



## Case report

## A case of primary pulmonary NK/T cell lymphoma presenting as pneumonia

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## ABSTRACT

Primary pulmonary lymphoma, particularly non-B cell lymphomas involving lung parenchyma, is very rare. A 46-year-old male was admitted to the hospital with fever and cough. Chest X-ray showed left lower lobe consolidation, which was considered pneumonia. However, because the patient showed no response to empirical antibiotic therapy, bronchoscopic biopsy was performed for proper diagnosis. The biopsied specimen showed infiltrated atypical lymphocytes with angiocentric appearance. On immunohistochemical staining, these atypical cells were positive for CD3, CD30, CD56, MUM-1, and granzyme B, and labeled for Epstein–Barr virus encoded RNA in situ hybridization. These findings were consistent with NK/T cell lymphoma. We report on a case of primary pulmonary NK/T cell lymphoma presenting as pneumonic symptoms and review the literature on the subject.

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## 1. Introduction

Involvement of pulmonary lymphoma can occur in three ways: 1) hematogenous dissemination; 2) contiguous invasion from nodal lymphoma; 3) primary pulmonary involvement [1]. Of these, only 3–4% of non-Hodgkin's lymphoma is primary pulmonary lymphoma, and most cases are B cell lymphoma arisen from bronchial mucosa associated lymphoid tissue [2]. Primary pulmonary involvement of non-B cell lymphoma is uncommon; in particular, natural killer (NK)/T cell lymphoma is very rare, and only nine cases have been reported. NK/T cell lymphoma has a very aggressive behavior pattern, and a delay in diagnosis can result in a fatal outcome. We report on a case of primary pulmonary NK/T cell lymphoma presenting as pneumonia and review previous cases.

## 2. Case report

A 46-year-old male was admitted to our hospital with chief complaints of 10 days history of intermittent febrile sense and

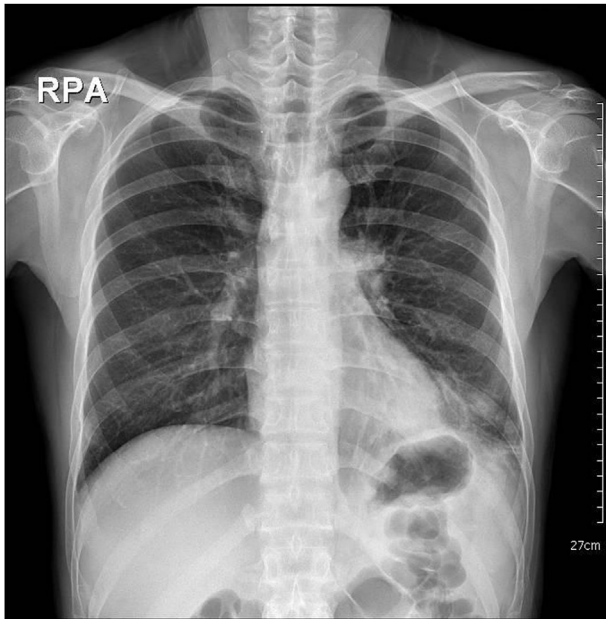
cough. He had scanty sputum. On review of the system, he denied weight loss and night sweat. He had no past medical history, but had a 20-pack-year smoking history, however he had stopped smoking five years ago. On admission, his vital signs included blood pressure 130/70 mmHg, pulse rate 74 beats/min, respiratory rate 20 breaths/min, and body temperature 38.6 °C. On physical examination, his face had an acutely ill-looking appearance. No palpable lymph nodes were detected on the neck and supraclavicular area. Also, no throat injection and no specific lesion were detected on oropharyngeal cavity. On chest auscultation, crackles without wheezing were detected on the left lower lung (LLL) field, but paranasal sinus Water's view was no active lesion.

Laboratory findings showed white blood cell count 5600/mm<sup>3</sup>, hemoglobin 13.0 g/dL, platelet count 206,000/mm<sup>3</sup>, aspartate aminotransferase 167 IU/L, alanine aminotransferase 176 IU/L, total bilirubin 0.7 mg/dL, and CRP 1.66 mg/dL. Chest radiography showed LLL consolidation, particularly retrocardiac space (Fig. 1).

He was initially treated with ceftriaxone (1 g bid intravenously), but, despite receiving empirical antibiotic treatment, he showed persistent cough and febrile senseduring one-week treatment. The attending physician considered pneumonia treatment failure, thus antibiotics were changed to piperacillin/tazobactam (4.5 g tid) and levofloxacin (500 mg qd) intravenously with no further studies for one week. Despite change in antibiotic treatment, he showed

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**Fig. 1.** Chest X-ray showed consolidation on left lower lung fields, especially retrocardiac space.

aggravated dyspnea. Laboratory findings at that time showed white blood cell counts  $2900/\text{mm}^3$ , hemoglobin 11.7 g/dL, platelet count  $146,000/\text{mm}^3$ , aspartate aminotransferase 211 IU/L, alanine aminotransferase 118 IU/L, total bilirubin 0.4 mg/dL, total protein 3.0 g/dL, albumin 1.9 g/dL, and serum LDH 1050 IU/L. Arterial blood gas analysis on room air showed pH of 7.471,  $\text{PCO}_2$  of 29.1 mmHg,  $\text{PO}_2$  of 59.7 mmHg,  $\text{HCO}_3^-$  of 20.7 mmol/L, and  $\text{SaO}_2$  of 92.8%. He underwent chest computed tomography (CT), which showed consolidation at LLL and dominant left pleural effusion (Fig. 2). Sputum studies revealed three consecutive negative results for acid-fast staining and non-specific cytology. Results of pleural fluid analysis showed a slightly red color, specific gravity 1.010, pH 7.5, no white blood cells were found, red blood cell count  $2650/\text{mm}^3$ , pleural total protein 2.5 g/dL, LDH level 1900 IU/L, and adenosine



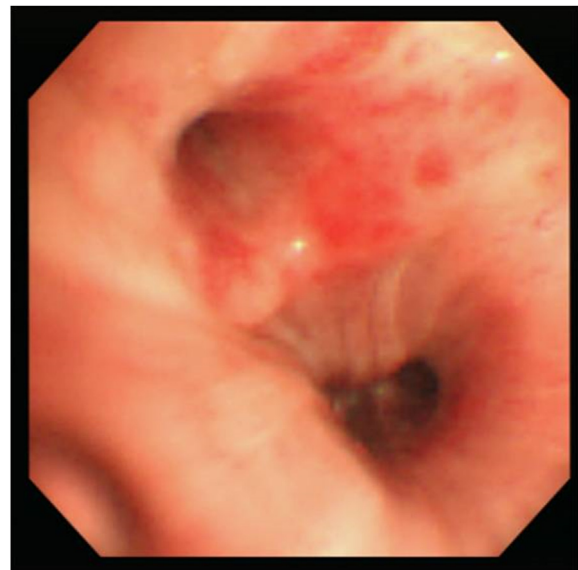
**Fig. 2.** After two weeks treatment, chest CT showed mass like consolidation on left lower lobe with pleural effusion, especially left dominant.

deaminase 80.2 U/L. For proper diagnosis, he was referred to a pulmonologist and bronchoscopic examination was performed.

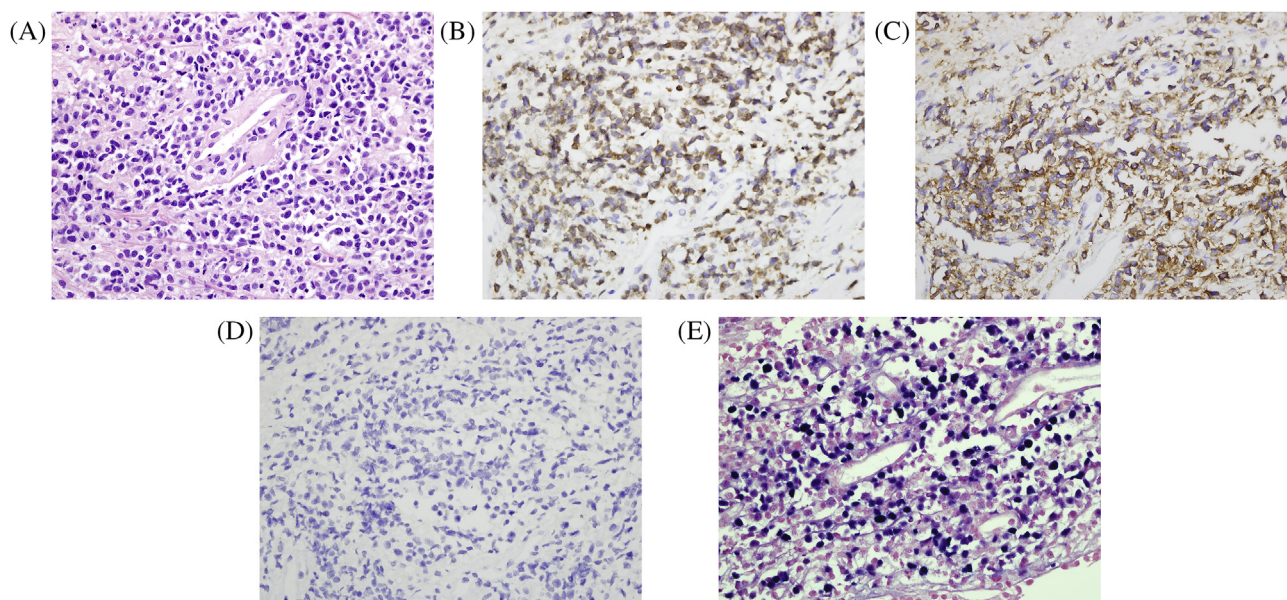
Bronchoscopic findings showed reddish mucosal nodular lesions with edematous mucosa on superior segmental bronchus of the left lower lobe (Fig. 3). On microscopic findings, the mucosa showed infiltration of medium-sized cells with irregular nuclei, inconspicuous nucleoli, high nuclear cytoplasmic ratio, and many apoptotic bodies. Angiocentric growth pattern and coagulative necrosis were also observed (Fig. 4A). On immunohistochemical staining, the atypical cells were positive for CD3, CD30, CD56, MUM-1, and granzyme B but negative for cytokeratin, CD10, CD20, bcl-2, bcl-6, and ALK (Fig. 4B–D). In situ hybridization for Epstein–Barr virus (EBV) encoded RNA (EBER), most atypical cells were labeled (Fig. 4E). These findings were consistent with NK/T cell lymphoma. There was no evidence of lymphoma involvement in the extrapulmonary site, thus, he was diagnosed as primary pulmonary extranodal NK/T cell lymphoma. He showed rapid deterioration and was transferred to another hospital after final diagnosis. Unfortunately, he died shortly thereafter.

### 3. Discussion

NK/T cell lymphoma shows extranodal presentation characterized by angiocentric and angiodestructive growth, and is associated with EBV [3]. It occurs most often in elderly adults, and is more common in males than females [4]. This disorder is rare in the United States and Europe, but common in Asia, South and Central America, and Mexico [4,5]. Extranodal NK/T cell lymphoma commonly occurs in the upper aerodigestive tract (nasal cavity, nasopharynx, paranasal sinuses, and palate) [4]. The preferential sites of extranasal involvement are skin, gastrointestinal tract, testis, and soft tissue, and primary lung involvement is very rare [2,3,6–8]. Histologically, the site of involvement shows extensive ulceration, diffuse and permeative infiltration of atypical lymphocytes, and many apoptotic bodies and mitotic figures. An angiocentric and angiodestructive growth pattern with coagulative necrosis is a frequent finding. Atypical lymphocytes are diverse in size, from small to large or anaplastic. The atypical nuclei are folded or elongated, and the chromatin pattern is granular or vesicular. The cytoplasm is moderate in amount with pale or clear



**Fig. 3.** Bronchoscopic finding showed reddish mucosal nodular lesions with edematous mucosa on superior segmental bronchus of left lower lobe.



**Fig. 4.** Pathologic findings of bronchoscopic biopsy. (A) Atypical medium-sized cells with irregular nuclei, inconspicuous nucleoli, high nuclear cytoplasmic ratio, and many apoptotic bodies. The atypical cells also showed an angiocentric growth pattern (H&E staining, X400). (B) Immunohistochemical stains showed positive reactivity for CD3 (X400). (C) Immunohistochemical stains showed positive CD56 (X400). (D) Immunohistochemical stains showed negative CD20 (X400). (E) In situ hybridization for Epstein–Barr virus-encoded RNA showed positive reaction in atypical cells (X400).

appearance. Mitotic figures are common [3,4].

The characteristic immunophenotyping of NK/T-cell lymphoma is: CD2+, CD56+, surface CD3- and cytoplasmic CD3ε+. Among these, CD56 is a particularly useful marker [3,4]. The etiology of NK/T cell lymphoma has shown strong association with EBV, thus, EBER is the most reliable standard in diagnosis of NK/T cell lymphoma [3,4].

Primary pulmonary NK/T cell lymphoma is rare, with only a few reported cases. We reviewed nine cases [2,5–12], whose clinical characteristics are summarized in Table 1. Including the current case, the patients ranged in age from 31 to 80 years (mean age was 53.2 years). The patients included four males and six females, who presented with cough, sputum, febrile sensation, and generalized weakness. The radiologic findings were mass [5,8], multiple nodular lesions [2,6,12], consolidation [7,9,11] or atelectasis [10]. Our case also showed alveolar infiltration, consolidation, and

pleural effusion.

Diagnosis of the primary pulmonary NK/T cell lymphoma was made by lobectomy in two cases, open lung biopsy in two cases, percutaneous transthoracic needle biopsy in three cases, mediastinal lymph node biopsy in one case, and postmortem examination in one case. However, our diagnosis was made by bronchoscopic biopsy.

There are still no recommended treatment strategies for pulmonary NK/T cell lymphoma. In reviewed literature studies, one patient underwent lobectomy alone, lobectomy with radiotherapy was performed in one case, and chemotherapy in four cases; however, three patients died before treatment due to rapid progression. Despite treatment, five patients died. Only one patient who underwent lobectomy with radiotherapy survived.

In our case, the patient was presumed as pneumonia and initially treated with empirical antibiotics. Despite antibiotic

**Table 1**  
Demographic, clinical and radiologic characteristics, treatment and outcome in 10 patients.

Reference	Age	Sex	Diagnosis	Presentation	Radiologic findings	Treatment and outcome
Kwon	50	F	Lobectomy	Dry cough	Well-demarcated mass in the right lower lobe	Right lower lobectomy and radiotherapy, alive
Jung	48	F	Open lung biopsy	Cough, sputum, and febrile sensation	Patch and reticular densities in both lung field	Chemotherapy, died
Laohaburanakit	72	F	Percutaneous transthoracic needle biopsy	Shortness of breath, cough, and fever	Bilateral consolidation, cavitation and diffuse nodules	Died
Jeong	49	F	Mediastinal lymph node biopsy	Cough, sputum and dyspnea	Bilateral multiple ill-defined nodules	Died
Davis	31	M	VATS <sup>a</sup> lung biopsy	Shortness of breath, cough, and fever	Bilateral diffuse patch parenchymal consolidation	Chemotherapy, died
Liu	80	M	Percutaneous transthoracic needle biopsy	Cough and blood-streaked sputum	Soft tissue mass with ground-glass attenuation in left lower lobe	Chemotherapy, died
Gong	73	F	Lobectomy	Fever	Atelectasis in right upper lobe	Right upper lobectomy, died
Oshima	50	M	Postmortem examination	Fever and general fatigue	Multiple nodules in both lung fields	Chemotherapy, died
Lee	34	F	Percutaneous transthoracic needle biopsy	Fever and generalized weakness	Lobar consolidation in the left lower lobe	Died
Present case	45	M	Bronchoscopic biopsy	Cough, sputum and fever	Alveolar infiltration and consolidation in left lung, pleural effusion, left	Died

<sup>a</sup> VATS: Video-assisted thoracoscopic surgery.



treatment, he showed rapid deterioration. In addition, marked elevations of serum and pleural fluid LDH might provide a clue to suspicion of malignancy. Therefore, bronchoscopic examination was performed for proper diagnosis. Bronchoscopic biopsy in these areas revealed NK/T cell lymphoma.

In conclusion, primary pulmonary NK/T cell lymphoma is extremely rare, and it can present with pneumonic symptoms. These nonspecific clinical symptoms can cause delay of proper diagnosis and treatment. Therefore, due to its aggressive nature, a fatal outcome is common; bronchoscopic study and biopsy should be considered in cases where pneumonia shows deterioration in spite of adequate antibiotic therapy.

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