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Case Study

Histiocytic Sarcoma Originating in the Lung in a 16-Year-Old Male

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We report a 16-year-old male with histiocytic sarcoma (HS) originating in the lung. Partial resection of the lung was performed for a 3-cm mass with a clear boundary detected in the right inferior pulmonary lobe on a health checkup. Histologically, the tumor infiltrated into the surrounding tissue, and was comprised of spindle cells, mainly, and foam cells accompanied by mild nuclear atypia. The tumor cells were immunohistochemically positive for CD68 and CD163, indicating histiocytic lineage and the MIB-1-positive rate was low. Spindle cell morphology of HS is quite rare and only 3 cases of pulmonary HS have previously been reported. 〔*J Clin Exp Hematop 55(1) : 45-49, 2015*〕

Keywords: histiocytic sarcoma, lung, spindle cells, foamy cells

INTRODUCTION

Histiocytic sarcoma (HS) is a malignant hematopoietic tumor consisting of cells similar to mature histiocytes.[1-4] It is extremely rare and the age of onset widely ranges from 6 months to 89 years, with no gender difference; the incidence is high in adults, showing a large peak at 50-69 years, but also a small peak at 0-29 years.[4] It is considered to be a highly malignant tumor with a poor prognosis comprised of large tumor cells showing histiocyte markers. HS develops in a multiple or solitary pattern in lymph nodes, skin, and other extra-lymph node organs, and some cases of HS subsequently or concurrently occur with non-Hodgkin lymphoma.[1-4] Morphologically, the tumor cells are large and contain a round or oval nucleus, and multinucleated cells are frequently noted. Immunohistochemically, the tumor cells are positive for one or more histiocyte markers and negative for accessory/dendritic cell markers, and the exclusion of acute monocytic leukemia, malignant lymphomas with T/B/NK cells, and Hodgkin lymphoma is necessary. Only 3 cases of HS originating in the lung have previously been reported.[2,5,6] We encountered a young patient with HS of the lung containing spindle cells, mainly, and foam cells.

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CASE REPORT

The patient was a 16-year-old male who exhibited an abnormal shadow detected on a health checkup. He had no particular past or familial medical history. An abnormal shadow was noted on chest X-ray radiography in a health checkup upon entering senior high school, and he visited a physician. A 3-cm mass with a clear boundary was present in S6 of the right inferior pulmonary lobe on chest computed tomography and a magnetic resonance image, and it was suspected to be a benign lesion because no infiltrative change was noted (Fig. 1). He visited our respiratory surgery department for a second opinion. On trans-bronchial lung biopsy, outgrowth of spindle cells in a bundle pattern was noted. The diagnosis on biopsy was spindle cell tumor, and it was difficult to evaluate whether it was benign or malignant. Segmental excision of S6 of the right inferior pulmonary lobe was performed, and a portion of the mass was subjected to intraoperative rapid examination. The findings were the same as those in the biopsy specimen. The lesion was diagnosed as spindle cell tumor, and the possibility of epithelial lesion was low. An extensive infiltrative shadow was noted in the residual right inferior pulmonary lobe on postoperative chest computed tomography, and postoperative hemorrhage or atelectasis was suspected. Since it took time to make a pathological diagnosis, and malignancy could not be ruled out at the time of the diagnosis, resection of the residual right inferior lobe was performed one week after surgery. No residual tumor was noted in the excised specimen. The course was favor-

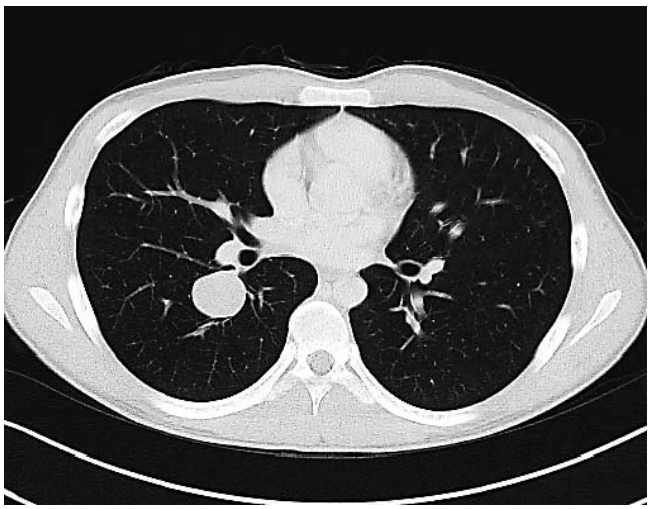

Fig. 1. Preoperative chest computed tomography image shows a 3-cm mass with a clear boundary in S6 of the right inferior pulmonary lobe. No infiltrative change was noted.

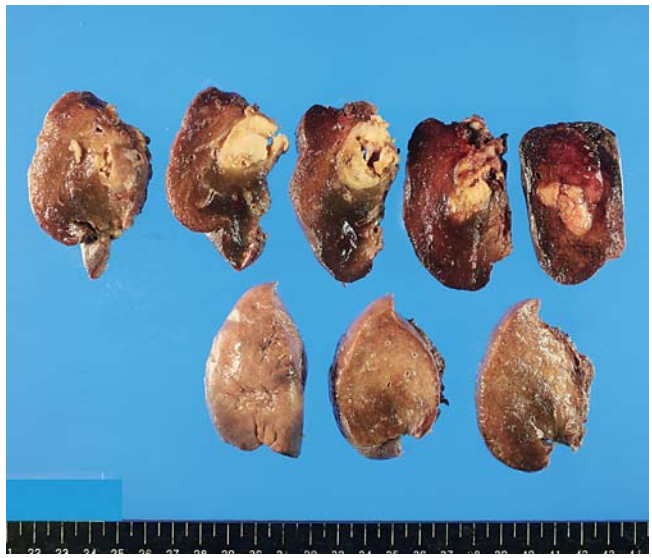

Fig. 2. The cut surface of respective tissue. A 20 × 20 × 32-mm yellowish white mass present near the bronchus.

able, and the patient was discharged. He is being followed by periodic chest X-ray radiography, but no findings suggesting recurrence have been observed within 2 years.

PATHOLOGICAL FINDINGS

The excised specimen was a 20 × 20 × 32-mm yellowish white mass present near the bronchus (Fig. 2). Under a magnifying glass, a solid mass with a relatively clear boundary was noted in the H&E preparation. Necrosis was found in part of it. The tumor was comprised of proliferating spindle cells, and infiltrated into the surrounding bronchial and vascular walls. The tumor was composed of mainly spindle cells. Some tumor cells contained relatively abundant cytoplasm, while others were thin and spindle-shaped, containing scarce cytoplasm. Clusters of cells containing foamy cytoplasm, foam cells, were occasionally noted. Tumor cells appearing to contain 2 nuclei were also mixed in, although the number of such cells was small, and nuclear division was noted in a few cells (Fig. 3). Phagocytosis of the tumor cells was not found.

On immunohistochemistry, the spindle and foam cells showed the same stainability, except for CD68 (Table 1). In terms of histiocytic markers, the tumor cells were positive for CD68 and CD163, but negative for lysozyme. CD68 reacted with most of the spindle cells and some of the foam cells. CD4 and CD45 reacted with some of the tumor cells. They were negative for lymphocytic markers (CD3, CD20), epithelial cell markers (AE1/3, CAM5.2, EMA, TTF-1), mesenchymal cell markers (smooth muscle actin, desmin, S-100 protein, HMB45, Melan A), follicular dendritic cell markers (CD21, CD23), and bone marrow cell markers (CD15, CD34, myeloperoxidase). The MIB-1 index was low (about 10%) (Fig. 4 and Table 1). On the basis of the infiltrative tumor growth and immunohistochemistry findings, the mass was diagnosed as HS.

DISCUSSION

Although tumors in the lung showing spindle cell outgrowth that need to be differentiated include epithelial tumors, mesenchymal tumors (fibrous, muscular, and nerve tissue tumors), hematopoietic tumors, and inflammatory pseudo-tumors,[7-10] the current patient could be roughly diagnosed with a hematopoietic tumor based on CD45 positivity by first immunohistochemistry. Among hematopoietic tumors, not only malignant lymphoma, but also tumors derived from histiocytes, Langerhans cells, and dendritic cells were candidates. Second immunohistochemistry with many markers demonstrated that the tumor cells were positive for two histiocyte markers (CD68 and CD163) and negative for B- and T-cell, Langerhans cell, follicular dendritic cell, and bone marrow cell markers, showing that it was a histiocytic tumor. Positive staining of CD163 and negative staining of S-100 protein were important results for the differential diagnosis; they could rule out tumor of Langerhans cells, such as Langerhans cell histiocytosis. Malignant fibrous histiocytoma was also ruled out by the absence of tumor cell polymorphism with multi-nucleated cells.

Lysozyme was negative in this case. Reactive macrophages in the necrotic area were lysozyme-positive; on the other hand, both the spindle cells and the foam cells were lysozyme-negative. Although CD68 and CD163 as well as

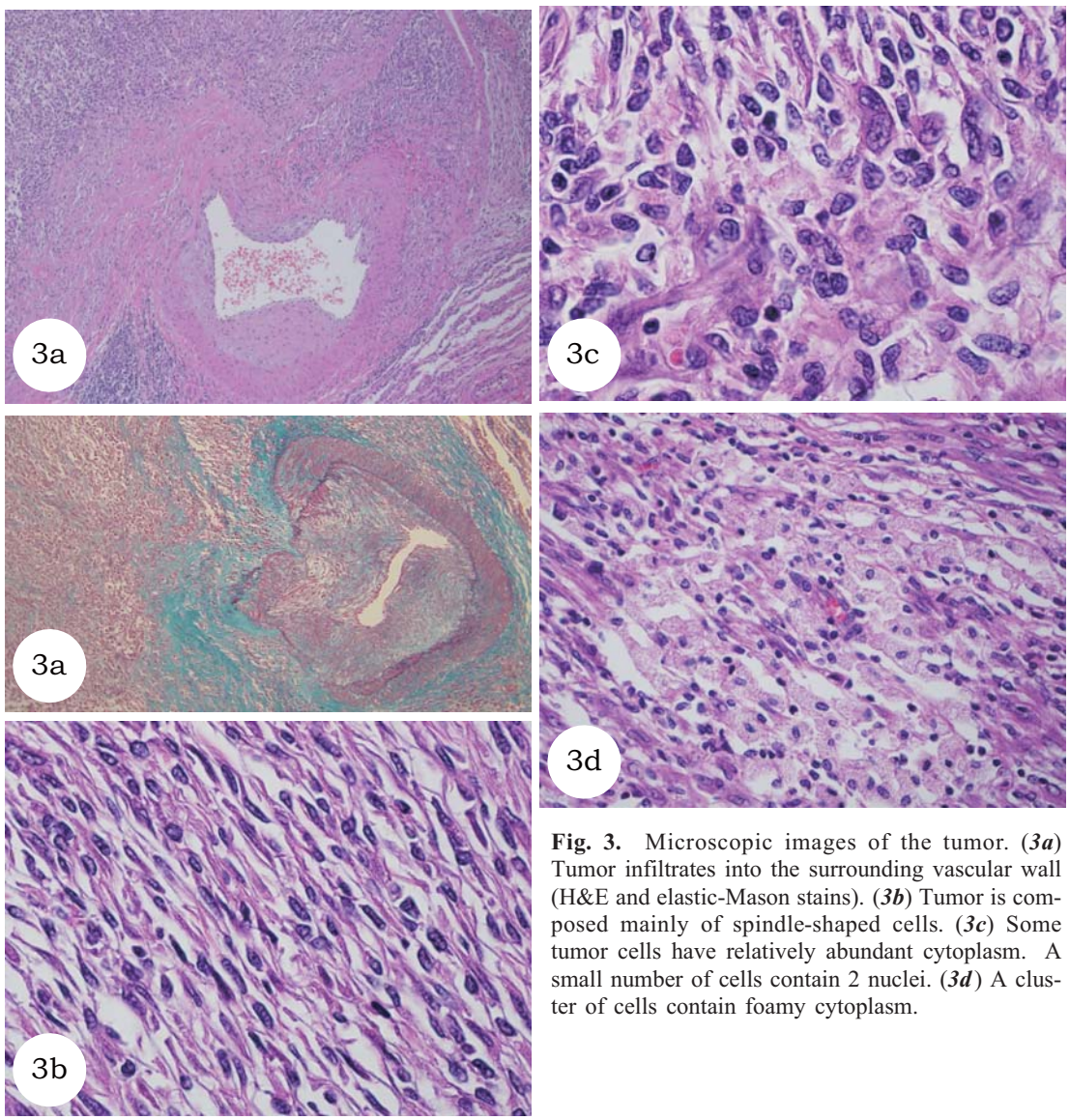

Fig. 3. Microscopic images of the tumor. (***3a***) Tumor infiltrates into the surrounding vascular wall (H&E and elastic-Mason stains). (***3b***) Tumor is composed mainly of spindle-shaped cells. (***3c***) Some tumor cells have relatively abundant cytoplasm. A small number of cells contain 2 nuclei. (***3d***) A cluster of cells contain foamy cytoplasm.

lysozyme were positive in most of the reported HS cases, a lysozyme-negative HS case was also reported.[11] That case had two populations of $CD68^{+}CD163^{-}$lysozyme^{+} oval cells in cervical lymph node and $CD68^{+}CD163^{+}$lysozyme^{-} spindle cells in hilar lymph node. The tumor cells in our case are quite similar to this latter cell component.

It was difficult to judge whether the case was malignant or benign because the grade of cellular atypia was low and the proliferative ability was also suggested to be low. Benign diseases such as Rosai-Dorfman disease and ALK^{+} histiocytosis should also be differentiated.[12-13] Since an infiltrative tumor growth pattern and necrosis were noted in our case and tumor cells were negative for ALK and S-100 protein, it was likely that these two diseases could be ruled out.

No concept of histiocytic tumor as a benign disease has been established in the current WHO classification,[7] and there is no index of malignancy or classification of low and high grade of malignancy. MIB-1 index of reported HS cases varied case by case from 5% to 90%, regardless of cellular atypia. MIB-1 index of HS, in general, cannot predict its clinical behavior. However, a low MIB-1 index, 10% in this case, may be related to no recurrence within 2 years.

Two HS cases with spindle-shaped tumor cells like this case have been reported, such as Alexiev *et al*. presenting a 41-year-old man with a tumor in the head and neck region[14] and Vos *et al*. (case no. 4) presenting a 55-year-old man with hepatosplenomegaly, abdominal adenopathy, and colonic mass.[3] Both of these cases were positive for CD68, CD163, and lysozyme. Clinical information of the former case with an MIB-1 index of 70% was unavailable and the latter case

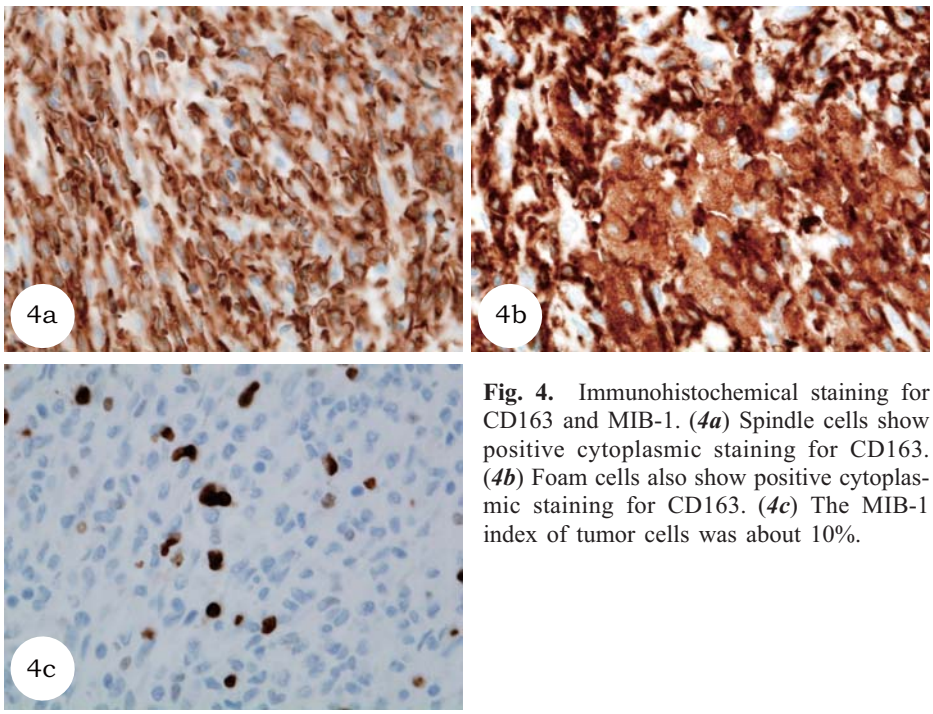

Fig. 4. Immunohistochemical staining for CD163 and MIB-1. (***4a***) Spindle cells show positive cytoplasmic staining for CD163. (***4b***) Foam cells also show positive cytoplasmic staining for CD163. (***4c***) The MIB-1 index of tumor cells was about 10%.

Table 1. Immunohstochemical results of histiocytic sarcoma

Antigen	Clone	Source	Condition	Results	
				Spindle cells	Foam cells
CD1a	JPM30	Leica	×50	−	−
CD3	2GV6	Roche	RTU	−	−
CD4	4B12	Dako	×100	+/−	+/−
CD15	MMA	BD	×100	−	−
CD20	L26	Dako	×200	−	−
CD21	1F8	Dako	×50	−	−
CD23	1B12	Leica	×10	−	−
CD34	QBEnd/10	Leica	×100	−	−
CD45	2B11 + PD7/26	Dako	×200	+/−	+/−
CD68	KP1	Dako	×200	+	+/−
CD163	10D6	Leica	×100	+	+
Myeloperoxidase	Polyclonal	Dako	×1,000	−	−
Lysozyme	Polyclonal	Dako	×100	−	−
AE1/3	AE1/3	Roche	RTU	−	−
CAM5.2	CAM5.2	BD	×2	−	−
EMA	E29	Dako	×2,000	−	−
Smooth muscle actin	1A44	SIGMA	× 5,000	−	−
Desmin	D33	Dako	×400	−	−
Vimentin	V9	Dako	×600	+	+
S-100 protein	Polyclonal	Dako	×1,000	−	−
HMB45	HMB45	Dako	×100	−	−
Melan A	A103	Dako	×100	−	−
TTF-1	SPT24	Leica	×50	−	−
ALK	5A4	Leica	×100	−	−
Ki-67	MIB-1	Dako	×200	10%	10%

RTU, ready to use; +. positive for ≧ 50% of tumor cells; +/−, positive for < 50% of tumor cells; −, negative

Table 2. Histicytic sarcoma in the lung

Case No.	Authors	Published year	Age	M/F	Symptom	Tumor involvement	Therapy	Outcome	Tumor size	Cell morphology	MIB-1 index
1	Hornick, *et al*.	2004	68	M	Cough, respiratory disturbance, weight loss	Lymph node (mediastinum, lung hilar, tracheal bifurcation) & lung	Chemotherapy	N.D.	68 mm	N.D.	N.D.
2	Buonocore, *et al*.	2005	3	M	Back to waist pain	Tumor in 4th vertebrae & lung	Chemo-radiation	N.D.	N.D.	Large-sized cells with marked pleomorphism	N.D.
3	Stacher, *et al*.	2009	23	M	By chance (surgical resection of recurrent pneumothrax)	Right lung	Surgical resection	No recurrence within 1 year	4 mm	Histiocyte-like cells with moderate pleomorphism	10-15%
4	This case		16	M	No symptom and by chance (health care examination)	Right lung (S6)	Surgical resection	No recurrence within 2 years	20 × 20 × 32 mm	Spindle cells and foam cells	10%

M, male; F, female; N.D., not described

with an MIB-1 index of 10% died of disease within 2 months. Although our case has shown a good prognosis so far, the clinical outcome of HS with spindle cells is controversial.

HS is treatment-resistant, the prognosis is poor, many cases are progressive, and 60-80% of cases exhibit tumor progression.[1-4] The prognosis of local small lesions is favorable.[1,2] The tumor size of this patient was moderate compared with reported cases of HS originating in the lung (Table 2). It was localized in the lung, and the postoperative course has been favorable for 2 years without additional treatment, showing that the histologically suggested low malignancy is consistent with the clinical condition.

In conclusion, we have reported a unique case of HS of the lung with spindle cells, mainly, and immunohistochemical markers of $CD68^+$, $CD163^+$, and $lysozyme^-$.

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