

Follicular bronchiolitis in a child

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Background: Follicular bronchiolitis (FB) is an uncommon but important pulmonary manifestation in children.

Methods: In this report, we present the clinical presentations and histopathological data of an 8-year-old boy with FB.

Results: The patient had a history of recurrent cough and dyspnea for 5 years with progressive worsening of symptoms. An initial pulmonary function test showed an obstructive ventilatory defect. Chest X-ray demonstrated miliary nodules. High-resolution computed tomography showed reticulonodular opacification and central consolidation. Histopathological examination revealed that lymphoid follicles with reactive germinal centers distributed along the bronchioles. The boy responded favorably to corticosteroid therapy and recovered well.

Conclusions: Diagnosis of FB should be considered when a child presents with chronic bronchial obstruction. Open lung biopsy is necessary for confirmation of the diagnosis.

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Key words: diagnosis;
follicular bronchiolitis;
histopathology

Introduction

Follicular bronchiolitis (FB), first described by Bienenstock in 1973, is a rare childhood disease, histopathologically characterized by bronchiolar narrowing caused by external compression due to

lymphoid follicular hyperplasia and often associated with lymphocytic infiltration in the bronchiolar wall. FB is an uncommon but important pulmonary manifestation. In adults, most cases are associated with collagen vascular diseases, immunodeficiency, or hypersensitivity reaction. However, the etiology of the disease in children is unknown, and few cases have been reported. In this report, we present one case of pediatric FB with an emphasis on the clinical presentation and diagnostic modalities of the disease.

Case report

An 8-year-old boy was admitted to our hospital because of cough and dyspnea. He had a history of several hospital admissions for recurrent respiratory infections in the preceding 5 years. Bronchitis and pneumonia had been diagnosed in the previous admissions with progressively worsened symptoms. Increased respiratory rate (30/min) and intermittent cough were found on this admission.

Physical examination for the boy showed delayed growth compared with his normal peers (weight: 20 kg; height: 112 cm). Moderate moist rales were detected in the left infra-axillary region with an increased respiratory rate and a prolonged expiratory phase. Laboratory evaluation revealed a normal sweat chloride test, normal total blood cell count, and normal sputum culture. The results of immune workup were normal, including routine auto-antibody screening, test of T-cell response to mitogens, flow cytometry, phagocytosis assay as well as tuberculin skin test. An initial pulmonary function test (PFT) revealed a mild obstructive defect with a vital capacity of 56% of predicted, forced expiratory volume in the first second (FEV1)/forced vital capacity (FVC) of 59%, and flows at 50% and 75% of exhaled vital capacity were 61% and 52% of predicted, respectively. Chest X-ray demonstrated miliary nodules. High-resolution computed tomography (HR-CT) showed reticulonodular opacification and central consolidation. Flexible bronchoscopy revealed an inflamed tracheobronchial mucosa. The results of bronchoalveolar lavage fluid examinations were

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negative. An open lung biopsy showed that hyperplastic lymph follicles with germinal centers were located around the bronchi and bronchioli, with infiltration of interstitial lymphocytes and foam cells (Fig. A and B). Furthermore, staining showed that follicular structures were mainly constituted by CD20/CD79a-positive B cells and CD3/CD43-positive T cells in the pulmonary interstitial areas and the follicular surrounding places. The ratio of CD3/CD20 was about 60%.

The boy was not responsive to the treatment with antibiotics, but partially to bronchodilators

and corticosteroids. He had a normal growth and development during a 2-year follow up.

Discussion

The pathogenesis of FB remains unclear. It may be associated with airway hyperresponsiveness due to unknown antigen or latent infection. Primary FB is rare, particularly in children. No evidence suggests a close correlation between FB and connective tissue disorders. Recent studies have indicated that FB may be typical

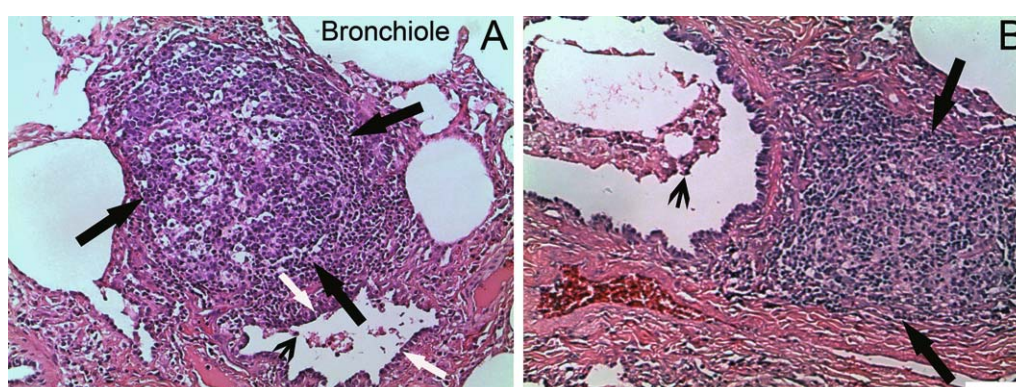


Fig. Histological features of follicular bronchiolitis. Hyperplastic lymphoid follicles with reactive germinal centers distributed along the bronchioles (black arrows, **A** and **B**), bronchiolar narrowing by external compression due to lymphoid follicular hyperplasia, and alveolar expansion (white arrows, **A**). Inflammatory cells leaked to the bronchiole cavity (arrow heads) (HE staining, scale bar = 100 μ m).

Table. The characteristics of children with follicular bronchiolitis reported in the literature

Year/n	Sex (F/M)	Age of first symptoms (n)	Symptoms (n)	Underlying disease (n)	Etiology (n)	Chest radiograph (n)	HR-CT (n)	Main histologic findings
1993/5 ^[3]	2/3	Birth (2); 10 d (1); 6 wk (2)	Respiratory distress (5); pyrexia (4); cough (2); TTN (1)	None (5)	None (5)	IP (5); PC (2)	-	FB
1995/1 ^[4]	-	-	-	Hypertrophic osteoarthropathy	Hypertrophic osteoarthropathy	IP	-	FB
1997/1 ^[5]	M	4 mon	Respiratory distress, cough, tachypnea, fever	None	None	Disseminated ill-defined nodular pattern	Centrilobular nodules, FB peribronchial nodules	
2001/2 ^[6]	1/1	5 mon (1) 1 y (1)	Cough and wheezing (2); dyspnea (1)	None (2)	None (2)	Bilateral patchy perihilar consolidations and reticular pattern of opacification (1),	Centrilobular nodules (1); bronchiectasis (2); emphysematous rarefaction of the parenchyma (1)	FB
2002/1 ^[7]	F	8 y	Respiratory distress and stridor	None	Legionella pneumophila	-	-	FB
2007/1 ^[8]	F	8 y	Recurrent hemoptysis	Lung abscess	None	Abscess cavity	Abscess cavity	FB
2008/1 ^[9]	F	8 y	-	HIV	HIV	Miliary nodules and perihilar consolidation	Reticulonodular opacification and central consolidation	FB
Present/1	M	3.2 y	Recurrent cough, and tachypnea	None	MP and CP	IP	Centrilobular nodules	FB

F: female; M: male; HIV: human immunodeficiency virus; IP: interstitial pneumonia; PC: pneumocystic carinii; MP: mycoplasma pneumoniae; CP: chlamydia pneumoniae; HR-CT: high-resolution computed tomography; FB: follicular bronchiolitis.

changes belonging to nylon, floc-related interstitial lung diseases.^[1,2] We reviewed all 13 cases reported in the literature over the last two decades, and found that the causes of 69.2% (9/13) of the pediatric cases were unknown. Few cases might be resulted from connective tissue disorders, immunodeficiency syndromes, or serious infections (Table).^[3-9]

Most patients with FB present with cough, dyspnea, respiratory distress, tachypnea, or pyrexia. The symptomatology in children also includes recurrent hemoptysis, failure to thrive, tachypnea, paratrophy, and growth lag. The onset of symptoms ranges from early infancy to adolescence (Table). The diagnostic modality includes chest radiography, PFT, HR-CT, and open lung biopsy. PFT generally reveals either an obstructive or a restrictive ventilatory defect; mixed defects and nearly normal lung functions have also been reported. Nonspecific characteristics of chest radiograph findings during the acute period of FB such as bronchiectasis/bronchiolectasis and emphysema are common. Characteristic chest radiograph findings for FB are gradually evident with bilateral interstitial disorders at subacute stage, including increased lung markings around the bronchus, mixed alveolar and interstitial infiltrates and consolidation or atelectasis. Radiological features may be normal during the recovery. It is important that FB in children could have an atypical radiological presentation such as the bilateral reticulonodular shadowing, which would be confused with other diseases such as miliary tuberculosis.^[3] Nodules were commonly found by HR-CT in a centrilobular distribution, ranging in size from 1 to 12 mm. Peribronchial nodules may also be present.

Open lung biopsy is necessary for confirmation of FB diagnosis since it is difficult to differentiate FB from other interstitial lung diseases only by clinical courses, laboratory findings and radiological features. Open lung biopsy is thought to be a safe procedure in children with diffuse interstitial lung disease, and contributes to the diagnosis and treatment of the challenging cases.

Treatment of FB is mainly directed against the primary diseases. Similar to previous reports, FB is associated with a generally good prognosis and responds

favorably to corticosteroid therapy. We conclude that FB can occur without underlying connective tissue diseases or immunodeficiency syndromes, and has a relatively favorable clinical course.

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Competing interest: None declared.

Contributors: Jiang KW wrote the main body of the article and reviewed the literature. Dai YW and Tang HF collected the data. Lin L collected part of the specimens.

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