An Uncommon Cause of Bronchiectasis: A Case Report

UI Qadir A1*, Afsar A2 and Aslam M2
1Department of PULmonary Medicine, POF Hospital, Wah Medical College, Wah Cantt, Pakistan
2Department of Internal Medicine, POF Hospital, Wah Medical College, Wah Cantt, Pakistan

Abstract

Bronchiectasis is a common respiratory condition and has a number of causes. One of the causes of bronchiectasis is immunoglobulin deficiency. Common variable immunodeficiency (CVID) is the most common symptomatic primary immunodeficiency disorder characterized by an increased incidence of recurrent infections, autoimmune phenomena and neoplastic diseases. This article describes a 37-year-old gentleman who was diagnosed as a case of CVID on the basis of recurrent respiratory tract infections and laboratory findings. He improved with monthly intravenous immunoglobulin (IVIG). The diagnosis is often difficult and delayed but should be considered for patients with recurrent infections.

Keywords: Bronchiectasis; CVID; Hypoimmunoglobulinemia; IVIG

Introduction

CVID is a primary immunodeficiency disorder [1] that involves low levels of most or all of the immunoglobulin classes, lack of B lymphocytes and frequent bacterial infections [2]. Increased susceptibility to infections with encapsulated organisms is the hallmark of this condition. Recurrent sinusitis, bronchitis, otitis, pharyngitis and pneumonia are commonly encountered infections. About 20% of patients present with gastrointestinal infections and sprue-like syndromes. The prevalence of CVID is about 1 in 25000 in the United States and one case per 50,000 population worldwide [3]. CVID manifests itself between ages of 5-10 years and 20-40 years [4]. Genetics of CVID is still unknown. Demonstration of functional or qualitative defects in antibody production is essential and all patients have reduced levels of Immunoglobulin G (IgG), Immunoglobulin (IgA) and/or Immunoglobulin (IgM) [5]. Most incidences of pneumonia occur before the diagnosis of CVID and hence result in sequelae like bronchiectasis, lung volume loss and empyema. Paradoxically there is increased incidence of autoimmune diseases (20%). Treatment includes lifelong immunoglobulin administration by subcutaneous (SC) or intravenous (IV) route. Here we report case of a 37-year-old gentleman with bronchiectasis secondary to recurrent infections of respiratory tract who was diagnosed to have CVID.

Case Report

A 37-year-old gentleman presented with history of recurrent lower respiratory tract infections since 2001 and was diagnosed as a case of bronchiectasis. In primary care setting he was treated with repeated courses of antibiotics but was never worked up appropriately for any underlying cause of his bronchiectasis. He was fertile. In 2003, he was started on anti-tuberculosis therapy (ATT) empirically based on history of chronic productive cough and radiological findings. Patient did not recall whether his smear was positive or not. He took ATT for 3 months which was then stopped because his symptoms did not improve and there was no definitive evidence of Mycobacterium Tuberculosis (MTB) infection. In 2008 his condition deteriorated and he was hospitalized. He had developed left-sided empyema thoracis for which he was referred to thoracic surgeon. He underwent video-assisted thoracoscopic surgery (VATS) and decortication was done for empyema. He continued to have recurrent chest infections for which he had to take antibiotics (Figure 1).

He underwent left lower lobectomy in January 2014. Initially he showed improvement but then he was lost to follow-up. He presented again in our department in June 2017 with poor health. On examination, he was an emaciated young gentleman with clubbing, cervical lymphadenopathy, hepatosplenomegaly and bibasilar coarse crepitations more on right lower chest. He had developed sensorineural deafness probably due to repeated courses of macrolides. He also developed Bell’s palsy from which patient did not recover fully resulting in residual facial muscle weakness. At this point he was thoroughly worked up. HRCT chest showed bilateral extensive bronchiectasis.

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Bronchiectasis is permanent and abnormal distortion of one or more of conducting bronchi. Although congenital causes respond from developmental abnormalities of the airways, the more common acquired forms of bronchiectasis are usually caused by repeated lung infections with respiratory pathogens. Immune defects resulting in hypogammaglobulinemia are strongly associated with bronchiectasis. Primary immunodeficiency, CVID and X-linked agammaglobulinemia, and secondary immunodeficiencies due to chemotherapy, immunosuppressants, lymphoproliferative malignancies and allogeneic bone marrow transplant are all strongly related to bronchiectasis. Up to 7% of adULTs and one third of pediatric population presenting with bronchiectasis will have a primary immunodeficiency [6].

CVID is a rare cause of bronchiectasis. It is characterized by hypogammaglobulinemia and varying degrees of defective T-cell and macrophage functions. Patients typically have low levels of IgG, IgA and/or IgM with loss of antibody production. CVID is a diagnosis of exclusion; thus gene defects, medications, protein loss or malignancies as cause of hypogammaglobulinemia must be excluded [6]. Another necessary criterion for diagnosis is lack of specific IgG antibody responses to at least two or more vaccines such as Hemophilus, measles, mumps, rubella, and pneumococcal polysaccharide vaccines, and diphtheria or tetanus toxoids. There is also a lack of adequate (laboratory-defined protective levels) antibody production after hepatitis A or B vaccines or after disease exposure. Detailed antibody testing is not important in those with very low levels of serum IgG (<150 mg/dL). Subjects with greater levels of IgG (more than 450 mg/dL) and those with only minimally reduced IgA, require more detailed evaluation. These patients are less likely to benefit from immunoglobulin therapy as they have relatively preserved IgG antibody production [6]. CVID is usually diagnosed in adULTs between 20-40 years. The diagnosis is typically delayed by 6-8 years. Patients with antibody deficiency with normal immunoglobulin levels or those with IgG deficiency alone do not have CVID. A careful past medical history is the first step in diagnosis. The clinical relevance of underdiagnosis of CVID is that it precludes the appropriate management by use of IVIG. Recurrent infections peculiarly of chest can thus occur.

The disease was first described by Charles Janeway Sr in 1953 in a 39-year-old patient who had recurrent infections, bronchiectasis and meningitis [7]. Besides recurrent acute infections, CVID patients have an increased tendency to develop autoimmunity, lymphoproliferative disease, chronic granulomatous disease and malignancy [8]. The disease has a complex and heterogeneous phenotype with 4 distinct clinical presentations [9]:

1. No disease-related complications (infections only)
2. Cytopenias (thrombocytopenias, autoimmune hemolytic anemia, neutropenia)
3. Polyclonal lymphoproliferation (granuloma, lymphocytic interstitial pneumonia, persistent unexplained lymphadenopathy)
4. Unexplained enteropathy

The patients often present with recurrent infections of respiratory or gastrointestinal tract. Otitis media, para nasal sinusitis, pneumonia and diarrhea are common infections. Chronic diarrhea is another mode of presentation but respiratory tract infections are predominant feature. Gastrointestinal manifestations include sprue-like illness, pernicious anaemia, autoimmune hepatitis, primary biliary cirrhosis and inflammatory bowel disease [10]. About 20% of patients develop herpes zoster infection. Same number of patients develops autoimmune phenomena such as hemolytic anemia, thrombocytopenia, vitiligo and rheumatoid arthritis [11]. Risk of certain malignancies like B-cell lymphomas, malignant melanoma and gastric carcinoma is high in CVID patients. A Sarcoidosis-like syndrome can occur in CVID with cutaneous and visceral granulomas. Other skin manifestations

<table>
<thead>
<tr>
<th>Immunoglobulin Type</th>
<th>ResULT</th>
<th>AdULT Reference Range</th>
</tr>
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<tbody>
<tr>
<td>Immunoglobulin A (IgA)</td>
<td>&lt;0.25 g</td>
<td>0.7-4.0 g/L</td>
</tr>
<tr>
<td>Immunoglobulin G (IgG)</td>
<td>&lt;3.20 g/L</td>
<td>5.4-18.22 g/L</td>
</tr>
<tr>
<td>Immunoglobulin M (IgM)</td>
<td>&lt;0.25 g/L</td>
<td>0.4-2.3 g/L</td>
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Table 1: Patient’s immunoglobulin levels.

Figure 2: HRCT chest at start of treatment (A). Repeat HRCT chest (B) after IVIG showing decrease in infective changes with background bronchiectasis.
can also occur. With passage of time, patients develop bronchiectasis or malabsorption leading to poor quality of health. On physical examination patients may look emaciated and have generalized lymphadenopathy or splenomegaly or both.

Mainstay of preventive therapy is with subcutaneous or IV immunoglobulins every 1-4 weeks, a monthly dose of 300-600 mg/kg [12]. The goal is to prevent infections. Trough serum IgG levels can be checked if patients do not respond adequately. Patients should be treated with antibiotics at the first sign of infection. The treatment is expensive but cost effective in decreasing the incidence of potentially life threatening infections, respiratory complications and hospital admissions.

CVID leads to several complications leading to significant morbidity and mortality. Bronchiectasis, empyema, sepsis, meningitis, and osteomyelitis are common. Streptococcus pneumonia, Haemophilus influenzae, or mycoplasma species are common causative organisms. Death usually occurs due to lymphoma, cor pulmonale secondary to bronchiectasis or liver failure caused by autoimmune or viral hepatitis.

Conclusion

This case highlights the importance of increasing awareness among primary healthcare doctors for suspecting the diagnosis of CVID in undiagnosed cases of bronchiectasis and early referral to confirm the disease so that early administration of IVIG provides improvement in these patients and prevents significant morbidity and mortality.

References