Follicular Bronchiolitis in an Adult Male with Common Variable Immune Deficiency

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BACKGROUND

- Follicular bronchiolitis (FB) in patients with common variable immune deficiency (CVID) is rarely described and knowledge is based on case reports, case series, and studies on the individual disease entities.[1-5]
- FB is a granulomatous-lymphocytic interstitial lung disease (GLILD). GLILD is a group of non-infectious lung diseases which also includes lymphocytic interstitial pneumonia, granulomatous disease, and lymphoid hyperplasia.[6,7]
- FB is caused by an external stimulus or abnormal immune response that incites lymphoid hyperplasia.[8]
- The etiology of FB is idiopathic or associated with collagen vascular disorders (e.g., Sjogrens, rheumatoid arthritis), hypersensitivity reactions, acquired immunodeficiencies (typically HIV), and less commonly, primary immunodeficiencies.[9,10] In case reports, FB has also been linked to primary ciliary dyskinesia, multicentric Castleman's disease, primary tuberculosis, and eosinophilia with elevated IgE.[11-14]
- The differential diagnosis of FB includes other types of GLILD, low grade bronchus associated lymphoid tissue lymphoma, and sarcoidosis.[1]

CASE REPORT

The patient was a 43 year-old male with chronic obstructive pulmonary disease, obesity, sleep apnea, and allergic rhinitis who presented with increased dyspnea on exertion, chronic mild productive cough, and occasional wheezing. The patient's symptoms had previously improved with an ipratropium bromide/albuterol daily inhaler. Patient also had a 15 year history of recurrent sinopulmonary infections. At age 38, a chest radiograph demonstrated hilar adenopathy. At that time, bronchoscopy samples grew Mycobacterium gordanae and video assisted thorascopic surgery (VATS) lung biopsy showed a nonspecific lymphoid granulomatous process. It was thought to be noninfectious, and acid fast bacilli(AFB) stain was negative. He worked in a steel mill as a maintenance coordinator and was a member of the Hazmat and Fire Rescue team. The patient had a history of hives in reaction to penicillin and the tetanus vaccine. His family history was negative for collagen vascular disorders or immunodeficiency.

On examination, the patient's oxygen saturation was 97% on room air, respiratory rate 20 breaths per minute, and lungs were clear to auscultation bilaterally. He had a BMI of 33 kg/m^2 and slight left tympanic membrane retraction with scar. Pulmonary function testing (PFT) revealed a small airway obstructive pattern, FVC 4.7L(82%), FEV1 3.08L(68%), FEV1/FVC 65.5%(82%), FEF25-75 1.78L(41%).

CLINICAL COURSE

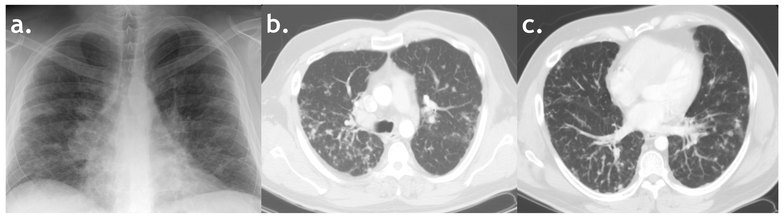

Figure 1. a) Chest radiograph shows an increase in interstitial markings and hilar adenopathy. Computed tomography demonstrates b) ground glass peribronchovascular nodules in tree and bud appearance and c) peribronchial thickening.

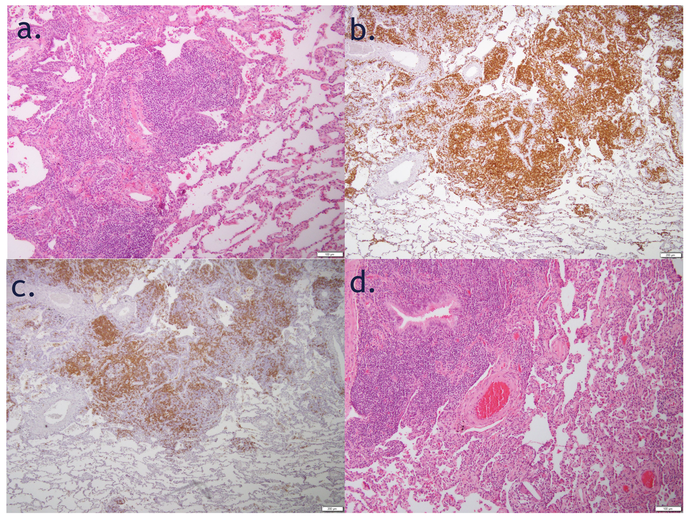

Figure 2. Lung biopsy with a) H&E staining reveals dense lymphoid aggregates with germinal centers around bronchioles with normal interstitium. b) CD3 staining shows the T-cell lymphocytes forming lymphoid aggregates around bronchioles. c) CD20 staining shows B-cell lymphocytes forming germinal centers within the lymphoid aggregates and also demonstrates, together with CD3 staining, the polyclonal nature of the lymphoid infiltrate. d) Follicular bronchiolitis with adjacent alveolar wall thickening indicative of Nonspecific Interstitial Pneumonitis (NSIP).

Laboratory results showed undetectable immunoglobulins (IgA< 6 mg/dL, IgG< 200 mg/dL, and IgM< 25 mg/dL) and negative isohemagglutinins. White blood cell count, anti-neutrophil cytoplasmic antibody, and erythrocyte sedimentation rate were within normal limits. Tuberculosis skin test, HIV, AFB stains, hypersensitivity pneumonitis panel and gallium scan were negative. Imaging was concerning for interstitial lung disease (Figure 1).

CLINICAL COURSE

After a diagnosis of CVID was made, the patient was started on 400mg/kg of IVIG. VATS was performed, and lung biopsy revealed follicular bronchiolitis on histopathology (Figure 2). The patient was then started on prednisone 60mg daily and he was given a month of clarithromycin to treat a respiratory infection. He required a prolonged course of corticosteroids that were weaned over one year. Interval imaging revealed improvement in ground glass opacities but progression of patient's NSIP. The patient's subsequent course was complicated by pancytopenia requiring splenectomy, and diabetes. Despite IVIG replacement and improved IgG levels, the patient continued to have recurrent sinopulmonary infections and was prescribed daily doxycycline. Infections further decreased after a 40% increase in dose of IVIG. Today the patient's respiratory symptoms are much improved, and he has continued treatment with IVIG for over six years.

CONCLUSION

- FB in CVID is a rare disease and associated with reduced survival.[7]
- Diagnosis may be difficult due to common presenting symptoms as well as variable PFTs and imaging findings.[3,8]
- Current treatment of FB suggests treating the underlying immunodeficiency. Some case series report favorable outcomes with corticosteroids.[2,15,16] Cyclosporine and infliximab have been used in case reports for inability to tolerate steroids and disease refractory to steroids, respectively.[17,18] In terms of treatment, long term effects and efficacy of IVIG has not been studied.[6]
- This case is presented to enhance awareness and discuss our management strategy.
- Further research is required to improve outcomes and management strategies.

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