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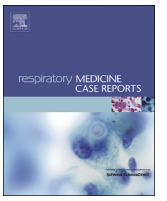

Case Report

Primary pulmonary extranodal natural killer/T-cell lymphoma of nasal type presenting as pneumonia in the right lower lobe: A case report

Xuefeng Li [a], Yang Zhu [b,*], Tao Yu [b], Liyu Cao [c], Aimin Sun [a], Zongtao Hu [a]

[a] Department of Thoracic Oncology, Hefei Cancer Hospital, Chinese Academy of Sciences, No. 68 Yangqiao Road, Hefei, 230000, China
[b] Department of Respiratory, Fuyang Hospital of Anhui Medical University, No. 99 Huangshan Road, Fuyang, 236000, China
[c] Department of Pathology, Fuyang Hospital of Anhui Medical University, No. 99 Huangshan Road, Fuyang, 236000, China

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ABSTRACT

Extranodal Natural Killer/T Cell Lymphoma Nasal Type (EN-NK/T-CL-NT) is a rare type of non-Hodgkin lymphoma in which the lesion is usually located in the upper respiratory tract, such as nasal cavity, palate, and nasopharynx. In addition, the primary lesion of EN-NK/T-CL-NT can rarely originate in extranasal sites such as the skin, gastrointestinal tract, testicles, central nervous system, and lungs. We describe an 82-year-old male smoker was brought to the hospital with 8 months of fever, cough, sputum production, chest pain, and chest tightness. Computed tomography (CT) of the chest showed subpleural high-density shadow in the lower lobe of the right lung with unclear borders and surrounding patchy ground-glass shadow. Initially, the patient's right lower lobe lesion progressed after receiving anti-inflammatory treatment. He subsequently underwent two computerized tomography (CT)-guided percutaneous transthoracic needle aspiration biopsies and a bronchoscopy, but no tumor cells were found. Through multidisciplinary team discussions, the patient was then transferred to the department of cardiothoracic surgery for right lower lobectomy. Finally, extranodal natural killer/T-cell lymphoma (ENKTCL), nasal type, was confirmed by pathology of the surgical specimen. The diagnosis of primary pulmonary ENKTCL was made because no evidence other than extrapulmonary site was found at the time of diagnosis and treatment. Here we report a case of primary pulmonary extranodal natural killer/T-cell lymphoma of nasal type presenting as pneumonia in the right lower lobe and enhance the understanding of the disease.

1. Introduction

Extranodal, natural-killer/T-cell lymphoma of nasal type is a rare type of non-Hodgkin lymphoma associated with Epstein–Barr virus (EBV) infection, and the lesion is usually located in the upper respiratory tract, such as nasal cavity, palate, and nasopharynx [1]. In addition, the primary lesion of EN-NK/T-CL-NT can rarely arise from extranasal sites such as the skin, gastrointestinal tract, testicles, and lungs [2,3]. Here we report a case of primary pulmonary extranodal natural killer/T-cell lymphoma of nasal type presenting as pneumonia in the right lower lobe and enhance the understanding of the disease.

* Corresponding author.
E-mail addresses: lxf06029311@163.com (X. Li), ayfy_zy@163.com (Y. Zhu).

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2. Case presentation

2.1. Chief Complaints

An 82-year-old male smoker was brought to the hospital with 8 months of fever, cough, sputum production, chest pain, and chest tightness.

2.2. History of present illness

Fever remained uncontrolled after receiving anti-infective treatment at the local hospital.

2.3. History of illness

A 10-year history of coronary atherosclerotic heart disease (6 stents in the coronary arteries and long-term oral antiplatelet medication), a 10-year history of hypertension, and a 10-year history of type 2 diabetes mellitus.

2.4. Personal and family history

The patient denied any family history of related disorders.

2.5. Physical examination

Physical examination revealed vital signs were stable, wet rales could be heard in both lungs, and no enlarged lymph nodes were palpable in the neck, supraclavicular region, axilla or groin.

2.6. Laboratory examinations

Blood routine examination: white blood cell count,6.52 × 109/L; hemoglobin, 119 g/dL; platelet count, 234 × 109/L. The C-reactive protein concentration was 37.13 mg/L (normal range, ≤4 mg/L). The procalcitonin level was 0.176 ng/ml (normal range,0–0.05 ng/ml). The G test, GM test, immune function tests, blood culture results and tumor markers were negative.

2.7. Imaging examinations

Computed tomography (CT) of the chest showed subpleural high-density shadow in the lower lobe of the right lung, the margin of which was relatively ill defined and ground-glass opacities (Fig. 1).

2.8. Futher diagnostic workup

Initially we used anti-infective treatment, but it was not effective and the lesion in the right lower lung gradually increased in extent. A CT-guided transthoracic needle biopsy of the right lower lung was first performed, and pathology suggested alveolar epithelial hyperplasia, alveolar interstitial tissue hyperplasia, and necrotic tissue was also seen with the addition of specific stains, which were negative for antacid staining and negative for glycogen staining. Intensified antimicrobial drug therapy was still ineffective, the lesion in the lower lobe of the right lung progressed. In order to reduce the error, a second CT-guided percutaneous lung biopsy was performed. At the same time, bone marrow examination, computed tomography (CT) of the sinuses and nasopharyngoscopy were performed to exclude lymphoma which were normal results. Pathological findings of the patient's second CT-guided lung puncture biopsy showed interstitial fibrotic tissue hyperplasia with inflammatory cell infiltration and a small amount of necrotic tissue. The patient's anti-inflammatory treatment remained ineffective and his fever was not controlled, so he underwent a bronchoscopy, which showed a patent ductal lumen in the lower lobe of the right lung with mucosal congestion and oedema (Fig. 2). Simultaneously, alveolar lavage fluid GM test, tuberculosis DNA, fiberscope brushing antacid staining, and gram staining for fungi and bacterial examination were all negative. Bronchial wash cytology showed ciliated columnar epithelium, erythrocytes and lymphocytes. Through multidisciplinary team discussions, the patient was then transferred to the department of cardiothoracic surgery for right lower lobectomy.

2.9. Final diagnosis

Extranodal natural killer/T-cell lymphoma (ENKTCL), nasal type, was confirmed by pathology of the surgical specimen. Pathology after right lower pneumonectomy showed some medium-sized lymphocytes visible at the edge of the necrotic tissue (Fig. 3). Immunohistochemical stains showed LCA (−), CK (−), TTF-1 (−), CD3 (+), CD7 (+), TIA-1 (+), granzyme B (+), CD56 (−), CD20 (−), CD4(−), CD8(−), CD68(−), PAX-5(−), CD30(−), CD117(−), MPO (−), TdT (−), ALK (−), Ki-67 (+, about 60 % cells). Furthermore, in situ hybridization for Epstein–Barr virus-encoded RNA showed positive reaction in atypical cells (Fig. 4). The diagnosis of primary lung lymphoma was made because no evidence of an extrapulmonary site was found at the time of diagnosis and treatment.

2.10. Treatment

The patient's pathology was clarified and she was subsequently referred to the department of hematology for chemotherapy. The patient received 2 cycles of chemotherapy. The patient's first chemotherapy regimen was a combination therapy of cyclophosphamide, chidamide and prednisolone. The second chemotherapy regimen was in chidamide combination with P-GEMOX (pegaspargase, gemcitabine, and oxaliplatin). The patient was eventually discharged automatically due to aggravation of his condition.

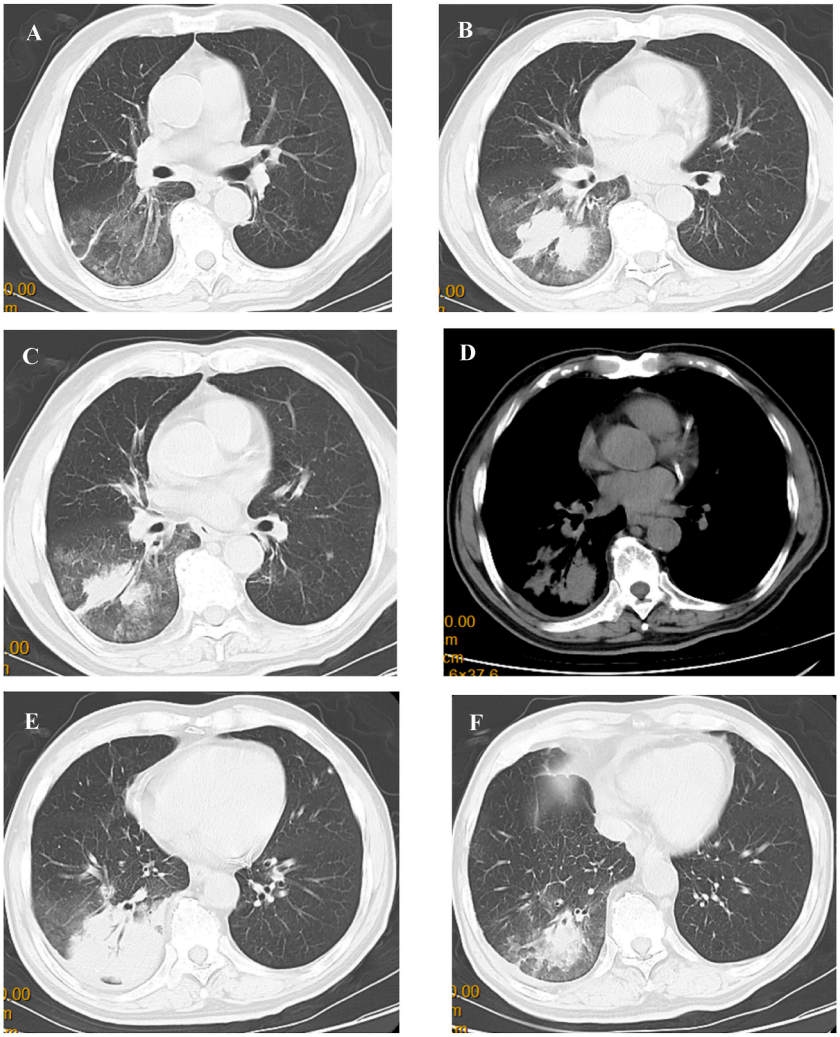

Fig. 1. (A–F) CT of the chest showed subpleural high-density shadow in the lower lobe of the right lung, the margin of which was relatively ill defined and ground-glass opacities; pleural effusion and air bronchogram sign were seen in the right lung.

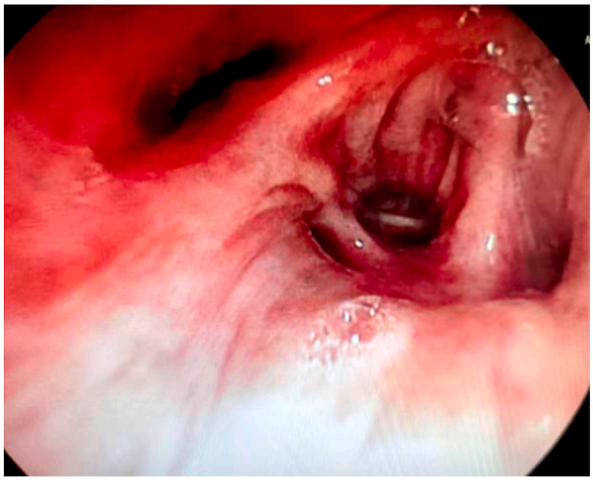

Fig. 2. Bronchoscopy revealed a patent lumen in the right lower lobe of the lung with mucosal congestion and oedema.

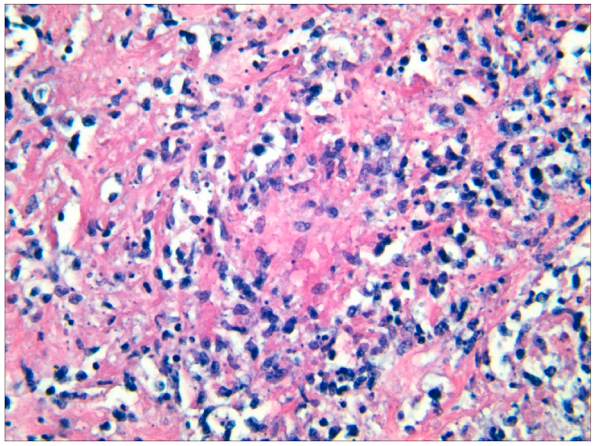

Fig. 3. Pathological biopsy after lower lobectomy of the right lung showed some medium-sized lymphocytes visible at the edge of the necrotic tissue (Hematoxylin-eosin staining; Magnification: × 10).

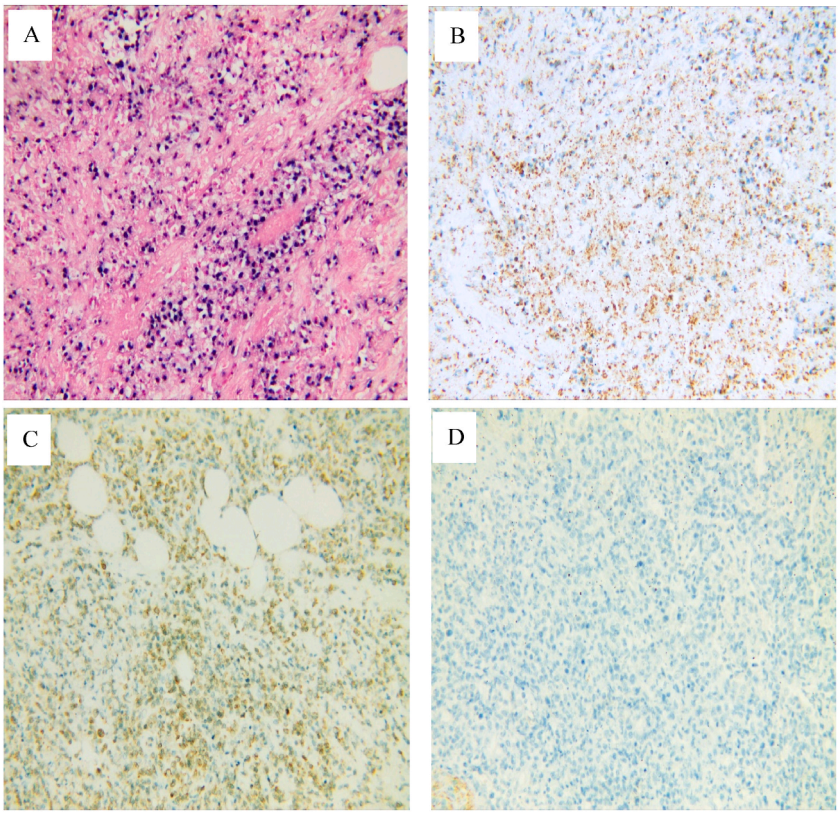

Fig. 4. A: In situ hybridization for Epstein–Barr virus-encoded RNA showed positive reaction in atypical cells (Magnification, × 10). (B–C): Immunohistochemical stains showed positive for CD3(Magnification, × 10)and granzyme B (Magnification, × 10).D: Immunohistochemical stains showed this cell was negative for CD56 (Magnification, × 10).

3. Discussion

Primary pulmonary lymphoma (PLL) is a rare malignant tumor that arises from mucosa-associated lymphoid tissue, usually belonging to the human B-cell lineage. PLL accounts for 3%–4% of extranodal non-Hodgkin's lymphomas and only 0.5–1% of all primary pulmonary tumors [4]. As a result, primary pulmonary extranodal natural killer/T-cell lymphoma of nasal type becomes extremely rare and is mostly reported in individual cases. The Pubmed database was searched with the keyword ‘primary pulmonary NK/T-cell lymphoma’, and a total of 19 articles were retrieved involving 19 cases of primary pulmonary NK/T-cell lymphoma, and the results were shown in Table 1. The age of the patients ranged from 23 to 83 years, with 13 males and 6 females. Most patients presented with fever, cough, sputum and dyspnea, and their chest images mainly showed multiple nodules, masses, pleural effusion,

Table 1
Clinical features, chest imaging features and diagnosis method of primary pulmonary NK/T-cell lymphoma.

Reference	Age/sex	Clinical symptom	Diagnostic method	Chest CT Imaging
Wang [5]	40/M	Cough, sputum, fever	CT-guided transthoracic needle biopsy	Multiple nodules, ground-glass opacities and bilateral pleural effusion
Hu [6]	49/M	Fever	CT-guided transthoracic needle biopsy	Massive infiltrates in both lungs
Hu [6]	74/M	Cough, fever	CT-guided transthoracic needle biopsy	Multiple nodes
Qiu [7]	34/F	Intermittent fever	CT-guided transthoracic needle biopsy	Multiple nodes, ground-glass opacities
Mori [8]	39/M	Cough, fever	Pleural puncture, liver biopsy(second time)	Multiple nodes
Zhang [9]	44/M	Cough, fever	CT-guided transthoracic needle biopsy(second time)	Multiple nodes and masses of variable sizes
Song [10]	55/M	Cough, sputum, dyspnea	Wedge resections of the lung under (VATS)	Ground glass opacities
Lee [11]	46/M	Cough, sputum, fever	Transbronchial biopsy	Consolidation on left lower lobe with pleural effusion
Fei [12]	83/F	Intermittent fever	CT-guided transthoracic needle biopsy	Multiple nodules and masses
Gui [13]	39/M	Cough, fever, dyspnea	Transbronchial biopsy	Consolidation on the right lower lobe
Liu [14]	80/M	Hemoptysis	CT-guided transthoracic needle biopsy	Mass-like lesion in the left lower lung, ground-glass attenuation and mediastinal lymphadenopathy
Gong [15]	73/F	Fever	Resection of her right upper lung	Space-occupying lesion in the upper lobe of right lung
Oshima [16]	50/M	Fever	Postmortem examination	Multiple nodes
Davis [17]	31/M	Cough, fever, dyspnea	VATS lung biopsy	Bilateral diffuse patchy lung parenchymal consolidation
Cao [18]	23/F	Cough, fever	CT-guided transthoracic needle biopsy	Multiple nodules and masses
Laohaburanakit [19]	72/F	SOB, cough, fever	Postmortem examination	Consolidation, cavitation of the right upper lobe
Chien [20]	53/M	Dyspnea, cough, fever	Transbronchial biopsy	Right lower lobe mass-like lesion, regional lymph node enlargement
Anai [21]	53/M	Anorexia	VATS lung biopsy	Ground-glass opacities
Zhang [22]	68/F	Cough, fever	CT-guided transthoracic needle biopsy	Soft tissue mass in the right lung

VATS: video-assisted thoracoscopic surgery; SOB: shortness of breath.
TBB: transbronchial biopsy.

ground-glass opacities, patchy infiltrates, and consolidation. Therapeutically, these patients were often ineffective on anti-infective treatments. The lung imaging features of the above patients could be broadly classified into three types. Types of nodules and masses: presenting as single or multiple, with high density in the center and slightly lower density around the periphery, and surrounded by ground-glass opacities at the margins. Pneumonia type: showing patchy inflammatory exudative or solid shadows distributed along lung segments and lobes with air bronchogram sign. Mixed-type: exhibiting both of these types. It is often difficult to diagnose primary pulmonary NK/T-cell lymphoma on the basis of the patient's clinical presentation and lung imaging features alone. Currently, lung tissue biopsy is the gold standard for confirming the diagnosis of the disease.

It has been suggested that CT-guided needle biopsy, bronchoscopy or even wedge biopsy should be performed if the lung lesion continues to worsen despite appropriate antibiotic therapy [23]. Among the 19 case reports retrieved by the Pubmed database, the diagnosis of primary pulmonary NK/T-cell lymphoma was confirmed by CT-guided lung puncture biopsy in 9 cases, by post mortem examination in 2 cases, by VATS lung biopsy in 2 cases, by lobectomy in 2 cases, by pleural puncture in 1case, and by TBB in 3 cases. In our case report, initially we used anti-infective treatment, but it was not effective and the lesion in the right lower lung gradually increased in extent. Finally, the case we reported was diagnosed by lobectomy.

The pathology of most patients with ENKTCL tends to show extensive vascular infiltration and necrosis, which makes it more difficult to clinically confirm the diagnosis of the lesion. Therefore, more than one invasive pathological biopsy is usually required clinically [24].There were a total of 19 patients with primary pulmonary NK/T-cell lymphoma, two of whom were diagnosed by VATS lung biopsy after a negative bronchial biopsy, one of whom was diagnosed by autopsy after both negative transbronchial and CT-guided transthoracic needle biopsies, and one of whom was diagnosed by a second CT-guided transthoracic needle biopsy. The case we reported was no exception. The patient underwent two CT-guided percutaneous transthoracic needle aspiration biopsies and a bronchoscopy, but no tumor cells were found. Finally, the diagnosis was eventually confirmed by lobectomy. In our case report, on the one hand, we found that tissue specimens obtained by CT-guided transthoracic needle biopsy were small and had the potential for false-negative results. On the other hand, most patients with NK/T-cell lymphoma showed extensive necrosis on histopathology, which were often mistaken for infectious lesions clinically, thus increasing the difficulty of early diagnosis of the disease. Repeat lung puncture biopsies are therefore useful, if need be, a sufficient number of specimens need to be obtained surgically to minimize misdiagnosis of this disease.

4. Conclusion

Primary pulmonary extranodal natural killer/T-cell lymphoma of nasal type has a low incidence and is difficult to diagnose and treat early. We reported a case of extranodal natural killer/T-cell lymphoma of nasal type in an elderly male, which provided valuable insight into the early diagnosis and treatment of this disease.

Ethics statement

Ethical approval to report this case was not required.

CRediT authorship contribution statement

Xuefeng Li: Formal analysis, Writing – original draft, Writing – review & editing, Data curation. **Yang Zhu:** Resources, Writing – review & editing. **Tao Yu:** Writing – review & editing. **Liyu Cao:** Conceptualization, Resources. **Aimin Sun:** Conceptualization, Data curation. **Zongtao Hu:** Data curation.

Declaration of competing interest

No one in the manuscript has a conflict of interest.

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