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Case Report

Bordetella pertussis pneumonia in adults: two case reports and diagnostic challenges

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Abstract

Introduction: In recent years, the number of pertussis cases has increased remarkably in our country and globally. However, the prevalence of pertussis in adolescents and adults is severely underestimated due to atypical symptoms. Here, we present two cases of pneumonia caused by *Bordetella pertussis* (*B. pertussis*) that were successfully treated, with etiologic diagnosis aided by targeted next-generation sequencing (tNGS).
Case Study: The first case involves a young man initially misdiagnosed with an acute attack of bronchial asthma and treated with corticosteroids therapy. The second case involves a man with hypoxemia who was co-infected with *Streptococcus pneumoniae* during treatment. In both cases, routine laboratory examinations for pathogen detection were negative. The bronchoalveolar lavage fluid (BALF) of patients was sent for tNGS, which identified sequence reads of *B. pertussis*.
Results: The diagnosis of the two cases was confirmed by tNGS detecting B. pertussis, and the patients showed positive results after treatment.
Conclusions: Adults with *B. pertussis* infection serve as an important source of infection and are frequently underdiagnosed or misdiagnosed. Early diagnosis and treatment can be achieved through typical cough symptoms and molecular biology tests.

Key words: *Bordetella pertussis*; pneumonia; targeted next-generation sequencing; tNGS; paroxysmal cough.

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Introduction

Pertussis, caused by *Bordetella pertussis* (*B. pertussis*), is a highly contagious respiratory tract infection associated with significant morbidity and mortality, particularly in young infants. The incidence of pertussis has decreased dramatically since the diphtheria-tetanus-pertussis (DTP3) vaccine. However, pertussis has not been eradicated, and small epidemics occur every three to five years. The prevalence of pertussis in adolescents and adults is severely underestimated due to atypical symptoms [1,2].

To the best of our knowledge, pneumonia due to *B. pertussis* is rare, and patients are often delayed in diagnosis. Here, we present two cases of pneumonia caused by *B. pertussis* that were successfully treated, with etiologic diagnosis aided by targeted next-generation sequencing (tNGS). By sharing the treatment history of these two patients, clinicians will have a better understanding of pertussis pneumonia.

Cases presentation

Case 1

A 37-year-old man presented with a cough and yellow sputum half a month prior. The yellow sputum decreased after the patient took amoxicillin. However, thirty minutes before admission, the patient experienced respiratory distress after a severe coughing episode. The emergency physician was hearing barking breathing, and physical examination was revealing audible rales in both lungs. An urgent chest computed tomography (CT) revealed patchy blurred shadows in the upper lobes of both lungs and the right middle lobe of the lungs. Neck CT showed no epiglottic swelling. The peripheral blood test revealed a white blood cell (WBC) count of 17.56×10^9/L. However, C-reactive protein (CRP) and procalcitonin (PCT) were normal. And liver, renal, coagulation, and myocardial-related tests were all normal. The patient was diagnosed with an acute attack of bronchial asthma and was treated with oxygen, prednisone acetate to reduce airway spasm, and levofloxacin empirical anti-infective therapy. The next day, the patient's dyspnea symptoms disappeared. To rule out concurrent tuberculosis infection, the patient underwent bronchoscopy, and lavage fluid was sent for tNGS. The results of the gene sequencing were unexpected. tNGS results *B. pertussis* (sequence reads 500) and rhinovirus type C (sequence reads 37121). No *Mycobacterium tuberculosis* was found. Finally, the patient was diagnosed with pertussis pneumonia and treated with azithromycin for one week. The patient's symptoms of cough and sputum were alleviated, and the chest CT re-examination showed that the bilateral pneumonia was improved (Figure 1, Table 1).

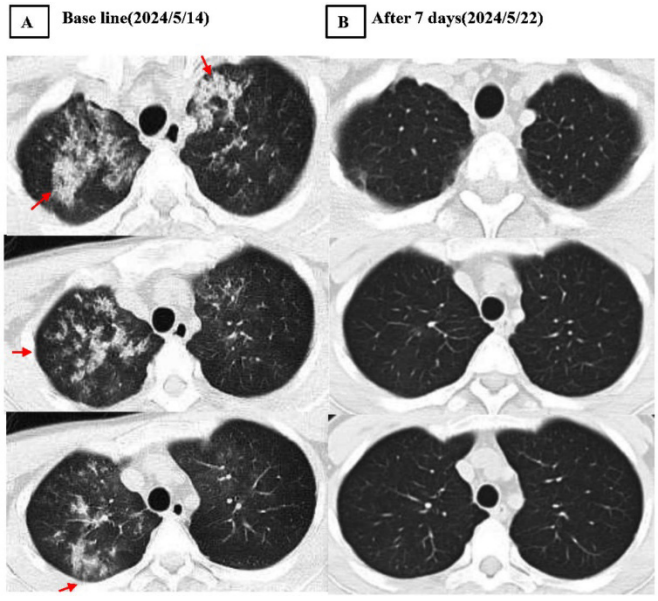
Table 1. Main laboratory indexes of two cases with *B. pertussis*.

	Blood routine				Arterial blood gas analysis				Biochemical indexes					tNGS
	Date	WBC	NEU	LYM	CRP	PH	PO2	PCO2	P/F	ALT	AST	ALP	GGT	-
Case 1	5.14	17.56	15.86	1.02	0.28	7.43	181	38	402	19	23	56	77	*Bordetella pertussis* (500), Rhinovirus C (37121)
	5.22	8.44	4.2	1.11	0.25	-	-	-	-	-	-	-	-	-
Case 2	7.20	18.64	14.22	3.63	214.45	7.45	61	36	290	90	74	163	260	*Bordetella pertussis* (230323), Human gammaherpesvirus 4 (1741), *Mycobacteroides chelonae* (60)
	7.31	14.73	9.23	4.15	16.56	7.43	73	38	348	53	28	142	199	*Streptococcus pneumoniae* (460), *Bordetella pertussis* (213), Human betaherpesvirus7 (7110), Human gammaherpesvirus 4 (1478)
	8.19	8.91	4.92	2.84	4.26	7.41	75	40	357	73	31	140	73	-

Case 2

A 39-year-old man presented to our hospital with a cough and sputum for one week. The patient was treated with cefuroxime, but the cough was not relieved. Even the patient developed dyspnea after climbing stairs. The patient's transcutaneous oxygen saturation was 88% at the time of admission to the hospital. Lung auscultation revealed no moist rales. Chest CT showed scattered inflammation in both lungs, with significant inflammation in the right lung. Peripheral blood count revealed WBC counts of 18.64 × 10^9/L, Lymphocyte counts of 3.63×10^9/L, and CRP levels of 214.45 mg/L. Liver function tests with elevated values of several transaminases. Arterial blood gas showed a significant decrease in oxygen partial pressure and oxygenation index. Therefore, high-flow nasal cannula oxygen therapy (HFNC) was given for assisted breathing. Levofloxacin was used as an anti-infective and glutathione hepatoprotective treatment. Bronchial mucosal congestion and copious purulent secretions were seen under electronic bronchoscopy. Bronchoalveolar lavage fluid (BALF) cultures were negative. But *B. pertussis* was identified by tNGS in the BALF, which was further confirmed by real-time polymerase chain reaction (RT-PCR) assay. After eleven days of treatment, the patient's cough and sputum symptoms were not relieved. The chest CT re-examination showed that multiple patchy solid shadows in bilateral pneumonic were increased compared to the previous one. Additionally, the WBC count level remained high. Subsequently, in the renewed BALF, we found *Streptococcus pneumoniae*, in addition to *B. pertussis*. Considering a mixed bacterial infection, the patient was treated with oral compound sulfamethoxazole and piperacillin-tazobactam. After two months, the chest CT showed reduced inflammation, and the patient's cough and sputum symptoms improved (Figure 2, Table 1).

Figure 1. The chest computed tomography CT of case 1.

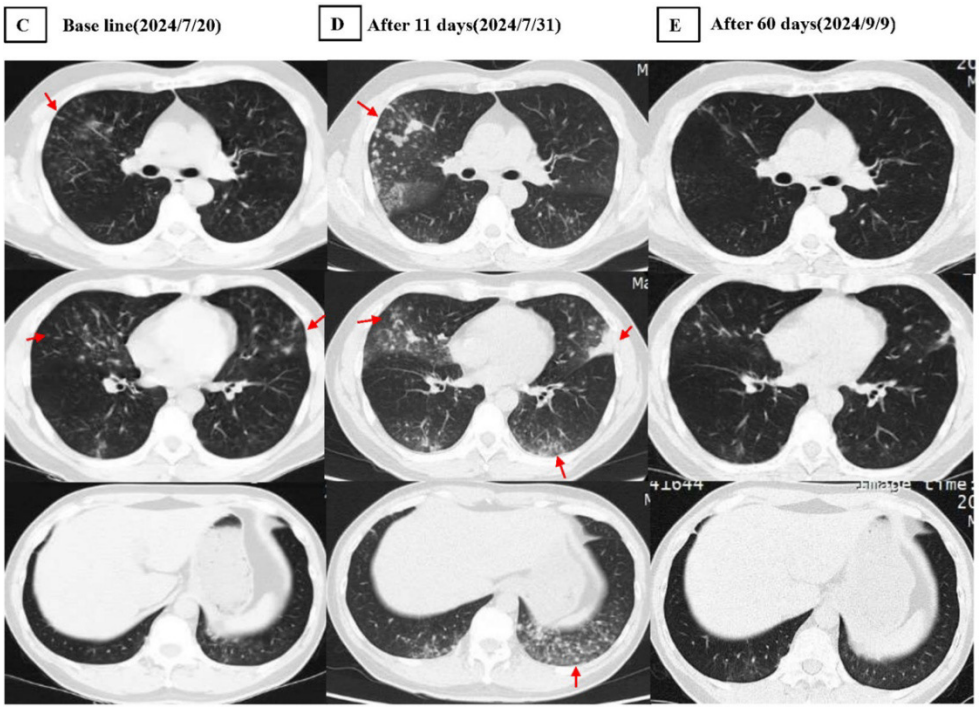


The chest CT showed that patchy blurred shadows in the upper lobes of both lungs and the right middle lobe of the lungs (A). After seven days of treatment, the inflammatory exudate from the lungs was largely absorbed (B).

Discussion

In recent years, the number of pertussis cases has increased significantly in our country and globally. Many factors contribute to this phenomenon. Pertussis nearly vanished alongside other respiratory infections following the implementation of non-pharmaceutical interventions in 2020 to reduce COVID-19 transmission [3]. It has been shown that 90% of adults visiting outpatient clinics lack protective antibody levels for pertussis [4]. This rise in pertussis cases may partly be attributed to waning immunity (protection from disease) among adults who were vaccinated during childhood [5]. Additionally, the widespread use of NGS has improved the detection rate of *B. pertussis*.

Figure 2. The chest computed tomography CT of case 2.



The chest CT showed that scattered inflammation in both lungs (C). After eleven days of treatment, the chest CT re-examination showed that multiple patchy solid shadows in bilateral pneumonic was increased (D). After two months, the overall trend of chest CT was decreased inflammation (E).

Pertussis is known to be underdiagnosed in adults, partly because the public and clinicians often regard pertussis as a childhood disease, so it is not considered. Moreover, pertussis is difficult to distinguish from other acute cough syndromes in adults [6]. In adult patients with pertussis, paroxysmal cough has a high sensitivity (93.2%) and low specificity (20.6%), whereas vomiting after coughing has low sensitivity (32.5%) and high specificity (77.7%) [7]. Ahmet [8] found that the prevalence of pertussis among adult patients presenting with acute cough was 3.5%, with the mean duration of paroxysmal cough within pertussis-positive cases lasting 20 days. It is known that there may be delays in the diagnosis because of not considering pertussis as a priority in differential diagnosis, even if the patients are admitted early.

Pertussis is difficult to distinguish from other acute cough syndromes in adults, particularly since some adult patients do not exhibit typical coughing symptoms. For example, bronchial asthma, acute exacerbation of chronic obstructive pulmonary disease (COPD), endobronchial tuberculosis, and so on. Therefore, auxiliary diagnostic methods are necessary to identify the underlying cause. It has been reported that patients with bronchial asthma have much higher values of exhaled nitric oxide than patients with pertussis (56.9 ± 20.3 ppb vs 18.2 ± 9.2 ppb, $p < 0.001$) [9]. Pneumonia can occur as a complication in a small percentage of pertussis patients. Chest CT findings in pertussis pneumonia typically include speckled and patchy exudates, solid lung lesions, and, in rare cases, pleural effusion. The most direct method for diagnosing pertussis is tNGS, which offers higher sensitivity, precision, and shorter processing times compared to bacterial culture and serological testing.

Clinical guidelines recommend azithromycin as the first-line treatment for neonates with pertussis. One study demonstrated that in the case of macrolide-susceptible strains, patients had a higher rate of bacterial clearance in the nasopharynx after 14 days of treatment with macrolides than with beta-lactams (80.0% vs. 58.8%) [10]. However, in China, the resistance rate to azithromycin exceeds 70%. For azithromycin-resistant patients with pertussis, cotrimoxazole is the preferred treatment for adults [11]. In Case 1, the patient was presumed to have a macrolide-sensitive strain of pertussis. In contrast, the patient in Case 2, who presented with hypoxemia, was treated with cotrimoxazole combined with piperacillin-tazobactam. The extended duration of anti-infective treatment was due to bacterial co-infection.

Conclusions

Adults infected with *B. pertussis* are a significant

source of transmission, yet the condition is frequently underdiagnosed or misdiagnosed. Many guidelines now recommend having a pertussis booster dose in adulthood in a way that one of the tetanus-diphtheria boosters be replaced by a tetanus-diphtheria-acellular pertussis (Tdap) booster [12]. Early detection and proper treatment of pertussis can reduce the transmission of the infection.

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Authors' Contributions

Ling Deng: Write a draft of the article; Zhong Hu: Collect case information and review literature; Jin Wang: Proofread the manuscript

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Conflict of interest

No conflict of interest is declared.

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