Peripheral Neuroectodermal Tumor Presenting Pleural Effusion

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Pleural effusion is a common finding of peripheral neuroectodermal tumor (PNET) of the chest wall (Askin's tumor), but little is known about the characteristics. A case of Askin's tumor with pleural effusion is reported. Repeated cytologies were negative for malignancy, but levels of lactic dehydrogenase (LDH) and neuron-specific enolase (NSE) in the pleural effusion were increased. Surgical biopsy was performed and immunohistochemical study of the tumor revealed the diagnosis.

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Introduction

Peripheral neuroectodermal tumor (PNET) is a rare, highly malignant small cell neoplasm that most often arises from the chest wall or paravertebral region. This entity is well recognized by pathologists but has been described rarely in the clinical journals. Clinical and radiological aspects of the tumor are not well documented, which may delay the correct diagnosis. To draw notice to this tumor, we report a case of PNET of the chest wall presenting with pleural effusion, which could not be diagnosed by repeated aspiration cytologies.

Case Report

A 26-year-old man was admitted to our hospital in January 1993 with left chest pain, cough and low grade fever persisting for a few days. Physical examination revealed decreased expansion, dull percussion note and reduced breath sounds over the left lower thorax. Laboratory data on admission (Table 1) showed no remarkable change except for mild anemia. A chest radiograph showed left-sided pleural effusion. Pleuritis was diagnosed but there was no response to antibiotics. Computed tomography on January 2 and February 4 (Fig. 1) revealed left pleural effusion but there was no mass or bone abnormality. Pleural biopsies and examinations of pleural effusion (Table 2) showed no malignant cells, but increased levels of lactic dehydrogenase (LDH), adenosine deaminase (ADA) and neuron-specific enolase (NSE). Computed tomography and magnetic resonance computed tomography on May 12 demonstrated a mixed attenuation mass with internal fluid and pleural

effusion (Fig. 2). No obvious involvement of lymph nodes, bone or diaphragm could be identified. An open surgical biopsy confirmed the diagnosis of PNET. Light microscopy showed small round tumor cells with hyperchromatic nuclei and scanty cytoplasm (Fig. 3a). Rosettes were also found. Periodic-acid-Schiff stain (PAS) was negative. Immunohistochemistry of the tumor demonstrated that the tumor was positive for NSE (Fig. 3b), synaptophysin and vimentin (data not shown). The patient received two courses of combination chemotherapy utilizing cisplatin (110 mg/day 1) and etoposide (100 mg/day 1, 2, 3). The tumor shrunk remarkably. Currently, he is receiving radiotherapy to the chest wall (55 Gy).

Discussion

The differential diagnosis of childhood and adolescent tumors composed of small round cells has classically involved Ewing's sarcoma, neuroblastoma, lymphoma, rhabdomyosarcoma and peripheral neuroectodermal tumor (PNET). PNET of the chest wall is now called Askin's tumor (1, 2). Histologically, it may be impossible to distinguish this tumor from other small round cell tumors and diagnosis may be established by immunohistochemical and electron microscopical features as discussed by Steiner (3). Diagnostically, the most characteristic and significant findings are the presence of rosettes and cytoplasmic staining for NSE (4). However, NSE-positive small cell carcinoma can not be distinguished without the localization of the tumor and other immunohistochemical features, such as synaptophysin, vimentin, etc (5). In this case, the tumor was an extrapulmonary mass, and synaptophysin and vimentin were

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Table 1. Laboratory Data on Admission

Peripheral blood		Alakline phosphatase	106 IU/L
White blood cell count	6,800/ul	Blood urea nitrogen	10 IU/L
neutrophil	63%	Creatinine	1.2 IU/L
basophil	0%	Na	143 mEq/L
eosinophil	3%	K	4.6 mEq/L
monocyte	10%	Cl	106 mEq/L
lymphocyte	24%	NSE	6.3 ng/ml
Red blood cell count	437×10 ⁶ /ul	Squamous cell cancer antigen	3.3 ng/ml
Hemoglobin	12.5 g/dl	Blood gas analysis	
Hematocrit	36.4%	pH	7.415
Platelet	37.3×10 ³ /ul	PaCO ₂	42.2mmHg
Erythrocyte sedimentation ratio	27 mm/1h	PaO ₂	82.5mmHg
Blood chemistry		Urinary total	
Total protein	6.2 g/dl	catecholamine	124 µg/day
Aspartate aminotransferase	11 IU/L		
Alanine aminotransferase	7 IU/L		
Lactic dehydrogenase	339 IU/L

Fig. 1. Computed tomography on February 4 revealed left pleural effusion but there was no mass nor bone abnormality.

Table 2. Data of Pleural Effusions

	January 18th	March 10th	April 26th	May 11th
Appearance	Bloody	Bloody	Bloody	Bloody
Protein	5.5 g/dl	5.3 g/dl	4.9 g/dl	2.8 g/ml
Sugar	99 mg/dl	78 mg/dl	54 mg/dl	34 mg/ml
Lactic dehydrogenase	2,546 IU/L	8,970 IU/L	5,500 IU/L	5,940 IU/L
Amylase	38 IU/L	16 IU/L	47 IU/L	36 IU/L
Adenosine deaminase	29.9 U/L	74.8 U/L	41.2 U/L	68.1 U/L
NSE		428 ng/ml		636 ng/ml
Cell subsets				
Neutrophils	14%	80%	69%	59%
Lymphocytes	15%	20%	26%	35%
Histiocytes	41%	0%	0%	0%
Eosinophils	30%	0%	5%	6%
Cytology	Negative	Negative	Negative	Negative
Culture	Negative	Negative	Negative	Negative
Rheumatic factor			< 18 IU/L	
Hyaluronic acid			Negative

Fig. 2. Sagittal thoracic MRI image (1.5 Tesla magnet, spin echo TR 1,090/TE90, 5 mm slice thickness) on May 13 demonstrated the high signal intensity left thoracic mass and pleural effusion.

also positive.

PNET of the chest wall is a very rare tumor in adults. Saifuddin et al summarized 46 cases of Askin's tumor (6) and 16 cases have been reported in Japan (7). The pathology of the tumor has been discussed in detail (1, 2), but little attention has been given to clinical and radiological aspects. The most common presenting symptom, in just over half the cases, is a painful chest wall mass. Chest pain without a mass is also common. Cough and dyspnea are less frequent features. Constitutional symptoms such as fever, anorexia and weight loss

Fig. 3. a) The hematoxylin-eosin stained slides demonstrated small round cells with sparse cytoplasm ($\times 100$). b) Immunostaining for NSE demonstrated cytoplasmic staining ($\times 400$).

may occur. Other modes of presentation are much more rare (6).

The most common radiological feature is a chest wall mass of soft tissue density, present in approximately two-thirds of cases (8). Over half of these have local rib destruction. Pleural effusion is a common radiological finding (70%), but the characteristics of pleural effusion are rarely known (8, 9). In the

present case, the pleural effusion was bloody throughout the course, and LDH, ADA and NSE in pleural effusion were elevated, however, repeated cytologies of the effusions were negative for malignant cells. Immunohistochemistry of the tumor and elevated levels of NSE in pleural effusions strongly supported the diagnosis, but negativity for NSE of tumor cells does not exclude the diagnosis because NSE is a soluble cytoplasmic constituent (4). Regarding the past literature, there were few case reports of PNET in which pleural effusion was positive for malignant cells (10). This seems to be important especially when pleural effusion is the only manifestation of the disease.

The Most common CT findings are extensive mixed attenuation soft tissue mass, associated rib destruction and pleural fluid (6). It should be emphasized that in the present case, the initial radiological sign was pleural effusion and chest wall mass was not been detected for over 3 months. In summary, PNET must be considered in the differential diagnosis of chest wall mass or unexplained pleural effusion in children and in young adults.

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