a malignant change in neurilemmomas typically presented with pain or rapid enlargement of a pre-existing lesion (9). In our case the patient presented
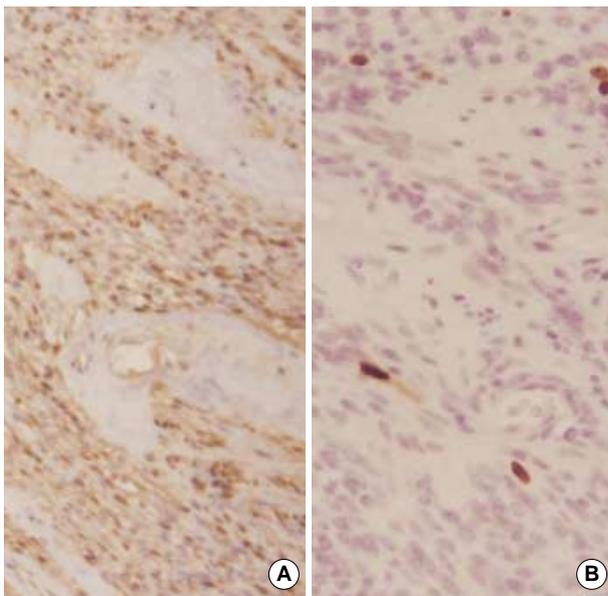
Fig. 5. Immunohistochemical stain for S-100 protein (A) and MIB1 (B) in benign areas reveal intense nuclear and cytoplasmic immunoreactivity for S-100 protein and a very low MIB1 index (×200).

Fig. 6. Immunohistochemical stain for S-100 protein (A) and MIB1 (B) in malignant areas reveal very weak immunoreactivity for S-100 protein and a very high MIB1 index (×200).

with right flank and chest pain for several months.

The characteristic pathologic features include encapsulation and distinct histologic features composed of Antoni type A and B tissues. Malignant peripheral nerve sheath tumors (MPNSTs) have a varied origin. A majority originate in patients with neurofibromatosis (NF)-1, presumably from an antecedent neurofibroma, often plexiform in type (14, 15). The remaining cases are tumors arising from neurofibromas in patients without stigmata of NF-1, de novo from a peripheral nerve (14, 15), from a peripheral nerve exposed to radiation (16, 17), from Schwann cells in a ganglioneuroma or ganglioneuroblastoma (18) and, most infrequently, from an antecedent benign neurilemmoma.

The present case had the following features of Woodruff et al. (8) criteria for the diagnosis of MPNST arising in a neurilemmoma: (a) presence of benign neurilemmoma; (b) failure to identify a primary tumor that might have metastasized to the neurilemmoma; and (c) presence within the substance of the neurilemmoma of a histologically malignant cell population. Regardless of their origin, the vast majority of MPNSTs are characterized histologically by densely packed, interlacing fascicles of hyperchromatic, mitotically active spindle cells. The exception to this is the MPNST arising from a neurilemmoma. In most cases of neurilemmoma with malignant transformation, the malignant component revealed predominantly or purely epithelioid differentiation (8, 9). In the minor cases, the malignant component showed small cells with neuroepithelial differentiation (8) and angiosarcoma (9, 19). Woodruff et al. (8) reviewed nine cases of MPNSTs arising in benign neurilemmomas and described clinical and pathologic differences between MPNSTs arising in neurilemmomas and conventional MPNSTs. MPNSTs arising in benign neurilemmomas show slight male predilection, occurrence in an older age group (a mean age of 56 yr, 20 yr older than the mean age for patients with conventional MPNSTs), a long history of an antecedent mass, and no association with NF type 1 or 2. Histologically, the malignant component was composed of commonly pure epithelioid (seven of nine cases) and small cells with neuroepithelial features (two of nine cases). McMenamin et al. (9) reported the spectrum of the malignant change in neurilemmoma. They reviewed 17 cases of neurilemmomas which undergoing a malignant change. They identified four cases of pure epithelioid MPNST, ten cases with a epithelioid malignant change, and four cases of angiosarcoma. The incidence and degree of epithelioid differentiation varied according to the origin of MPNST. A predominantly epithelioid differentiation occurs more frequently in MPNST from patients without NF-1 (8, 9, 20), while the epithelioid differentiation is uncommon in other forms of MPNST (20, 21). Thus, the neurilemmoma with malignant transformation is unique among MPNST for its high incidence of usually nonmucinous purely epithelioid differentiation (8). In contrast to the Woodruff et al. and McMenamin et al. reports, the present case was a 39-yr-old patient and the malignant component revealed conventional spindle cell cytomorphology. Epithelioid malignant change, epithelioid MPNST, or small cell neuroepithelial-like cytomorphology was not identified in our case. None of the cases of Woodruff et al. (8) and McMenamin et al. (9) showed the malignant component in an interlacing, fasciculated spindle cell tumor. Review of the available literature revealed only a few cases similar to our case (1-11).

Neurilemmoma with a malignant change showed several

distinctions from the conventional MPNST including an absence of geographic necrosis (15), heterologous elements such as glands (22), osteo/chondrosarcoma and rhabdomyosarcoma (23, 24), and the rarity of intercellular mucin in the epithelioid cell areas (8). No coincident heterologous elements were present in our case. The differential diagnosis of this lesion includes spindle cell sarcoma and cellular schwannoma. Presence of residual benign neurilemmoma tissues and immunohistochemistry can help to distinguish MPNST from spindle cell sarcoma and cellular schwannoma. The cellular schwannoma has similar clinical characteristics but has a higher recurrence rate (25). It consists mostly of hypercellular Antoni A tissue, is devoid of Verocay bodies, and 28% of the cases have been mistaken for a malignant tumor (25, 26). But a cellular schwannoma shows complete encapsulation, focal presence of subcapsular loose areas reminiscent of the Antoni B tissue, hyalinized thick-walled blood vessels, perivascular lymphoid infiltrates, collection of lipid-laden histiocytes, and diffuse strong expression of S-100 protein (8).

The prognosis for patients with neurilemmomas undergoing a malignant change is poor. The prognosis for epithelioid MPNST arising in a neurilemmoma has been poor, with less than 20% of patients surviving 5 yr (8). In our case the patient was well with no evidence of disease for 11 months.

In summary, we described a case of ancient neurilemmoma undergoing malignant trabsformation. The malignant foci demonstrated markedly increased cellularity with fascicular arrangement of hyperchromatic spindle cells with high mitotic activity and loss of the original neurilemmomatous feature.

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