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A Rare Case of Bronchiectasis Due To Common Variable Immunodeficiency

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Abstract

Bronchiectasis is a suppurative lung disease of varied etiology out of which Common Variable immunodeficiency (CVID) is a unique cause. Generally, most cases do not require routine workup unless suspecting Primary Immunodeficiency disorders like CVID. The clinical presentation of bronchiectasis in CVID constitutes recurrent exacerbations, severe non-resolving pneumonias and permanent structural damage predisposing to infections with resistant organisms. CVID is characterized by low levels of immunoglobulins coupled with a failure to mount adequate immunologic response after vaccination with pneumococcal and tetanus vaccines. Management poses significant challenges with control of bronchiectasis exacerbations along with IV immunoglobulin infusion. A high index of suspicion should be maintained when dealing with severe cases of bronchiectasis that span over a prolonged period in early adulthood that lack strong predisposing factors.

Keywords:

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Common Variable Immunodeficiency (CVID), Primary Humoral Immuneodificiency (PHI), High Resolution Computed Tomography (HRCT), Bronchiectasis, Broncho Alveolar Lavage (BAL), IV Immunoglobulins (IVIG)

Abbreviations

Common Variable Immunodeficiency (CVID), Intravenous Immunoglobulins (IVIG), Non-Contrast Computed Tomography (NCCT), High Resolution Computed Tomography (HRCT),Primary Humoral Immunodeficiency (PHI),Modified Medical Research Council (mMRC),Broncho Alveolar Lavage (BAL), Primary Ciliary Dyskinesia (PCD),Cystic Fibrosis (CF),Non‑Tuberculous Mycobacterial (NTM) infection.

Introduction

Bronchiectasis is a chronic respiratory condition characterized by irreversible widening and scarring of the bronchi in the lungs [1]. The damage leads to a vicious cycle of recurrent infections, inflammation with subsequent mucus build-up in the affected airways [2]. Over time, these changes can impair lung function and lead to debilitating symptoms [3]. Chronic or severe respiratory infections, such as pneumonia or tuberculosis are the most common causes of damage to the airways, leading to bronchiectasis. There are also other microbes like Non-Tuberculous Mycobacteria (NTM) that chronically infect the airways leading to bronchiectasis in individuals with structurally damaged lungs with cavities or emphysema. Conversely, there have been cases in apparently healthy individuals with localized bronchiectasis affecting the lingula or the right middle lobe.x Moreover, Bronchiectasis development has been linked to a number of lung infections from herpesvirus, adenovirus, and bacteria such as Pseudomonas aeruginosa, Klebsiella pneumoniae, and Staphylococcus aureus.y In addition, non-infective conditions that obstruct the airways, such as cystic fibrosis, inhaled foreign objects, or tumours, can also contribute to the development of bronchiectasis by preventing proper clearance of mucus and leading to recurrent infections.

Primary immunodeficiency disorders like Common Variable Immunodeficiency (CVID) or defects in the immune system can increase susceptibility to respiratory infections, which, if frequent or severe, can result in bronchiectasis [4]. CVID is a primary immunodeficiency disorder characterized by low levels of serum immunoglobulins with an increased susceptibility to infections. It can lead to recurrent respiratory tract infections with highly pathogenic organisms, which in turn can cause inflammation and damage to the bronchial tubes, ultimately leading to bronchiectasis [1]. The condition makes the lungs vulnerable to frequent exacerbations causing permanent structural damage to the airways.

Case Report

We present the case of a 25-year-old female patient who came to our Respiratory Medicine out-patient department with cough associated expectoration, shortness of breath (grade-2 mMRC) and fever with chills and rigor of 1 week duration. Patient was diagnosed with Left Lung Multi-Lobar Necrotizing Pneumonia and treatment was started on IV Piperacillin-Tazobactam and supportive therapy with mucolytics, bronchodilators and oxygen. The patient recollected multiple episodes of pulmonary infections and gastrointestinal infections since her early childhood. High resolution CT chest scan done at our hospital demonstrated multi-lobar consolidation of the entire left lung with patchy ground-glass opacities in the apico-posterior segments of the right lung **Figure 1 & Figure 2a&2b**. Similar, bronchiectatic changes are evident in the apical segment of left lower lobe **Figure 2c&2d.**

Figure1: Chest X-ray PA view showing massive consolidation of the left lung.

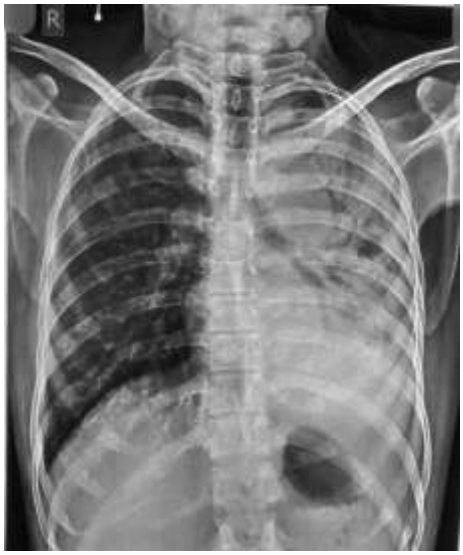


Figure 2a & 2b: High resolution CT chest scan showing areas of consolidation, necrosis.

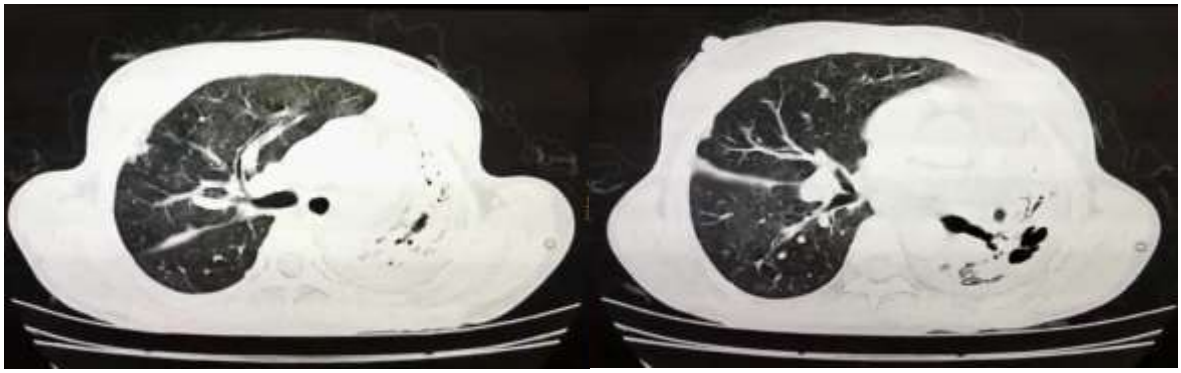
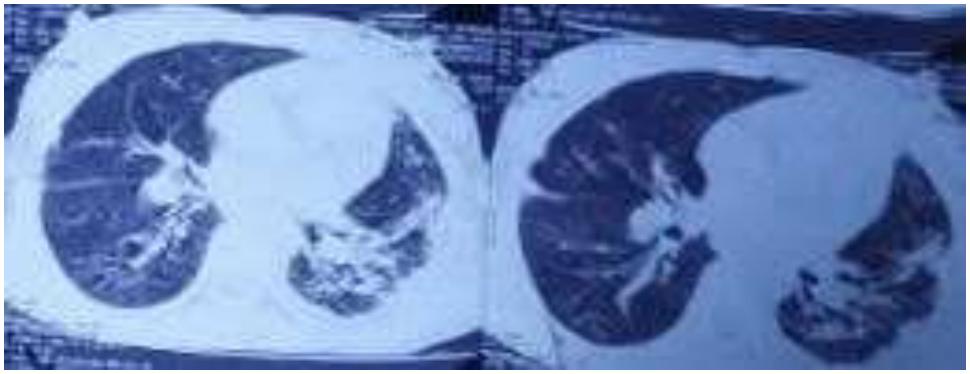
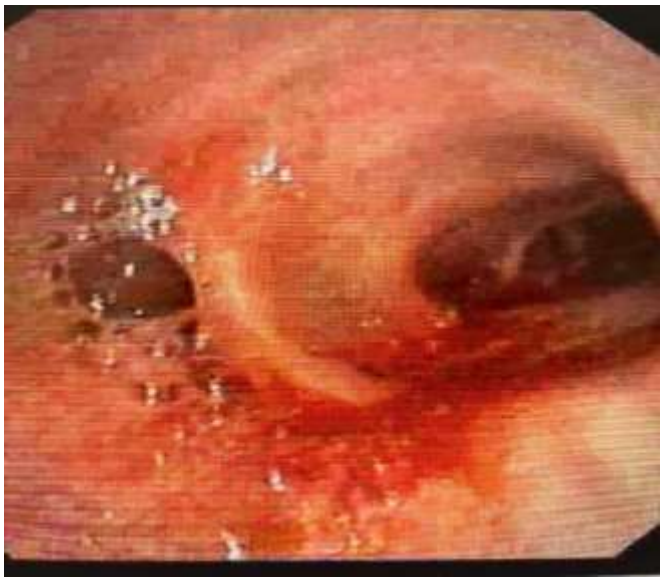


Figure 2c& 2d: HRCT of the same patient highlighting dilated bronchi and tram track appearance suggestive of bronchiectasis in the apical segment of left lower lobe.



Previous NCCT of chest done 5 months prior depicted consolidation which was limited to right upper lobe and left lower lobe. Eventually, the consolidation pattern worsened over the due course after which she presented to our hospital. Based on her WBC count and intermittent spikes of fever, antibiotics have been changed to I.V. Meropenem and Linezolid. A diagnostic bronchoscopy done on the day of admission revealed thick secretions from left principal bronchus and Broncho-Alveolar Lavage (BAL) was collected from the affected lobes which were sent for laboratory investigations. There was also obliteration of the apical segment of the left lower lobe which may have contributed to the development of necrotizing pneumonia and subsequent bronchiectasis. **Figure 3.**

Figure 3: Obliterated apical segment of left lower lobe with secretions.



The possibility of fungal infection was ruled out by a negative fungal smear and culture of the BAL. On the other hand, BAL cultures grew Acinetobacter baumanii which was sensitive to our empirical antibiotics. A comprehensive Connective Tissue Diseases profile ruled out subsequent disorders. Based on the chronic history of sinopulmonary and gastrointestinal infections, workup for Primary Immunodeficiency disorders was sought. Serum Immunoglobulin levels done for the patient revealed low levels of IgA and IgG with increased levels of IgM. A repeat Immunoglobulin profile done 6 days later showed the same findings which confirmed the abnormality. A C4 complement level was also low. The decision to start IV Immunoglobulins was deterred by the patient due to financial constraints [4].

Discussion

Bronchiectasis is a very common suppurative lung disorder in India of which tuberculosis is one of the leading causes [5]. Usually probe into the cause of Bronchiectasis is not done, but to prevent further progression of the disease the cause of the disease should be identified [4]. Primary Humoral Immunodeficiencies (PHI) are rare but potential cause of severe bronchiectasis. Primary humoral immunodeficiencies (PHI) encompass a range of disorders characterized by defective antibody production. PHI can be broadly classified into two groups [4]:

1. Defined Genetic Linkage: Includes diseases with known genetic causes, such as:

a. X-linked agammaglobulinemia: Characterized by the absence of B cells and very low levels of immunoglobulins, typically appearing in childhood.

b. Autosomal recessive agammaglobulinemia: Similar to X-linked but inherited differently, also presenting in childhood.

2. Unknown Genetic Basis: This larger group includes Common Variable Immunodeficiency (CVID): It is the most prevalent symptomatic form in adults, marked by hypogammaglobulinemia, recurrent bacterial infections, and autoimmune issues, IgG Subclass Deficiencies, IgA Deficiency & Selective Antibody Deficiency.

These disorders typically manifest in the early part of adulthood. CVID, in particular, has an incidence of 1 in 10,000 to 50,000, with familial occurrence in 1/5th of cases [4,6]. Symptoms often begin in the 2nd or 3rd decade of life, but diagnosis is frequently delayed by 6 to 8 years. [4,7]. This delay is due to lack of suspicion of primary immunodeficiency in adults and nonspecific initial symptoms, such as recurrent sinusitis or bronchitis.

CVID diagnosis involves excluding secondary immunodeficiencies and other primary immunodeficiency disorders. It is typically confirmed by measuring immunoglobulin levels (IgG, IgA, and/or IgM) and assessing the antibody response to vaccinations [3,4]. Patients with recurrent respiratory infections but normal immunoglobulin and complement levels may have a functional Ig deficiency, manifested by a poor response to pneumococcal vaccine and tetanus toxoid despite normal Ig levels. For most patients, the early symptoms of CVID are recurrent sinusitis or bronchitis [8]. Unfortunately, serum Ig levels are not measured routinely in such cases. The fundamental immunological defect in CVID is the reduced number of switch memory B cells with a failure to produce significant antibody response to specific antigens [9]. The diagnosis of CVID is made mostly by exclusion of secondary causes of immunodeficiency and other primary immunodeficiency disorders.4 Though there is no consensus regarding the definition of CVID, the most agreed one as proposed by European Society for Immunodeficiencies is reduced (2 SD below the mean) levels of IgG with reduced IgA and/or IgM, together with failure to mount a significant antibody response to vaccination, in the absence of a known cause [8] High-resolution computed tomography (HRCT) of the chest often shows bronchiectasis, a common manifestation in PHI patients, due to recurrent respiratory infections such as sinusitis, bronchitis, and pneumonia [9].

Bronchiectasis is a late manifestation in CVID and signatory to repeated infective insults in the past. Bronchiectasis remains the most common pulmonary pathology detected in CVID patients with a reported prevalence ranging from 17 to 76%.4 HRCT scan is the single best imaging tool for the diagnosis and

monitoring of bronchiectasis in CVID. Bronchiectasis is generally cylindrical, bilateral, and diffuse. It affects mostly the middle or lower lobes, and less commonly the upper lobes. The other pulmonary manifestations are emphysema, fibrosis, granulomatous disease mimicking sarcoidosis, and interstitial lung disease [4,9]. In addition to lung, virtually any organ system can be involved in CVID. Extrapulmonary manifestations of CVID include recurrent diarrhea, malabsorption, autoimmune disorders like idiopathic thrombocytopenic purpura and autoimmune hemolytic anemia, and malignancies like lymphoma and gastric cancer.8 Presence of bronchiectasis and liver disease at diagnosis carries a poor prognosis in CVID patients. Bronchiectasis is not a feature in isolated IgA or IgM deficiencies but more likely if these occur in association with selective IgG subclass deficiencies [4].

The differential diagnoses of CVID include Primary Ciliary Dyskinesia (PCD), adult‐onset Cystic Fibrosis (CF), alpha‐1 antitrypsin deficiency, and Non‐Tuberculous Mycobacterial (NTM) infection.4 Male infertility is a common feature in both PCD and adult‐onset CF. However, presence of rhinitis since neonatal period and a classic triad of sinusitis, situs inversus, and bronchiectasis (seen only in 50% cases) will differentiate PCD from adult‐onset CF, the later may also present with recurrent pancreatitis [4] The diagnosis of PCD is established by ultrastructural study of cilia, whereas sweat chloride estimation and/or genetic analysis is required to diagnose adult‐onset CF. On the other hand, alpha‐1 antitrypsin deficiency is usually associated with concomitant emphysema and affects the lower lobes, whereas NTM infection has a predilection for middle lobe and lingula with nodular bronchiectasis and tree‐in‐bud appearance [5].

IVIG remains the mainstay of therapy in CVID.10 The standard recommendation for IVIG is 400‐600 mg/kg body weight every 3‐4 weeks [4,8]. An IgG trough level (the IgG level before the next infusion) of at least 5 g/l should be attained. Patients with bronchiectasis or diarrhea may require higher IVIG doses (500‐600 mg/kg) to reach the mandatory trough level. The dose, frequency and route of administration of IVIG should be individualized to achieve maximum success. Antimicrobial therapy is the other main component of CVID therapy, because Ig replacement alone may not adequately prevent or treat local and/or persistent infections. Those with recurrent infections despite IVIG therapy may benefit from suppressive antibiotic therapy especially macrolides like azithromycin given three times a week.4,5 Other usual therapies for bronchiectasis include bronchodilators, inhaled corticosteroids, and airway clearance techniques which should be optimized for maximum benefit. In addition, the accompanying diseases and sequelae of CVID require adequate treatment. In selected cases, novel agents like Infliximab and Etanercept have been used with mixed results [11]. Larger clinical trials are needed to effectively manage complications related to CVID, especially bronchiectasis with emphasis on personalized therapy.

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