Clinical Case Report

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Primary pulmonary extranodal NK/T-cell lymphoma of nasal type misdiagnosed as pneumonia

A case report and literature review

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Abstract

Rationale: Primary pulmonary NK/T cell lymphoma is extremely rare, and only a few cases have reported so far. Its diagnosis is mainly dependent on open-lung biopsy.

Patient concerns: Here, we report a 44-year-old male who was initially misdiagnosed as having pneumonia according to the clinical characteristics and computed tomography (CT) findings.

Diagnosis: The first lung biopsy indicated a large number of coagulative necrotic lesions, and definite diagnosis was made after the second lung biopsy following non-response to 6-day wide spectrum antibiotic therapy. The second lung biopsy showed the tumor cells were positive for LCA, CD3ε, CD30, TIA-1, Ki67 and negative for CD20, CD56, CD1a, MPO, CK, S-100, desmin, and CD34.

Interventions: This patient refused to receive further therapy and died 1 month after confirmed diagnosis.

Outcomes: Clinically, it is difficult to differentiate pneumonia from NK/T cell lymphoma in pathology due to the presence of plenty of focal necrosis in primary pulmonary NK/T cell lymphoma.

Lessons: The diagnosis of primary pulmonary NK/T cell lymphoma should be based on lung biopsy (usually multiple lung biopsies are required), immunohistochemistry and clinical and imaging findings.

Abbreviations: CT = computed tomography, EBER = Epstein–Barr virus encoded RNA, ENKTL = Extranodal natural killer/T-cell lymphoma.

Keywords: extranodal NK/T cell lymphoma, literature review, misdiagnose, pneumonia

1. Introduction

Extranodal natural killer/T-cell lymphoma (ENKTL), nasal type, is deviated from either activated NK cells or cytotoxic T cells. Although it may involve nasal cavity, skin, upper respiratory tract, gastrointestinal tract, testes, brain, salivary glands, pancreas, soft tissues, adrenal glands, bone marrow and other extranodal sites, the nasal cavity is the most common site of involvement.[1,2]In cases of ENKTLs, only a few cases reported involving the lung.[3,4] Primary pulmonary NK/T cell lymphoma originates from lung parenchyma, bronchi, and/or its regional lymph nodes. Primary pulmonary NK/T cell lymphoma is extremely rare and represents 0.4% of all lymphoma, 3 to 4% of all extranodal manifestations and 0.5 to 1% of all primary pulmonary malignancies.[5,6] Although this lymphoma can occur in subjects of any age group, it appears has a higher incidence in subjects aged 20 to 80 years (median: 50 years) and occurs more commonly in men than women.[2,7,8] The imaging findings of primary pulmonary NK/T cell lymphoma are nonspecific, and thus it is easily misdiagnosed as pneumonia in the early stage. Here, we report a case of primary pulmonary NK/T cell lymphoma in a 44-year-old Chinese male patient and its clinical characteristics, computed tomography (CT) findings, pathological characteristics and immunophenotype are described.

2. Case report

A 44-year-old Chinese male presented with weakness, cough, and intermittent fever for half a month. Moist rales were noted at the base of both lungs on auscultation. Laboratory examinations showed white blood cell count and percentage of neutrophils elevated moderately (white blood cells: 11.2×10^9/L; neutrophils: 88%). The Epstein–Barr virus test showed positive. Immune function tests and sputum culture displayed negative. CT of the chest showed multiple lesions in both lungs (Fig. 1). Bronchoscopy failed to find abnormalities (Fig. 2). CT-guided lung biopsy revealed a large amount of necrotic tissues in the right lung, in which a small amount of inflammatory cells, fibroblasts and some atypical small–medium-sized cells were observed. Only a small

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This study was approved by the ethics committee of People's Hospital of DeYang city. The patient consented to the publication of this study.

The authors have no conflicts of interest to disclose.

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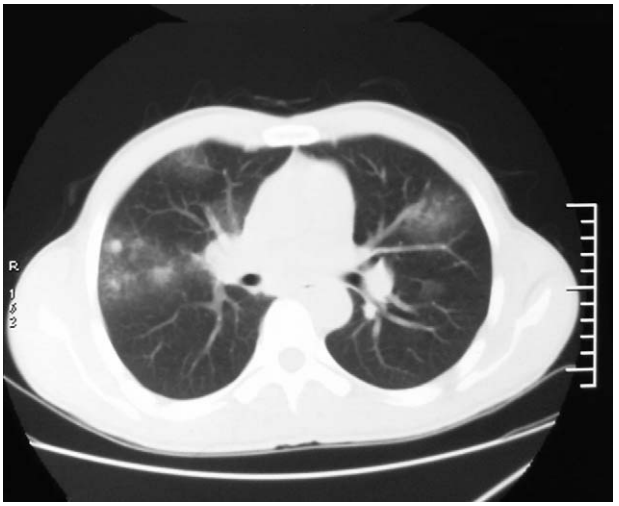

Figure 1. CT of the chest showed multiple nodules and masses of variable sizes in both lungs. Halo signs were observable in some masses. CT = computed tomography.

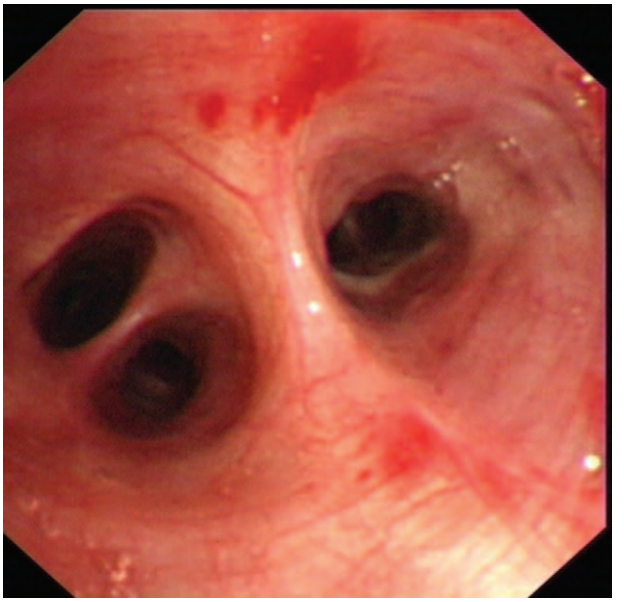

Figure 2. Bronchoscopy showed normal.

number of lymphocytes were found in the left lung. Staining of gram stain and special stains for atypical organisms including mycobacteria, fungi, and pneumocystis carinii also showed negative. He was diagnosed as pneumonia and treated with broad spectrum antibiotics for 6 days, but symptoms remained unchanged and he showed persistent fever, fatigue, and poor appetite. Meanwhile, the counts of white blood cells and platelets decreased progressively. A second CT of the chest showed diffuse infiltration in both lungs, measuring up to 7 cm in diameter, with consolidation and atelectasis in the middle lobe of right lung. Obvious mediastinal and hilar lymphadenopathy was not observed (Fig. 3).

Then, the patient received a second lung biopsy which showed atypical lymphoid cells infiltration with necrosis in the lung (Fig. 4). The tumor cells were positive for LCA, CD3ε, CD30, TIA-1, and Ki67, but negative for CD20, CD56, CD1a, MPO, CK, S-100, desmin, and CD34. In situ hybridization showed that tumor cells were positive for Epstein–Barr virus encoded RNA (EBER). Examination of the bone marrow showed the infiltration of diffused or clustering lymphocytes, and cells were positive for CD3ε and CD20, but negative for granzyme B and CD56. Therefore, the patient was diagnosed as having primary pulmonary extranodal NK/T-cell lymphoma of nasal type. Unfortunately, the patient refused further therapy and died 1 month later.

3. Discussion

Primary pulmonary NK/T cell lymphoma is a rare and aggressive malignancy, and only a few cases have been reported so far in Japan, Korea, the United States, China, and Taiwan.[1,2,5,9–12] It is rare in the United States and Europe, but more prevalent in Asia, South and Central America, and Mexico. Reviewing literatures indicated a total of 12 cases were reported between 1990 and 2017 except for the case we reported (Table 1). The clinical characteristics of these cases are summarized in Table 1. Of 12 patients, 2 were from Taiwan China, three from United States, and six from China mainland. The prevalence is significantly higher in yellow race than in white race, which might be ascribed to the geographical and ethnic susceptibility, but there are no specific epidemiological data available.[13–15] The available patients ranged from 23 to 83 years and with a female-to-male ratio of approximately 1:1. Patients present with fever, cough, dyspnea, and other symptoms, which however are nonresponsive to antibiotics. The common radiographical findings are the consolidation, nodules, and masses. Hilar adenopathy, pleural effusion, and atelectasis have also been reported.[10,15–18]

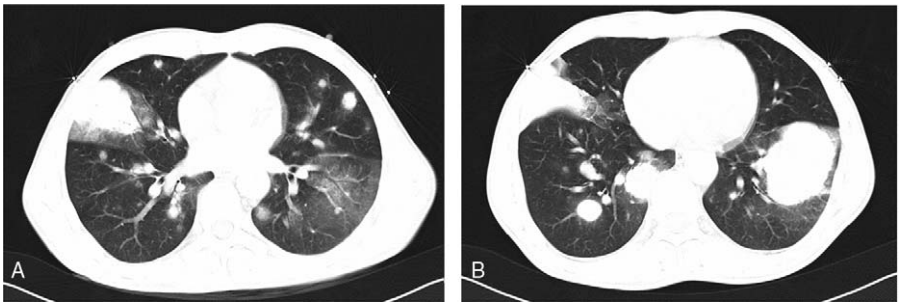

Figure 3. CT of the chest after 6-day treatment. (A) 20×30 mm mass was observed in the right lung and halo signs were observable. Some nodules of variable sizes were found in both lungs. (B) 30×40 mm mass was noted in the left lung, but not found on the previous CT. CT = computed tomography.

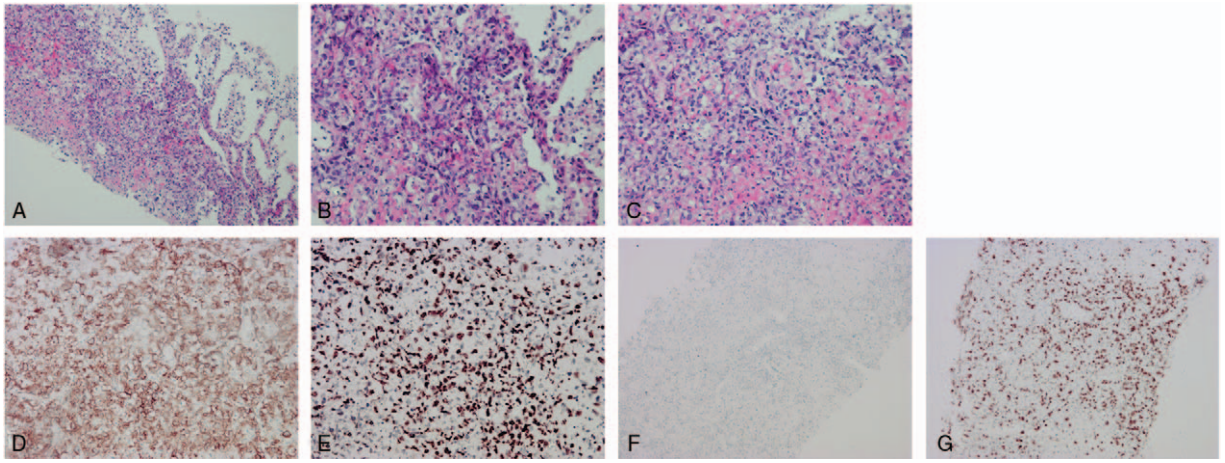

Figure 4. The lesions showed extensive coagulative necrosis and infiltration of atypical lymphoid cells. (A) Hematoxylin and eosin staining (200×); (B, C) hematoxylin and eosin staining (400×); (D) cells were positive for CD3 (400×); (E) tumor cells were positive for Epstein–Barr virus-encoded RNA (EBER) (in situ hybridization; 400×); (F) cells were negative for CD56 (200×); (G) cells were positive for KI67 (400×).

CT findings of the primary pulmonary NK/T cell lymphoma usually vary and are nonspecific. These findings can be divided into 3 types—nodular or mass-like, mesenchyma-like, and pneumonia-like.[12,16] Thus, it is difficult to differentiate primary pulmonary NK/T cell lymphoma from pneumonia if CT of the chest shows pneumonia-like features. In this patient, halo signs were also found, and bleeding was observed surrounding the halo signs. The halo signs can be found mostly in invasive aspergillosis, and rarely in tumor. Lymphoma cells can invade blood vessels leading to the bleeding of surrounding tissues. Thus, the halo signs can also be observed in primary pulmonary NK/T cell lymphoma.

The diagnosis of NK/T cell lymphoma is on the basis of following features: (1) Lesions occur in the nose, skin, facial midline, lung, and other soft tissues. (2) In situ hybridization shows being positive for EBER. (3) The lymphoma infiltrates in a diffuse pattern and is usually angiocentric and angiodestructive with coagulative necrosis and apoptotic bodies. (4) Cells are positive for CD2, cytoplasmic CD3ε, CD56, cytotoxic granule-associated proteins (such as granzyme B, TIA1, and perforin.).[19–21] This patient was positive for EBER, LCA, CD3ε, CD30, TIA-1, and Ki67. Although he was negative CD56 as a marker, this patient met the diagnostic criteria in the 2008 WHO classification of lymphomas. Most NK/T lymphoma patients show extensive necrosis in the lung and thus they are often misdiagnosed as having infectious lesions. Therefore, repeated lung biopsy is needed.

The prognosis of primary pulmonary NK/T-cell lymphoma is very poor and the longest survival time was less than 6 months in available reports.[1,5]Correct diagnosis and timely treatment may have benefits for prognosis. The patient we reported presenting with rapidly growing lung mass and positive EBER would mean a poor prognosis.[22] The optimal treatment has not been clearly established, although more than 70% of NK/T cell lymphoma patients received CHOP (cyclophosphamide, adriamycin, vincristine, and prednisone) based chemotherapy and surgical resection in the literatures.[23] It is reported that NK/T cell lymphoma is not sensitive to chemotherapy because of multidrug resistance gene expression. The recurrence rate is very high, and the skin and hypoderm are the most common sites of recurrence.[24] Some patients may be responsive to initial treatment, but this effectiveness lasts a short time, and patients will develop local recurrence, and distant metastasis soon after initial treatment. A definite diagnosis was not achieved in this

Table 1

Primary pulmonary NK/T cell lymphoma reported since 1990.

Year	Case	Country	Age	Sex	Presentation	Radiographic findings
2006	1	USA	72	Female	Shortness of breath, productive cough, intermittent fever	Consolidation, small nodules
2010	2	USA	41	Male	Dizziness, fainting spells	Masses, infiltrates
2016	3	USA	62	Male	Cough, progressive respiratory distress	Diffuse bilateral mixed interstitial and alveolar infiltrates
2015	4	Korea	46	Male	Fever and cough	Consolidation
2007	5	China	23	Female	Cough, dyspnea, fever	Consolidation
2007	6	China	30	Female	Cough, fever	Consolidation
2008	7	China	30	Female	Productive cough, fever	Multiple nodules and consolidation
2013	8	China	73	Female	Fever	Atelectasis, nodules
2015	9	China	83	Female	Intermittent fever	Nodules and masses
2017	10	China	48	Male	Fever, fatigue, Expectoration	Cord and patch shadow
2012	11	Taiwan	80	Male	Hemoptysis	Mass, mediastinal lymphadenopathy
2015	12	Taiwan	53	Male	Progressive dyspnea	Consolidation, moderate pleural effusion

patient until a second lung biopsy was performed. The disease condition of this patient deteriorated rapidly and he refused further therapy.

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