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MALIGNANT FIBROUS HISTIOCYTOMA OF THE LUNG: A Case Report and Immunohistochemical Examination of the Case

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SUMMARY : Malignant fibrous histiocytoma (MFH) arising in the lung of an autopsy case, a 52-year-old man, is reported with immunohistochemical findings. In most areas, a storiform patterns with fibroblast-like cells and histiocyte-like cells were noted. Extensive carcinoma invasion and multiple metastases were found in many organs such as mediastinum, heart, aorta, left pleural cavity, abdominal wall, omentum, peritomeum, liver, intestine, adrenal and kidneys. The tumor was mainly composed of spindle cells and had storiform and herring-bone patterns. immunohistochemically, these tumor cells were demonstrated to possess vimentin, alpha-1-antitrypsin, alpha-1-antichymotrypsin and lysozyme.

INTRODUCTION

Since malignant fibrous histiocytoma (MFH) was described in the 1960s[17, 19)], it has been recognized as the most common soft tissue sarcoma of older adults[23)]. The usual primary sites of MFH are the deep musculature of extremities, retroperitoneum, and trunk. Although over 75 % of deep-seated soft tissue MFH metastasizes to the lung, primary MFH of the lung is rare. The common primary pulmonary sarcomas have been reported to be leiomyosarcoma and fibrosarcoma.

MFH is characterized by both histiocyte-like and fibroblast-like cells usually arranged in a storiform pattern[2, 3, 23)]. By routine light microscopic examination, however, MFH may be difficult to be distinguished from other sarcomas[9)]. Therefore, immunohistochemical and electron microscopic examinations may be required for diagnosis.

We herein present an autopsy case of primary MFH of the lung, confused with fibrosarcoma and diagnosed by immunohistochemical study.

CASE REPORT

A 52-year-old man was admitted to our hospital in July, 1989, because of a chronic cough of two years' duration. Two weeks previously, the cough became productive of small amount of sputum which was occasionally blood-streaked. A chest X-ray film and chest CT scan showed an almost homogeneous density measuring 10 cm in diameter and reaching the aorta in the left upper lung. Left pleural effusion was also noted. Bronchoscopy demonstrated a finger-like projection with pulsation within the lumen of the left upper bronchus. On August 4, a bone scintigraphy revealed a metastasis to the left 8th rib. He underwent chemotherapies of cisplatin and vindesine from August 21, since malignant tumor of the lung with metastases

was strongly suspected. In September, he expectorated sputum with tumor fragments three times. One of the experctorated specimens showed the appearance of poorly-differentiated squamous cell carcinoma which had eosin-stained cytoplasm, many mitoses, and a few PAS-positive tumor cells with vacuoles. The other specimens revealed the histological appearance of fibrosarcoma which contained spindle-cells, interlacing fibers, and a few mitoses. On November 7, lymphokine activated killer-cell (LAK) therapy[7] was performed. On November 24 and December 22, cytotoxic T lymphocyte (CTL) therapy[7] was also done. The tumor, however, showed no response to these treatments. Multiple metastases from the pulmonary tumor were noted in the back, liver, stomach, ribs, sternum, and iliac bone. Pleural effusion and ascites appeared and gradually increased. Hemorrhagic ascites was also demonstrated by abdominal puncture, suggesting rupture of metastatic gastric tumor or perforation of the digestive ulcer, and his condition deteriorated due to respiratory insufficiency. He died of hemorrhagic shock on March 1, 1990. Postmortem examination was performed about one and a half hours after death.

RESULTS

Gross findings : The left lung weighed 900 gm. A solitary tumor of necrotic mass, man's fist size, was found in the upper lobe involving the left main bronchus, and the tumor was poorly delineated and had hemorrhahic central necrosis (**Fig. 1**). The tumor was seen to invade posterior mediastinum, aortic wall, and left atrium. Multiple metastases were found in the left pleural cavity, abdominal wall, omentum, peritoneum, liver, right adrenal, both kidneys and intestine resulting in conglomeration of entire intestinal loop. About 5 mm diameter hole with clear margin was seen at the greater curvature of the stomach.

Microscopic finding: The tumor of the lung consisted of fibroblast-like and histiocyte-like cells. The fibroblast-like cells were spindle-shaped and contained a single elongated nucleus surrounded by a thin rim of cytoplasm. The nuclear chromatin pattern varied from vesicular to evenly dispersed. A single, small nucleolus was usually present. Most areas of the lesion showed a distinct storiform pattern (**Fig. 2**) suggesting MFH, but few form cells or giant cells were noted. However, herring-bone-like

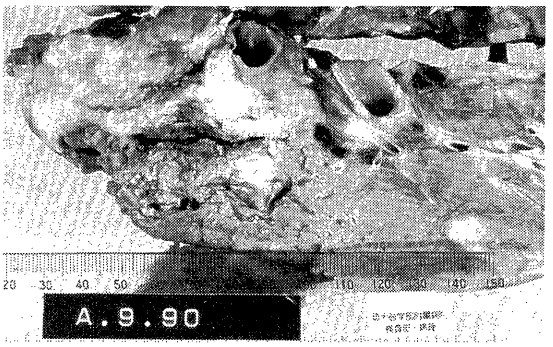


Fig. 1. Gross appearance of the primary tumor in the upper lobe of the left lung with central necrosis.

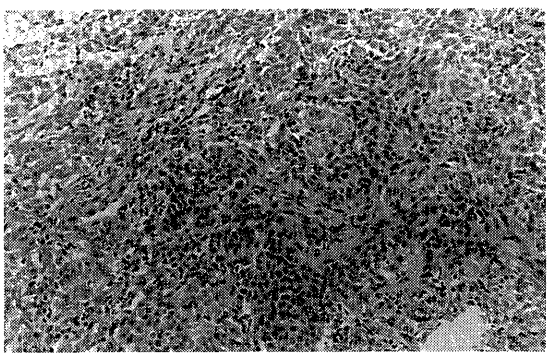


Fig. 2. Storiform pattern with a predominance of spindle-shaped fibroblast-like cells is noted. (Hematoxylin Eosin ×150)

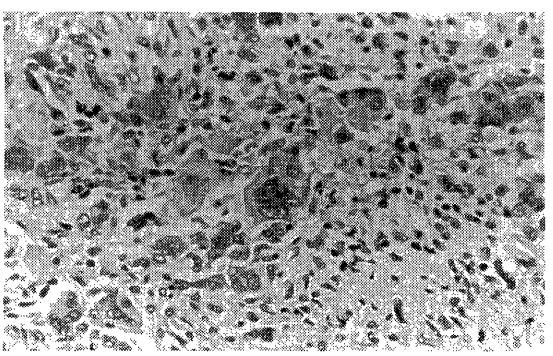
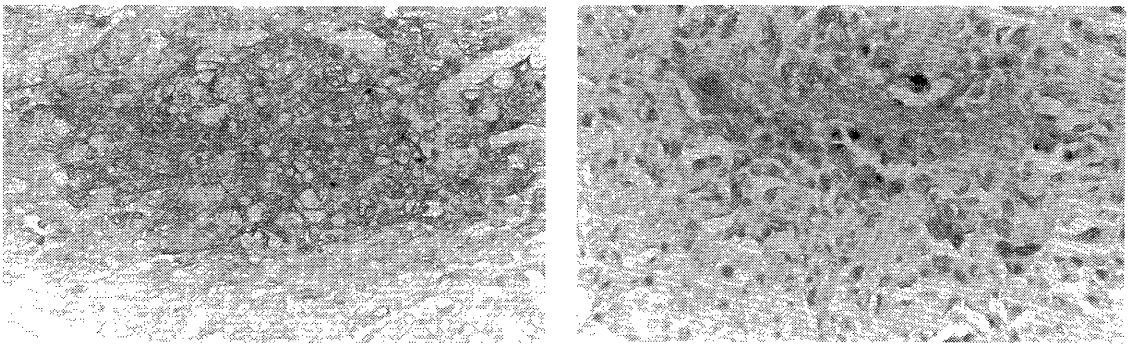


Fig. 3. High-power view of several pleomorphic tumor giant cells (Hematoxylin Eosin ×300)



(A) (B)

Fig. 4. Alpha-1-antichymotrypsin (A) and vimentin (B) are positively demonstrated in tumor cells (PAP stain ×300)

areas suggesting fibrosarcoma were occasionally present. The histiocyte-like cells were somewhat irregular outline and had abundant, eosinophilic cytoplasm than the fibroblast-like cells. Their nuclei were usually round to oval or vesicular, and possessed a single prominent nucleolus. The tumor cells exhibited moderate nuclear pleomorphism and hyperchromasia with up to 15 mitoses per 10 high-power field (HPF). The histological features of the metastatic lesion were almost identical to those of the primary lesion. However, the metastatic lesion contained occasional giant cells and showed more variegated histological appearance than the primary lesion. No malignant cells wrer noted in the stomach with perforated ulcerated lesion.

Immunohistochemical Findings: Formalin-fixed, paraffin-embedded specimens were immuno-histochemically examined using peroxidase-anti-peroxidase (PAP) techniques, as previously described[21]. Almost all the fibroblast-like, histiocyte-like, and giant cells showed diffuse positive cytoplasmic staining for vimentin, alpha-1-antitrypsin, alpha-1-antichymotrypsin, and lysozyme (**Fig. 4A and B**). There was no immunoreactivity for antibodies for keratin, desmin, S-100 protein, and neuron-specific antigen, and anti-smooth muscle antibody.

DISCUSSION

Primary pulmonary MFH is much rarer, and only fewer than 30 cases have been reported. It ranks third in incidence of pulmonary sarcomas, following leiomyosarcoma and fibrosarcoma[6, 15]. In Japan, it comes third, following leiomyosarcoma and rhabdomyosarcoma[14].

Patients with MFH of the lung must be carefully evaluated to rule out a metastatic origin, because MFH is primarily a tumor of the soft tissues of the extremities[3, 23] and metastases frequently appear in the lung[8]. However, patients have rarely presented with pulmonary metastases before the primary tumor was identified[3, 23]. In our case, although wide spread metastases were seen, the primary tumor was in the left lung, judging from the clinical course in which the tumor was first seen in the left lung.

It is speculated that few accurately diagnosed cases of MFHs have been reported so far in the literature, because of their low incidence above described and of being classified as a pleomorphic variant of fibrosarcoma, leiomyosarcoma, liposarcama, or rhabdomyosarcoma prior to the recognition of MFH as a distinct neoplasm[8]. There also may be tendency to interpret pleomorphic lung sarcomas as poorly differentiated carcinoma[6].

The lesions in our case showed storiform pattern with fibroblast-like and histiocyte-like cells. Such morphologic pattern is often present in most cases of MFH, but not specific for MFH[2]. MFH presents an extremely wide range in its cellular composition and pattern, not only from tumor to tumor, but also frequently in different portions of the same tumor[16]. In fact, in our case, herring-born-like pattern was seen

in the pulmonary lesion. The predominantly fibroblastic types of MFH may similar to fibrosarcoma, maligant schwannoma, synovial sarcoma, or leiomyosarcoma[16]. To support the light microscopic diagnosis of MFH, electron microscopic and immunohistochemical examination is required[9].

Antibodies to the various proteins are useful in distinguishing between epithelial and mesenchymal tumors. This is based on the relatively stable cell-type-specific expression of intermediate filament proteins in malignant tumor cells as follows ; keratins in epithelial, vimentin in mesenchymal, desmin and muscle-specific antigen in muscular, neuron-specific antigen in neural, and S-100 protein in neurosarcoma (malignant schwannoma), liposarcoma, and malignant melanoma[4, 18]. Numerous immunohistochemical studies of MFH have been reported that the cells of MFH contain only vimentin[5, 18], both desmin and vimentin[11], lysozyme, alpha-1-antitrypsin, and alpha-1-antichymotrypsin[1, 10], or subunit A of factor XIII[16].

Thus, the immunohistochemistry of intermediate filaments does not offer any universal defining pattern for MFH[9, 12]. However, Roholl *et al*[20] consider that the presence of alpha-1-antichymotrypsin or one of the other markers favors the diagnosis of MFH, and Miettinen and Soini[12] stated that the immunohistochemical study of MFH remains a diagnosis by exclusion rather than representing a specifically recognizable entity. The tumor cells in our case reacted to antibodies for vimentin, lysozyme, alpha-1-antitrypsin, and alpha-1-antichymotrypsin. However, these tumor cells showed no definite reaction to antibodies for keratin, desmin, neuronspecific antigen, and S-100 protein, and smoothmuscle antibody. Therefore, we ruled out the following diagnosis ; carcinoma or leiomyosarcoma, rhabdomyosarcoma, malignant schwanoma, malignant melanoma, and liposarcoma. Fibrosarcoma was also ruled out, because it has no reactivity for alpha-1-antichymotrypsin[9, 20].

The reported prognosis in patients with primary MFH of the lung is poor[8]. The predictive features of a worse prognosis are 1) advanced stage at diagnosis, 2) incomplete excision of the sarcoma (biopsy only), 3) tumor invasion of the mediastinum and chest wall seen at initial diagnosis, 4) recurrence or metastasis[22, 24]. In the present case, the initial examination revealed that the tumor invaded into the left bronchi and attached to the aorta of the tumor, and the later examination showed multiple metastases. Yousem *et al*[24] reported that half of the patients with MFH in the lung had metastatic patterns which reflect the propensity for vascular invasion of MFH in that distant disease was found in the brain, liver, and kidneys. Thus, the prognosis of the lung is poor, but surgical resection offers the chance of a cure[8, 22]. The role of either chemotherapy or radiotherapy as primary or adjuvant treatment in MFH is presently unclear[22]. Lymphokine activated killer-cell (LAK) therapy and cytotoxic T lymphocyte (CTL) therapy are immunotherapies expected as new treatments against malignant tumors. Kitsukawa[7] reported that CTL therapy produced effects on the life prolongtion of the patients with carcinomas in the terminal stage. However, CTL therapy produced no effect on the MFH in the present case. Clinical significance of various types of treatments must await the more studies of their use against pleomorphic sarcomas and their metastases.

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