

Type B3 thymoma complicated with *Chlamydia psittaci* pneumonia with rare features: A case report

JIANPING JIANG^{1*}, JINMENG DAI^{2*}, XUN HU³, XIUJUAN YAO⁴, WEIQIANG MO¹ and HAIQIN WANG¹

¹Department of Respiratory Medicine, The Second Affiliated Hospital of Jiaying University, Jiaying, Zhejiang 314000;

²Department of Respiratory Medicine, Jiashan County Yaozhuang Town Health Centre, Jiaying, Zhejiang 314117;

Departments of ³Thoracic Surgery and ⁴Pathology, The Second Affiliated Hospital of Jiaying University, Jiaying, Zhejiang 314000, P.R. China

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Abstract. The case of a patient with type B3 thymoma comorbid with *Chlamydia psittaci* (*C. psittaci*) pneumonia exhibiting rare features is presented in the current report. The patient was admitted at the Second Affiliated Hospital of Jiaying University (Jiaying, China) with a history of direct contact with poultry. Clinical manifestations included fever, shivers, cough, fatigue and poor appetite. Chest computed tomography (CT) indicated right lung pneumonia, while metagenomics next-generation sequencing using bronchoalveolar lavage fluid confirmed infection with *C. psittaci*. Additionally, positron emission tomography-CT suggested the presence of thymoma. After surgery and treatment with doxycycline and imipenem cilastatin, the patient was discharged showing signs of improvement.

Introduction

Chlamydia psittaci (*C. psittaci*) pneumonia is a rare type of pneumonia, accounting for ~1% of community-acquired pneumonia cases (1). This type of pneumonia is caused by a Gram⁻, obligate intracellular bacterium called *C. psittaci*, typically detected using metagenomics next-generation sequencing (mNGS) examination. Patients with thymoma are more susceptible to immune dysfunction compared with individuals with common pneumonia (2), and they have an increased risk of infection with *C. psittaci*. In patients with thymoma, the entry of *C. psittaci* in the bloodstream can involve the lungs, leading to pneumonia and potentially affecting multiple

organs, resulting in organ failure. In the current case report, the clinical data of a patient with type B3 thymoma comorbid with *C. psittaci* pneumonia exhibiting rare features are presented, with the view of providing a basis for clinical diagnosis and treatment.

Case report

A 69-year-old male patient was admitted at the Second Affiliated Hospital of Jiaying University (Jiaying, China) due to fever in April 2021, following 1 week of treatment. The patient developed a fever after exposure to cold, with a peak body temperature of 40°C. The fever was irregular and accompanied by chills, shivers, cough, fatigue and poor appetite. There were no symptoms of phlegm, hemoptysis, night sweats, chest tightness or other discomfort. The patient, a professional chef, had a history of direct contact with poultry prior to the onset of the disease. Upon admission, auscultation revealed significant moist rales in the right lower lung, while the rest of the physical examination was unremarkable. Laboratory examination showed a hypersensitive C-reactive protein level of 122.06 mg/l (normal range, 0-8 mg/l), a white blood cell count of 5×10^9 cells/l (normal range, 3.5-9.5 mg/l), neutrophil percentage of 81.80% (normal range, 40-75%) and a procalcitonin level of 0.227 ng/ml (normal range, 0-0.05 ng/ml). Chest computed tomography (CT) showed inflammation in the lower lobe of the right lung with partial consolidation and bilateral pleural reaction, as well as a soft tissue nodule in the anterior mediastinum, suggesting examination with contrast-enhanced imaging (Fig. 1A and B). The diagnoses made upon admission were community-acquired pneumonia and mediastinal mass.

After admission, the patient received anti-infection therapy (0.5 g per day levofloxacin and 0.5 g q6h imipenem cilastatin), anti-inflammatory treatment (40 mg single methylprednisolone injection), anti-pyretics and expectorants. However, after 3 days of treatment, the patient continued to experience recurrent fever. Tests for the presence of *Cryptococcus neoformans* and tubercle bacillus antigens, fungal smears and bacterial culture of bronchoalveolar lavage fluid yielded negative results. The results of mNGS showed infection with *C. psittaci* (sequence number, 10) and cytomegalovirus (sequence number, 28). The mNGS analysis was outsourced by Mobai Biotechnology Co.,

Correspondence to: Dr Haiqin Wang, Department of Respiratory Medicine, The Second Affiliated Hospital of Jiaying University, 1518 Huanchen North Road, Jiaying, Zhejiang 314000, P.R. China
E-mail: w_haiqin@163.com

*Contributed equally

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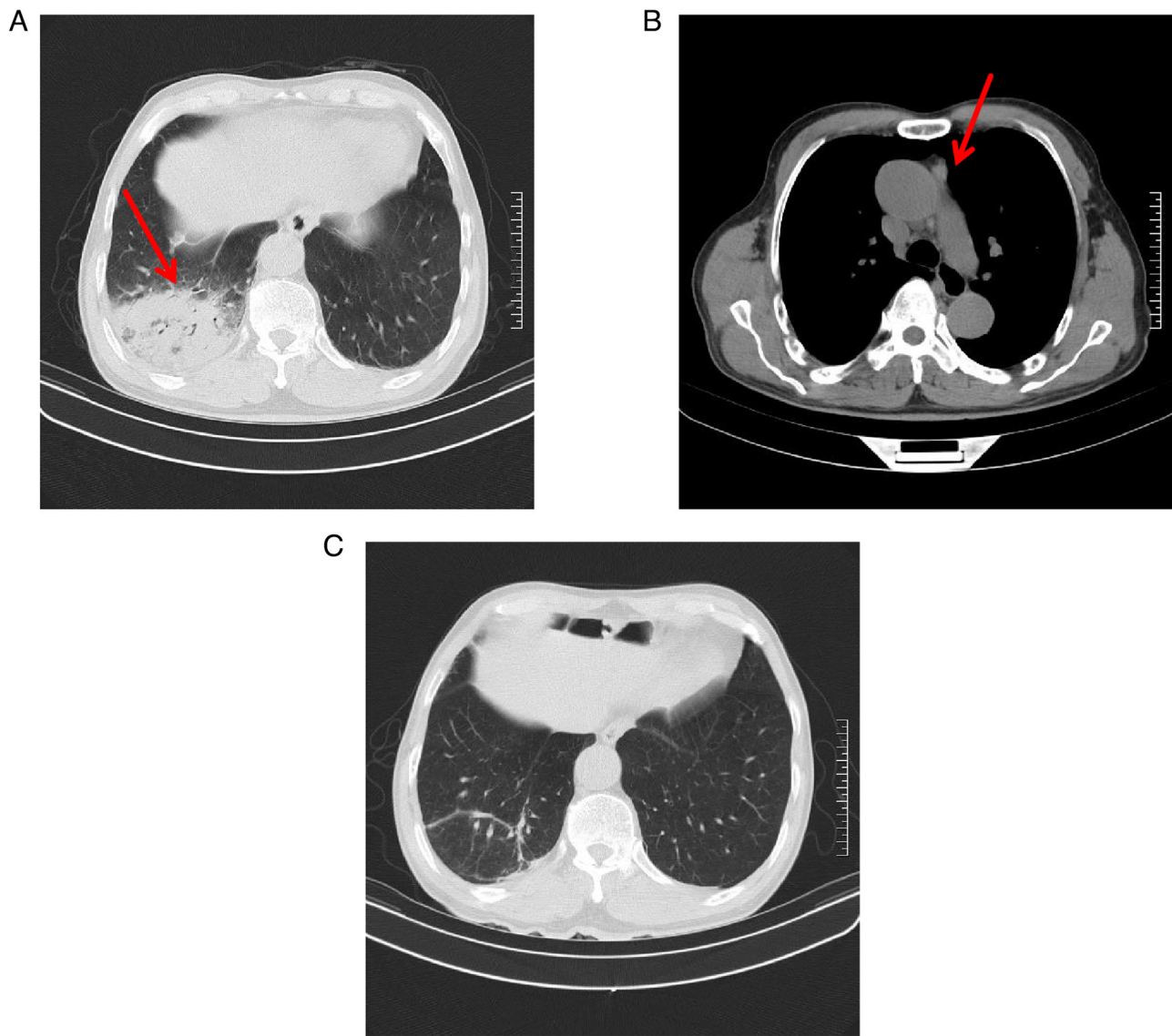


Figure 1. Results of chest CT examination in April 2021. (A) A patchy hyperdense shadow in the lower part of the right lung with partial consolidation, as well as (B) a soft tissue nodule in the anterior mediastinum with a size of $\sim 1.8 \times 2.0$ cm (indicated by red arrow). (C) Re-examination of chest CT in May 2022 showed a patchy hyperdense shadow in the lower lobe of the right lung with partial consolidation, which was evidently absorbed compared with the CT scan carried out in April 2021. CT, computed tomography.

Ltd (Hangzhou, China). Usually CT images of cytomegalovirus pneumonia are characterized by multiple patchy or diffuse ground-glass nodules in both lungs; however, the CT image of the present patient showed a large patchy consolidation of the lungs (Fig. 1A). Combined with CT images and poultry contact history, the patient was initially diagnosed with *C. psittaci* pneumonia, but did not rule out cytomegalovirus infection. The treatment regimen was adjusted to 100 mg doxycycline twice a day and 0.5 g imipenem cilastatin q6h for a duration of 10 days. A re-examination of chest CT in May 2022 showed a significant reduction in lung lesions (Fig. 1C). The absence of evidence generated through imaging that would point towards cytomegalovirus infection as well as the observation that absorption of inflammatory lesions following treatment of *C. psittaci* infection without treating a possible cytomegalovirus infection confirmed that cytomegalovirus was not the causative pathogen.

Positron emission tomography-CT carried out during patient hospitalization in April 2021 revealed a nodule in the

ascending aorta of the anterior mediastinum with increased fluorodeoxyglucose metabolism. Thymoma was suspected, and classified as mild aggressive and B2 grade (World Health Organization histologic classification divided thymomas into A, AB, B1, B2, B3 and C according to the degree of malignancy) (3). In May 2021, the patient underwent thoroscopic resection of the mediastinal lesion. Intraoperative exploration confirmed the presence of a visible nodule measuring $\sim 2.1 \times 1.6$ cm on the left side of the ascending aorta in the anterior mediastinum, involving the pericardium. Pathological examination revealed tumor infiltration in a lobular pattern with fibrous septa (Fig. 2A), vascular invasion (Fig. 2B) and evident perivascular interstitial space (Fig. 2C) under the low-power lens. The high-power lens showed round- to oval-shaped tumor cells with deeply stained nuclear chromatin, increased nuclear-to-cytoplasmic ratio and notable cell atypia (Fig. 2D). Immunohistochemistry (IHC) results showed CD20⁺ B lymphocytes (+), CD5 (+), CD117 (+), TdT (-), CK19

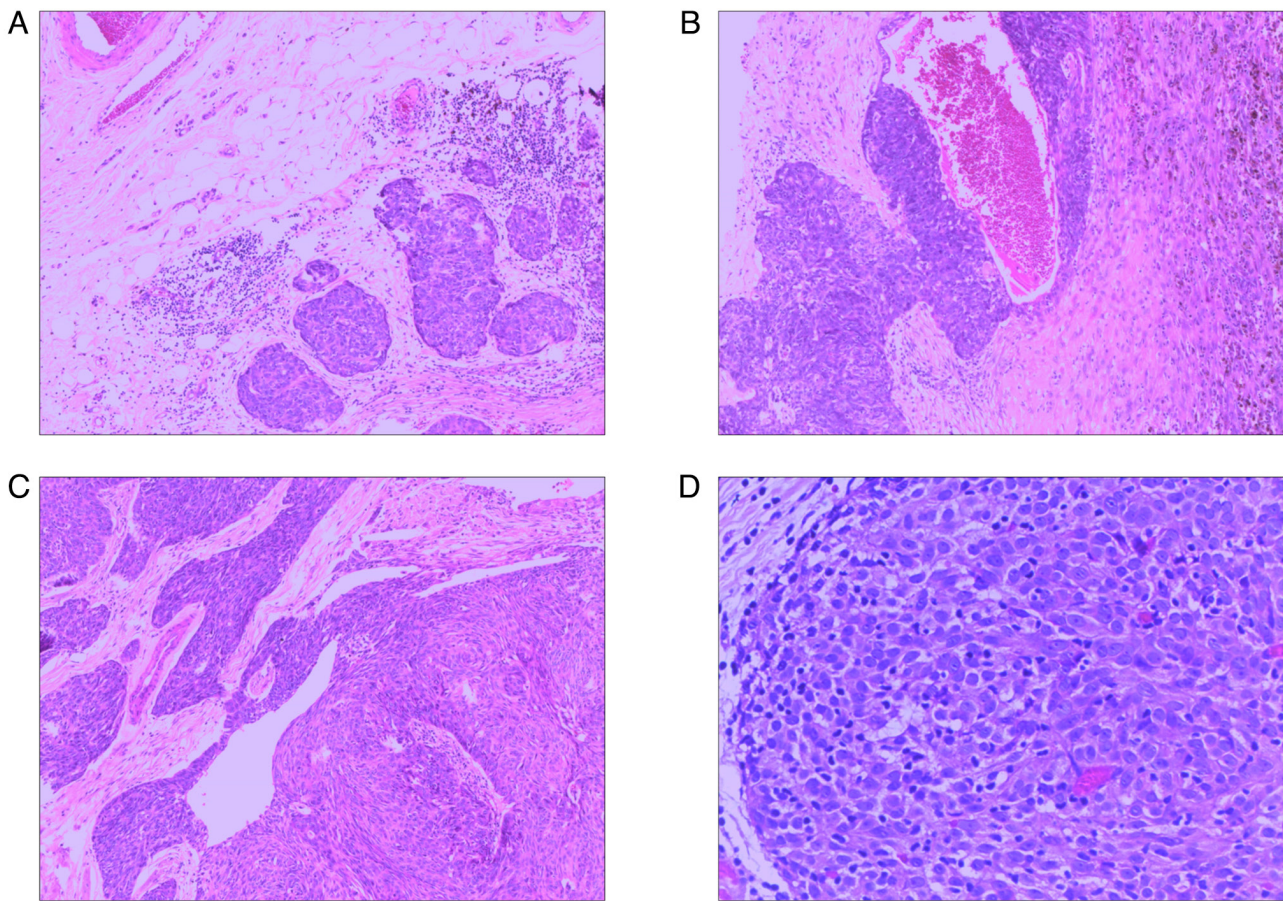


Figure 2. Pathological examination involving hematoxylin and eosin staining. (A) Invasion of tumor tissue into surrounding tissue (magnification, x50). (B) Invasion of tumor tissue into blood vessels (magnification, x50). (C) Perivascular space visible in tumor tissue (magnification, x50). (D) Tumor cells (magnification, x200).

(+), AE1/AE3 (+), P63 (+) and P53 partial (+) in Fig. 3A-H. Based on the morphology and the IHC results, the diagnosis of a rare type B3 thymoma was established [CD5 (+), CD117(+) and TdT(-)] (1). The patient recovered well after surgery and was discharged in May 2021.

Re-examination chest CT in May 2021 revealed no abnormalities (Fig. 4A and B). Subsequent routine follow-up chest CT scans in March and October 2022 revealed no abnormalities at the surgical site and absorption of the original lung lesion with no evidence of recurrence was noted (Fig. 5A-D).

Discussion

In the current case report, the patient presented with an acute onset of symptoms, including high fever, and was admitted at the Second Affiliated Hospital of Jiaxing University. Laboratory tests showed a normal white blood cell count and an increased neutrophil percentage, while a CT scan revealed pulmonary inflammation. Immunocompromised patients without acquired immunodeficiency syndrome, who have cytomegalovirus pneumonia, generally demonstrate a combination of ground-glass attenuation, air-space consolidation and small nodules on HRCT (4). Although mNGS results showed cytomegalovirus infection, CT scan was more inclined to *Chlamydia psittaci* pneumonia. Additionally, during the diagnostic process for identifying the pathogen, a mediastinal mass

was incidentally identified. *C. psittaci* pneumonia accounts for ~1% of community-acquired pneumonia cases (2). Most patients with this condition have a history of contact with infected birds or poultry (5).

The patient in the present case report also had extensive patchy lungconsolidation. Conventional anti-infection therapy was not effective. The detection of *C. psittaci* in the bronchoalveolar lavage fluid of the patient using mNGS confirmed the diagnosis. The clinical manifestations and examination results of the patient were consistent with those of previous studies (6), supporting a relatively typical case of *C. psittaci* pneumonia. Additionally, the patient had a concurrent type B3 thymoma, and it is known that patients with this type of thymoma often have immune dysfunction (7,8), which may explain possible co-infection with cytomegalovirus. In patients with type B3 thymoma and infection with *C. psittaci*, the disease can progress rapidly, potentially leading to severe pneumonia, multiple organ failure and death if not treated in time (9).

The incidence rate of thymoma in China is ~3.93 cases per million (10), with type B3 accounting for ~13% of all cases. B3 thymoma has a higher degree of malignancy and aggressiveness compared with other subtypes (11). Patients with type B3 thymoma may be asymptomatic and are often incidentally diagnosed during physical examination or routine check-ups. As the tumor grows, a subset of patients may experience symptoms such as chest tightness and pain,

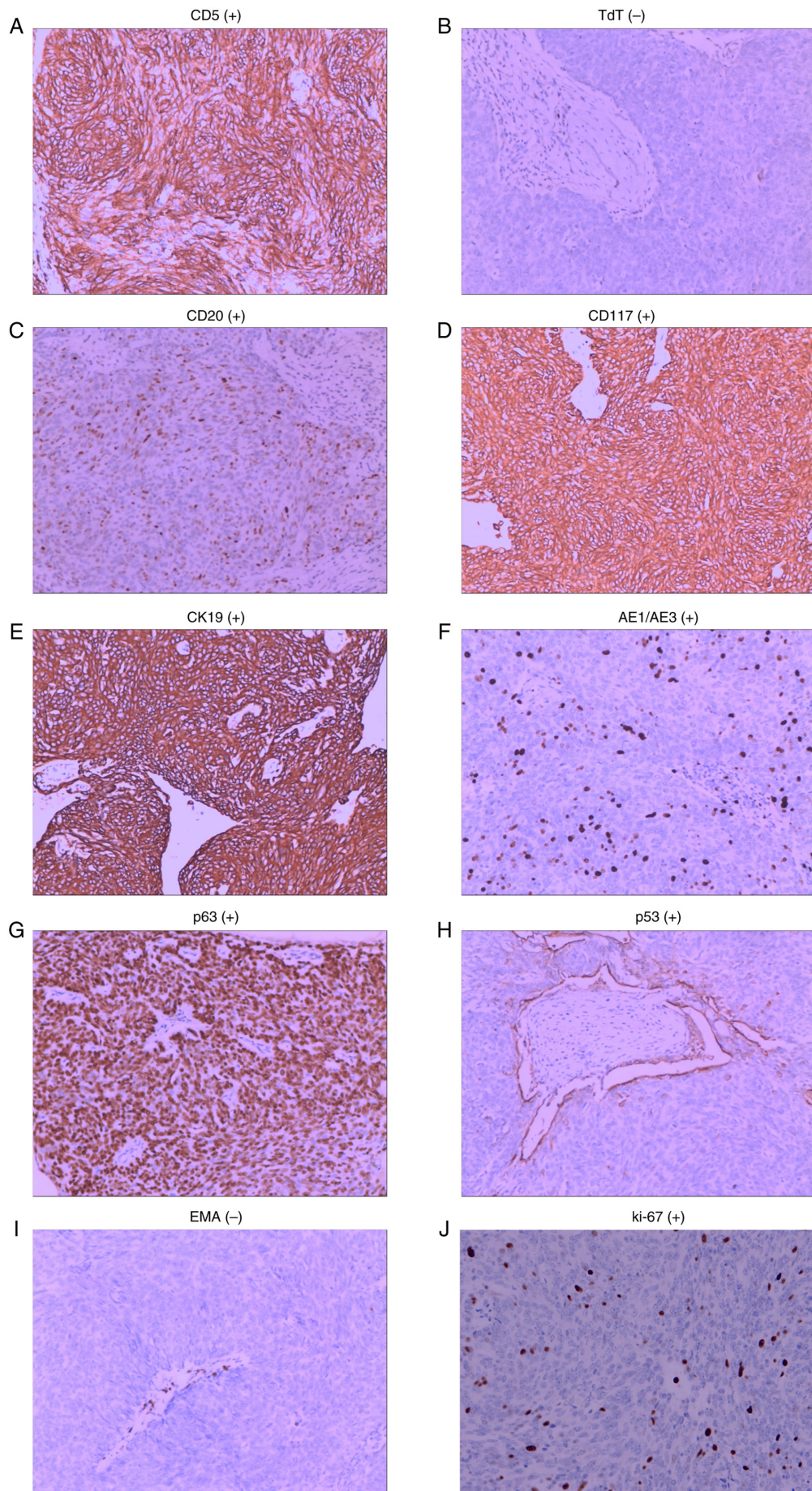


Figure 3. Immunohistochemical staining. (A) Diffuse expression of CD5 in tumor tissues. (B) TdT (-) stained lymphocytes; (C) CD20 (+); (D) CD117 (+); (E) CK19 (+); (F) AE1/AE3 (+); (G) p63 (+); (H) p53 (+); (I) EMA (-); and (J) ki-67 (+). Magnification, x200.

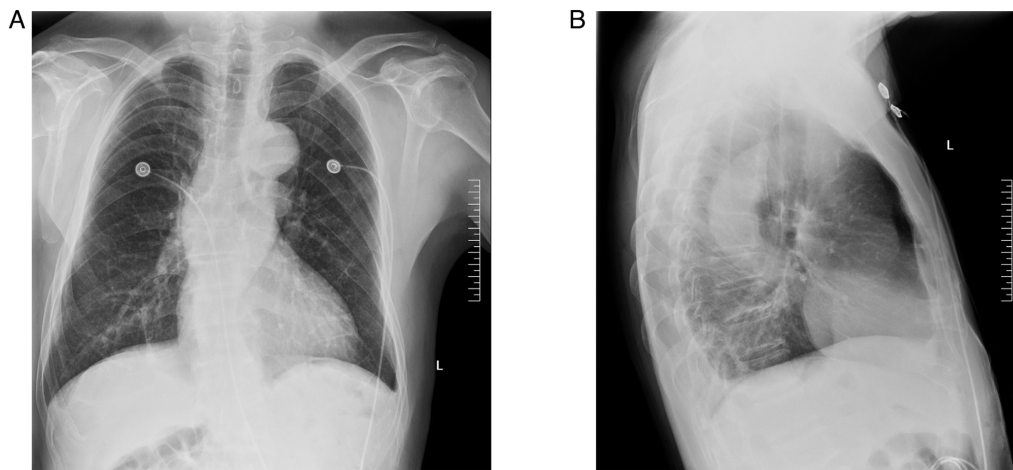


Figure 4. X-ray performed in May 2021. (A) Anteroposterior film, after thoracoscopic mediastinal lesion resection, clear lung fields with no substantial lesions were observed in both lungs. (B) Lateral film, no obvious abnormality in the lungs.

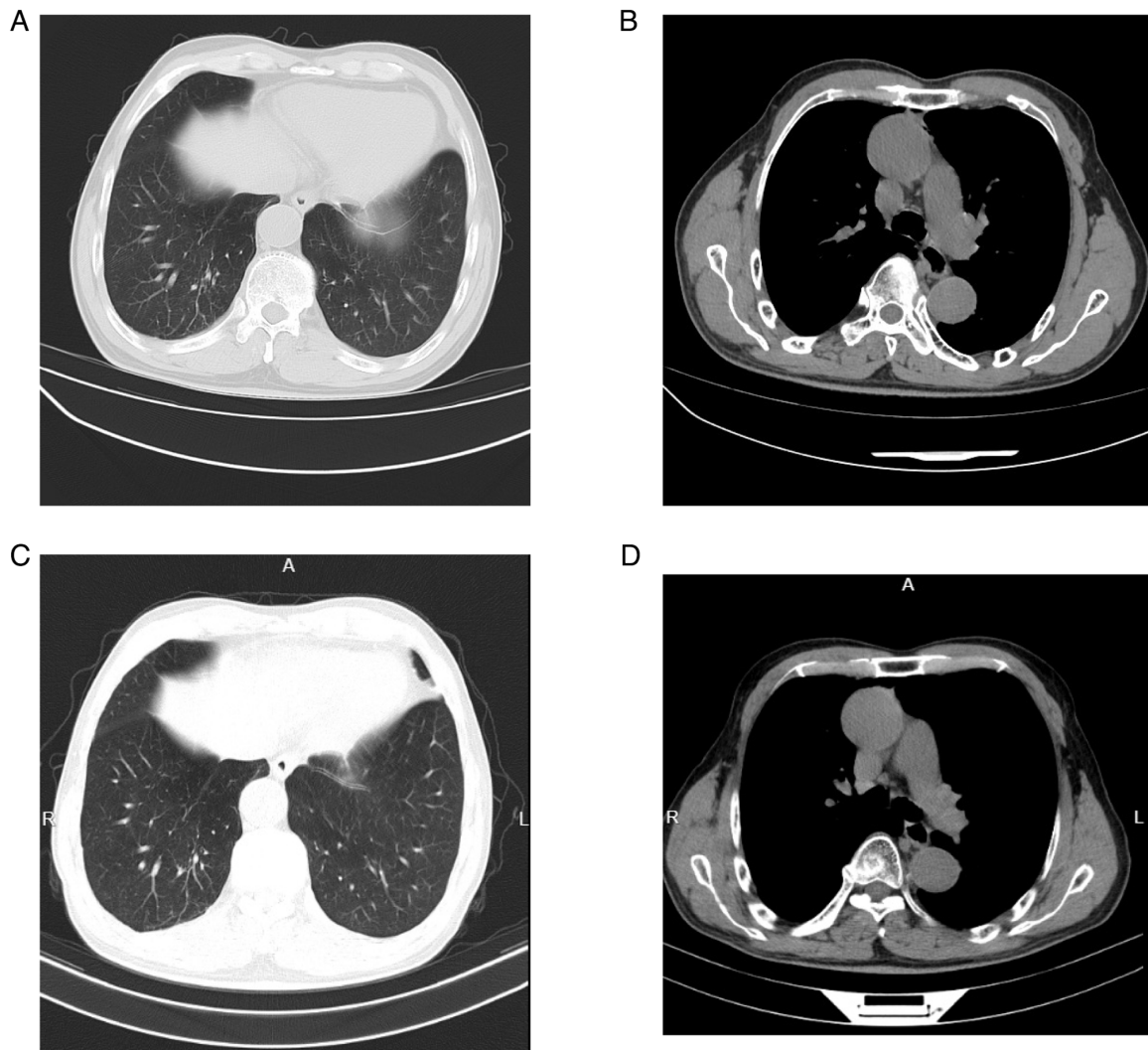


Figure 5. Results of the chest CT examination in March 2022. (A) A dense cord-like shadow in the lower lobe of the right lung, and (B) the thymoma results after resection. The results of the chest CT examination in October 2022 showed (C) no obvious abnormalities in the right lower lung, and (D) the thymoma results after resection. CT, computed tomography.

head and facial swelling, which may be accompanied by autoimmune diseases (12). In the present case report, the

patient was shown to have a mediastinal mass and no history of other immune diseases.

Tetracycline is the first-line treatment for *C. psittaci* pneumonia, with a recommended treatment duration of 10-14 days (13). After inhalation through the respiratory tract, *C. psittaci* first enters the bloodstream and proliferates in the liver, spleen and mononuclear macrophage system, and then involves the lungs, spleen, liver, kidneys and central nervous system through hematogenous dissemination (9). In patients with immune deficiency or malignant tumors, *C. psittaci* infection tends to involve the lungs and other systemic organs earlier (1). Therefore, early control of infection is necessary, and targeted treatments should be considered based on the organs affected.

In the present case report, *C. psittaci* infection was mainly confined to the lungs and did not involve the liver, kidneys or other organs. The treatment plan was the same as that for conventional cases of *C. psittaci* pneumonia, and the patient responded well to treatment, which may be attributed to the early and accurate pathogen identification, allowing for timely adjustment of the treatment plan. A previous study has shown that patients with thymoma have a higher risk of bacterial or viral infection associated with more severe cellular immunodeficiency compared with those without thymoma (14). Agarwal and Cunningham-Rundle' showed that ring-formed parasites in red blood cells are in the peripheral blood smear of a patient with thymoma (15). Another report showed that there are multiple viral particles or viral genes such as cytomegalovirus, enterovirus and herpes simplex virus in patients with thymoma, which is related to thymoma disease (16). To the best of our knowledge, there is little evidence of an association between chlamydia infection and thymoma. Therefore, it was hypothesized that thymoma can indirectly increase the susceptibility to *C. psittaci* infection in humans.

After complete resection of the thymoma, the patient was recommended to undergo adjuvant radiotherapy and chemotherapy but they declined. No tumor recurrence was observed during the routine 17-month follow-up after surgery. Currently, there is no consensus guidelines on the treatment of type B3 thymoma, but complete resection is generally considered an important independent prognostic factor (5). Treatment strategies mainly involve surgical resection followed by adjuvant radiotherapy and chemotherapy. Type B3 thymoma has a poor prognosis with reported 5- and 10-year survival rates of 84 and 65%, respectively, and ~22% of patients experience postoperative recurrence (11). Therefore, long-term follow-up is recommended for these patients to investigate survival time and recurrence status.

The current report presents the case of a patient with type B3 thymoma [CD5 (+), CD117 (+) and TdT (-)] comorbid with *C. psittaci* pneumonia exhibiting rare features. There is limited research on type B3 thymoma, and the biological behaviors of the tumor remain unclear. Additionally, *C. psittaci* pneumonia is not commonly encountered in clinical practice. A higher number of cases and in-depth research are needed to understand the clinical characteristics and prognosis of patients with type B3 thymoma comorbid with *C. psittaci* pneumonia.

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Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Authors' contributions

JJ, HW and JD performed conception and design of the study. JJ, JD, XH, XY, WM and HW performed acquisition of the data and medical images, analysis and interpretation of data. JJ and HW prepared the manuscript, performed critical revision and gave final approval. JJ and HW confirm the authenticity of all the raw data. All authors read and approved the final version of the manuscript.

Ethics approval and consent to participate

This study complied with the tenets of the Declaration of Helsinki and was approved by the Medical Ethics Committee of the Second Affiliated Hospital of Jiaxing University (approval no. JXEY-2022SW067). The patient provided verbal and written consent for publication.

Patient consent for publication

A written consent from the patient was obtained prior to collecting the case material and accompanying images, operating histopathological biopsy, writing the final manuscript and publishing the case report.

Competing interests

The authors declare that they have no competing interests.

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