Recurrent Chest Infections Leading to Bronchiectasis in a Patient with Common Variable Immune Deficiency

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Introduction

Common variable immune deficiency (CVID) is late onset humoral immune deficiency with onset after 24 months of age.1 Incidence is reported as 1:50,000 to 1:75,000.2 These patients have increased susceptibility to infections and diminished or poor response to vaccination with protein and polysaccharide vaccines.3 CVID patients experience frequent respiratory tract infections, bronchiectasis, gastrointestinal disorders, autoimmune disorders and malignancies.4 We report a young boy with bronchiectasis secondary to recurrent pulmonary infections with underlying common variable immunodeficiency which remained undiagnosed for quite long time.

Case Report

A nine year old boy presented to Quaid-i-Azam International Hospital first time with c/o fever, cough and rash all over the body for 10 days along with history of drowsiness for 1 day. Family history revealed consanguineous parents and four female healthy siblings. He was developmentally normal for age and fully immunized according to EPI schedule. There was no history of chronic illnesses in the family. According to his parents, he remained well till two years of his life after which he started having recurrent ear and chest infections which were treated with multiple oral and intravenous antibiotics, steroids and bronchodilators. He also received antituberculous treatment for nine months at 7 years of age for suspected pulmonary tuberculosis. In spite of that he remained symptomatic having productive cough with fever off and on.

On examination he was a febrile, drowsy, agitated boy with red puffy eyes and a fading maculopapular rash all over his body. Anthropometric measurements showed height and weight between 25th and 50th centiles. Chest examination revealed coarse crepitations on right middle and lower zones. Glasgow coma scale (GCS) was 12/15 with no signs of meningeal irritation and focal neurological deficit. He was managed as a case of measles encephalitis with pneumonia and conjunctivitis. Base line investigations including complete blood count, serum electrolytes, liver function tests, renal functional tests and urine examination were unremarkable. Lumbar puncture revealed cerebrospinal fluid (CSF) routine examination as unremarkable. Blood and cerebrospinal fluid culture revealed no growth. Electroencephalogram (EEG) and computed tomography (CT) Scan of brain were also normal. Chest x-ray revealed pneumonic infiltrates in both lung fields along with areas of bronchiectasis especially in right middle and lower zones. His condition gradually improved. He became fully conscious, rash subsided and was discharged in stable condition after 3 days with advised to follow up for further workup. Later he needed 3 admissions in next 4 months (Table 1).

Figure 1: CT Scan chest showing areas of atelactasis with bronchiectasis in middle lobe of right lung

Immunology department was consulted and final diagnosis of common variable immune deficiency (CVID) was made; which led to recurrent infections especially pulmonary and resulted in bronchiectasis. Specific therapy for CVID was then started as intravenous immunoglobulin 400mg/kg/dose every 4 weeks regularly. Co.trimoxazole(septran) prophylaxis was also started and was advised to have complete therapeutic course of antibiotics in case of reinfections.
He is on regular follow up and has shown much clinical improvement. He is maintaining infection diary regularly and immunoglobulins levels are monitored every 4 weeks. He had only two mild episodes of chest infection in last one year. Repeat CT scan chest has revealed significant resolution of bronchiectatic lesions. Parents were counselled in detail about the disease, its possible future complications, prognosis and lifelong treatment with immunoglobulin infusions as no other definite treatment is available.

**Discussion**

CVID is the most prevalent form of symptomatic primary antibody deficiency. Patients with CVID have a marked decrease in serum IgG and IgA or IgM of at least 2 standard deviations (SD) below the mean for age in the presence of normal or low number of circulating B cells. Significant deficit in humoral immunity directly leads to increased susceptibility to infections and impaired response to protein and polysaccharide vaccines. Most infections are sinopulmonary and bacteria involved are encapsulated organisms likes streptococcus pneumoniae, haemophilus influenzae and mycoplasma pneumoniae. They are prone to have meningitis, recurrent skin and eye infections, recurrent pneumonias, gastrointestinal infections and autoimmune disorders. They also have increased susceptibility to malignancies particularly lymphomas. Healthcare providers should exercise high index of suspicion in such cases of recurrent infections so that they can be diagnosed in time to avoid long term complications. As in this case it took about 6 to 7 years till correct diagnosis was made and he had developed bronchiectasis. Long term prognosis of these patients depends upon the number and severity of bacterial sinopulmonary infections. Mortality rate ranges from 22-30%. It is expected that the long term outcome of these patients may improve in future with increasing use of immunoglobulin infusion and aggressive antibiotic therapy. Diagnosis is established by a low serum IgG along with reduced concentration of other immunoglobulins like IgA and IgM in the presence of normal or low number of circulating B cells. IgG level as low as less than 100mg/dl may be encountered as in our patient.50 to 77% of individuals with CVID have reduced numbers of switched memory B-cells. Response to protein antigens such as diphtheria or tetanus component of DT vaccine may be reduced but are often preserved as a result of high immunogenicity of these vaccines, as seen in our patient. Abnormalities in T cell include low CD4 count, reduced proliferative responses to mitogens, reduced cytokine response to mitogens and recall antigen and reduced T regulatory cells. Low CD4 count is usually associated with normal to increased CD8 count.

The test to diagnose disorders likes CVID are not freely available and many health professionals are not aware of these tests. These factors lead to delay in diagnosis and development of complications. Most cases of CVID are sporadic, however 10% may be familial with predominance of autosomal dominant over autosomal recessive inheritance pattern. Carrier testing and prenatal diagnosis for pregnancies at risk are possible if disease causing mutations have been identified in an affected family member. Treatment involves regular immunoglobulin replacement therapy, antibiotics and periodic surveillance for monitoring of complications including bronchiectasis, malignancies and autoimmune phenomenon. But due to high cost of treatment and poor hygienic conditions in developing countries like us, Prognosis is expected to be poor. In this patient, parents are getting exhausted and they are likely to discontinue costly IV immunoglobulins as there is no support available at government or NGO levels.

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<th>Admisson date</th>
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<th>Investigations</th>
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<tr>
<td>2nd 20-1-2013</td>
<td>Fever, Cough</td>
<td>Bilateral coarse crepitations more on right side</td>
<td><strong>Chest x ray:</strong> Pneumonia and Bronchiectasis. <strong>HR CT scan chest</strong>&lt;sup&gt;(Fig 1)&lt;/sup&gt; Areas of atelectasis with bronchiecstasy in middle lobe of right lung <strong>Mantoux test:</strong> - Negative. <strong>Sputum for AFB:</strong> - Negative. <strong>Sweat chloride:</strong> - Normal. <strong>Delta 580 mutation:</strong> - Not Detected</td>
<td>Broad spectrum antibiotics Supportive care</td>
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<tr>
<td>3rd 4-02-2013</td>
<td>Worsening of cough, Fever, Tachypnea, Bilateral Crepitations</td>
<td>X ray chest followed by HR CT scan chest - New areas of consolidation in right lung middle and lower lobes and a right sided pleural effusion</td>
<td></td>
<td>Broad spectrum Antibiotics</td>
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<tr>
<td>4th 7-05-2013</td>
<td>Fever, Headache, Vomiting</td>
<td>Fever Irritability Signs of meningial irritation</td>
<td><strong>Cerebrospinal fluid analysis:</strong> - Total leukocytes count: 213/μL, Neutrophiles: 63%. Lymphocytes: 35%, Glucose: 128mg/dl, Protein: 71mg/dl, Blood CFS - No growth, CSF C2S - Pneumococci sensitive of all first line antibiotics. <strong>CT scan brain:</strong> - Unremarkable. <strong>Serum immunoglobulins levels:</strong> - IgA: &lt;0.1, IgG: 1.2, IgM: &lt;0.1. <strong>Blood group O Positive with Negative Anti A and Anti B titres, Antidiaphtheria and anti tetanus antibody titres:</strong> - Positive. <strong>CH50 levels:</strong> - Normal. <strong>Burst suppression test for chronic glaucomatous disease:</strong> - within reference limits. <strong>Lymphocyte subsets analysis:</strong> - Relatively low no of natural killer (NK) cells.</td>
<td>Intravenous Ceftriaxone.</td>
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References


