

## CASE REPORT

# Squawks as an important physical finding for differentiation of diffuse panbronchiolitis from asthma in children: A case report

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## Abstract

Diffuse panbronchiolitis (DPB) is an idiopathic chronic inflammatory pulmonary disease clinically characterized by cough, sputum, and chronic sinusitis. Although the average age of onset is 40 years, DPB occasionally occurs in children and is often misdiagnosed as asthma. Long-term therapy with macrolide antibiotics significantly improves survival in DPB. Herein, we report the case of a 16-year-old man who had been treated for asthma and was referred to our department as transition from the Department of Pediatrics. Adequate auscultation to detect squawks and history taking of purulent sputum led to the correct diagnosis and appropriate treatment, which improved his quality of life.

## KEYWORDS

asthma, diffuse panbronchiolitis, squawk

## 1 | BACKGROUND

Diffuse panbronchiolitis (DPB) is an idiopathic chronic inflammatory pulmonary disease of the bilateral lungs that is clinically characterized by cough, sputum, dyspnea, and chronic sinusitis.<sup>1</sup> The average age of onset of DPB is 40 years; it has rarely been reported in children and is mistaken for asthma.<sup>2</sup> Untreated DPB can result in bronchiectasis and respiratory failure.<sup>1</sup> Long-term therapy with macrolide antibiotics significantly improves survival in DPB.<sup>1</sup> Therefore, early diagnosis of DPB is crucial, especially in children.

Herein, we report the case of a 16-year-old man who was previously treated for asthma. Adequate auscultation with the detection of squawks and history taking of purulent sputum led to the correct diagnosis and accurate treatment, which improved his quality of life.

## 2 | CASE PRESENTATION

A 16-year-old Japanese man presented with persistent dyspnea and fatigue. He had been diagnosed with asthma and had visited

several pediatricians since he was 1 year old. He had experienced an episode of recurrent respiratory infection for several years. Two months prior, his condition had exaggerated, and he had difficulty attending school. He was referred to the Department of General Internal Medicine for transition from the Department of Pediatrics.

The findings pertinent to his condition included rhinorrhea and nasal obstruction. Furthermore, he mentioned the discharge of large amounts of sputum when hiding at school. He was treated with inhaled budesonide/formoterol fumarate hydrate and leukotriene receptor antagonists; however, these drugs did not improve his symptoms.

Upon examination, the temperature, blood pressure, pulse, respiratory rate, and oxygen saturation while breathing ambient air was 36.5°C, 112/68 mmHg, 72 beats per minute, 20 breaths per minute, and 94%, respectively. Lung auscultation revealed early to mid- and late-inspiratory crackles and rhonchi in various lung fields. Notably, squawks were heard in the bilateral lower lungs, which had never been described in his medical charts. Other physical examination findings were unremarkable.

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Laboratory values were as follows: leukocyte count, 6400/ $\mu$ L (57% neutrophils, 34% lymphocytes, 5% monocytes, 3% eosinophils); hemoglobin, 14.4 g/dL; platelet count, 281,000/ $\mu$ L; creatinine, 0.5 mg/dL; C-reactive protein, 1.5 mg/dL (normal <0.3 mg/dL). His past sputum cultures revealed *Pseudomonas aeruginosa* and *Hemophilus influenzae* with a tendency toward antimicrobial resistance. Despite recurrent respiratory infections, the patient did not have immunodeficiency, such as primary immunodeficiency.

Chest radiography revealed granular shadows in both lower lung fields. Computed tomography (CT) of the chest performed at the time of our patient's referral revealed bilateral diffuse centrilobular infiltrative shadows with mucoid impaction and bronchial wall thickening but no bronchiectasis (Figure 1A). Similar findings were observed on past CT images (Figure 1B), taken 18 months earlier in the Department of Pediatrics; thus, acute exacerbation of bronchial asthma with bronchitis was considered. Lung function tests showed a decrease in forced expiratory volume in 1 s of 2.03 L (71.7% of predicted).

Although he had obstructive ventilatory deficit, squawks with purulent sputum and recurrent findings of diffuse centrilobular infiltrative shadows on CT led to the diagnosis of DPB, rather than asthma. Moreover, the patient's condition met the Ministry of Health and Welfare of Japan (MHLW) criteria in his for DPB, including a cold agglutinin titer of 256 (normal <64).

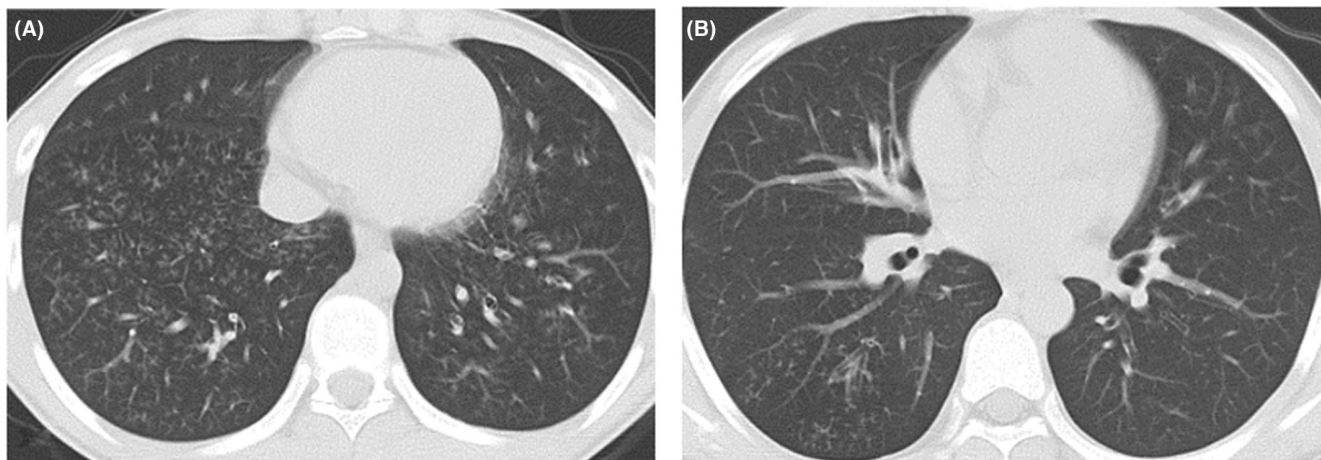
Macrolide antibiotics (erythromycin 200 mg/day to 400 mg/day) were initiated. In addition, when his respiratory symptoms worsened, his sputum culture was repeatedly submitted, and narrow-spectrum antibiotics were administered as needed. His sputum culture seldom detected *P. aeruginosa* and *H. influenzae*, which are often cultured in DPB.<sup>1</sup> Although he took a year off school due to his physical condition, he entered graduate school and was well enough to go to the beach and pool.

### 3 | DISCUSSION

Diffuse panbronchiolitis is an idiopathic chronic inflammatory pulmonary disease of the bilateral lungs characterized by bronchiolitis and chronic sinusitis.<sup>1</sup> The current diagnostic criteria for DPB are proposed by the MHLW: having all three major criteria (1: persistent cough, sputum, and exertional dyspnea; 2: history of recurrent chronic sinusitis; 3: bilateral diffuse small nodular shadows on plain chest X-ray film or centrilobular nodular shadows on chest CT images), and at least two of the three minor criteria (1: coarse crackles, occasionally wheezes, rhonchi, or squawks; 2: forced expiratory volume in 1 s /forced vital capacity <70% and partial pressure of oxygen <80 mmHg, 3: cold agglutinin titer  $\geq$ 64).<sup>3</sup>

The pathogenic mechanism of DPB remains unknown. Various genetic, environmental, and systemic factors may contribute to the development of this condition. In Japan, specific HLA haplotypes, such as HLA-B54, are associated with the development of DPB.<sup>4</sup> *Pseudomonas aeruginosa* can cause persistent airway inflammation and structural damage to the airway.<sup>5</sup> In our case, *P. aeruginosa* was detected until the initiation of long-term macrolide antibiotics and appropriate antibiotic use.

Although DPB typically occurs in middle age, it occasionally occurs in children and can be mistaken for asthma.<sup>2</sup> To the best of our knowledge, several cases of DPB in children have been reported after reevaluation of refractory asthma, similar to our case. None of these patients was correctly diagnosed at the initial presentation,<sup>2,6-8</sup> and the duration of misdiagnosis ranged from 6 months to 12 years. Although the patient was referred to our department for transition from pediatric to adult care with a diagnosis of refractory asthma, the presence of squawks and purulent sputum, which are atypical for asthma, led to the correct diagnosis. Although DPB is rare in children, these findings can help distinguish DPB from asthma.



**FIGURE 1** Computed tomography of the chest. (A) Computed tomography (CT) of the chest performed at the time of our patient's referral revealed bilateral diffuse centrilobular infiltrative shadows with mucoid impaction and bronchial wall thickening but no bronchiectasis. (B) Past CT images, taken 18 months earlier in the Department of Pediatrics, showed similar findings.

Squawks are unfamiliar abnormal lung sounds—short inspiratory wheezes that have been described in hypersensitivity pneumonitis, pneumonia, and interstitial lung disease.<sup>9</sup> Squawks, the key finding in our case, are listed as one of the MHLW criteria.<sup>3</sup>

Untreated DPB can result in bronchiectasis and respiratory failure.<sup>1</sup> Long-term macrolide antibiotics are crucial for DPB treatment.<sup>1</sup> Erythromycin therapy has been reported to improve symptoms, lung function, and survival rates.<sup>1</sup> The duration of treatment remains unclear, and most patients are treated for >6 months.<sup>10</sup> Our patient has been receiving treatment for over 5 years and is doing well.

## 4 | CONCLUSION

In conclusion, DPB occasionally occurs in children and is often misdiagnosed as asthma. DPB should be considered even in children with refractory asthma, especially if squawks and a history of purulent sputum are present.

### CONFLICT OF INTEREST STATEMENT

The authors have stated explicitly that there are no conflicts of interest in connection with this article.

### ETHICS STATEMENTS

This study has been approved by the research ethics committee of Fukuchiyama City Hospital.

### PATIENT CONSENT STATEMENT

The authors have obtained patient consent.

### CLINICAL TRIAL REGISTRATION

None.

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