CASE REPORT
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Giant Aneurysm of Thoracic and Proximal Abdominal Aorta in a Patient with Common Variable Immunodeficiency

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ABSTRACT

Common variable immunodeficiency (CVID) is the most common symptomatic primary immunodeficiency disease, predisposing the patients to various tissue involvement and organ damage.

Here a 16-year-old boy is presented who was referred to our center with cough, dyspnea, cyanosis, and history of recurrent pneumonia. The diagnosis of CVID was made according to reduction all serum immunoglobulin levels, normal numbers of T, B and NK lymphocyte subpopulations, poor antibodies responses.

Considering abnormality in heart examination and chest X-ray, echocardiography and computed tomography angiography were performed which showed large thoraco-abdominal aortic aneurysm in this patient.

Although there are some reports of cardiovascular disease associated with primary antibody deficiencies, this is the first time that such large thoraco-abdominal aortic aneurysm is reported in CVID. This may be secondary to recurrent pulmonary infections or an unknown mutation process. Cardiovascular abnormalities are an entity that should be kept in mind in patients with primary immunodeficiency diseases.

Keywords: Aneurysm; Aorta; Common Variable Immunodeficiency

INTRODUCTION

Common variable immunodeficiency (CVID) is a heterogeneous group of disorders, characterized by low serum levels of IgG, IgA and/or IgM and impaired antibody responses to immunization antigens.1-4 They are very susceptible to recurrent infections, autoimmunity and cancers. Respiratory and gastrointestinal systems are the major organs that can be involved in CVID.2-4 Aneurysm of the aorta is generally considered as a rare condition in children. It is believed that most of aorta aneurysms are attributed
to secondary causes such as recurrent infections, collagen vascular disease, trauma, Kawasaki disease, congenital arterial malformation, or even unidentified cause. There are some reports of cardiovascular disease in association with primary antibody deficiencies, which could be due to recurrent infections and release of various inflammatory cytokines; however, hitherto thoraco-abdominal aortic aneurysm has not been reported in CVID patients. Development of vascular disease can be a serious problem and should be managed promptly. Herein a young boy with CVID is reported who suffered from an extensive involvement of thoracic and abdominal aorta.

**CASE PRESENTATION**

A 16-year-old Caucasian boy was admitted to the Pediatric Department for evaluation of worsening dyspnea, productive cough, and fever. His medical problem had commenced from early infancy, when he experienced recurrent upper respiratory tract infections and pneumonia. There was no evidence of any adverse reaction with routine immunizations.

At the time of admission, the indices of weight and height were below 5th percentile. He was febrile, cyanotic, tachycard, and tachypneic. In chest examination, increased anteroposterior diameter of chest wall and coarse rales in right lung were detected. Physical examination of heart revealed a regular heart rhythm, ranged from 100 to 120 beats per minutes. Heart auscultation had normal S1, loud A2 component and ejection systolic click. There was no symptom of hyperelastic skin, hypermobile joints and other musculoskeletal abnormalities. Laboratory findings are summarized in the table 1.

Arterial blood gas analysis showed PH: 7.45, O₂ saturation: 84%, PO₂: 45% and PCO₂: 27 mmHg. Cultures of blood and tracheobronchial secretion were negative for pyogenic organisms, fungi and mycobacterium. Polymerase chain reaction (PCR) for aspergillus and candida albicans was also negative. Plain chest x-ray revealed infiltration in right lung with prominent left ventricle and aneurismal dilatation of thoracic aorta especially ascending aorta (Figure 1) with significant calcification which confirmed by high-resolution computed tomography (CT) scan. Pulmonary function tests showed FVC: 104%, FEV1: 78%, FEV1/FVC: 69%, which were compatible with mild obstructive pattern.

**Table 1. Laboratory and immunologic results on this patient**

<table>
<thead>
<tr>
<th>Test</th>
<th>Laboratory results</th>
</tr>
</thead>
<tbody>
<tr>
<td>White blood cell</td>
<td>17,400 cell/mm³</td>
</tr>
<tr>
<td>Neutrophil</td>
<td>78%</td>
</tr>
<tr>
<td>Lymphocyte</td>
<td>17%</td>
</tr>
<tr>
<td>Monocyte</td>
<td>5%</td>
</tr>
<tr>
<td>Hemoglobin</td>
<td>11.1 gr/dL</td>
</tr>
<tr>
<td>ESR</td>
<td>113 mm/h</td>
</tr>
<tr>
<td>CRP</td>
<td>320 gr/dL</td>
</tr>
<tr>
<td>Serum IgG</td>
<td>&lt;10 mg/dL (700-2,100 mg/dL)</td>
</tr>
<tr>
<td>Serum IgM</td>
<td>&lt;10 mg/dL (100-430 mg/dL)</td>
</tr>
<tr>
<td>Serum IgA</td>
<td>No detectable</td>
</tr>
<tr>
<td>Serum IgE</td>
<td>0.01 IU/mL</td>
</tr>
<tr>
<td>CD3+ T cells</td>
<td>84%</td>
</tr>
<tr>
<td>CD3+CD4+ T cells</td>
<td>24%</td>
</tr>
<tr>
<td>CD3+CD8+ T cells</td>
<td>69%</td>
</tr>
<tr>
<td>CD19+ B cells</td>
<td>13%</td>
</tr>
<tr>
<td>CD56+ NK cells</td>
<td>8%</td>
</tr>
<tr>
<td>NBT</td>
<td>90%</td>
</tr>
</tbody>
</table>

Considering history of recurrent infections and failure to thrive, immunological work up was done (Table 1). Low serum levels of immunoglobulin as well as minimal IgG response after booster immunization with tetanus and diphtheria were detected. HIV serology test was negative. Results of tests for serum antinuclear antibodies, perinuclear and cytoplasmic antineutrophil cytoplasmic autoantibodies were negative.

**Figure 1.** Chest x-ray showed infiltration in right lung with prominent left ventricle and dilated root, arch and descending aorta
The diagnosis of CVID was made for this patient, according to the low serum Ig levels, normal enumeration of peripheral T and B lymphocytes and impaired antibody response to protein antigens. Meanwhile, other well-defined causes of hypogammaglobulinemia were excluded. Treatment with intravenous immunoglobulin was added to antibiotics infusion after three days admission, while he showed mild clinical improvement in the following days.

As of abnormal heart sounds and chest X-ray, echocardiography was performed which showed aortic root of 32 mm and ascending aorta dilatation with mild to moderate aortic insufficiency and dilated cardiomyopathy. CT-angiography showed huge dilated calcified thoraco-abdominal aorta (TAA) extending from the ascending to descending aorta above division of renal arteries (Figure 2).

Accordingly, major and minor clinical criteria of Ghent were reviewed in the patient for exclusion of Marfan syndrome.

The patient continues to take intravenous antibiotics, immunoglobulin infusion and also captopril, whilst there was gradually more clinical improvement. The patient was discharged after two weeks in a good health. Repeated echocardiography, at one and four weeks later, revealed no increasing size of aneurysm. The patient was closely followed under regular immunoglobulin replacement therapy and prophylactic antibiotics, whilst hemodynamic abnormality or aneurismal-related complication ultimately necessitated surgery.

DISCUSSION

Patients with CVID usually tend to present with recurrent respiratory tract infections, whilst other organ damage could also be common. Hypoxemia, hypercapnia, acidemia and airway resistance consequent chronic pulmonary damage are associated with pathological changes that predominantly affect the blood vessels. However, there are few reports of cardiovascular abnormalities in primary antibody deficiencies, including giant cell myocarditis, right aortic arch, ventricular dilatation and hypertrophy, valvular regurgitation, pulmonary hypertension, atrial dilatation, anterior pericardial effusion, and mild dilated aortic root.

The exact cause and pathogenesis of thoraco-abdominal aorta is not clear. There are some evidences indicating that infection could significantly transform human aortic smooth muscle cells from a contractile to a proliferative phenotype, resulting in an increase in cell proliferation in vitro, which can be accompanied with vascular injury, chronic inflammation and aneurismal lesions by different infections. Considering the fact that CVID is characterized by hypogammaglobulinemia, poor specific antibody responses, and recurrent infections, this condition could potentially affect susceptible cases to develop aneurismal lesions. Presence of serological autoantibodies and systemic autoimmune disease has been reported in patients with thoraco-abdominal aorta. The growing body of evidence suggests antigen stimulation of T lymphocytes and poorly controlled inflammatory cytokines may exert an important role on involvement of cardiovascular system in patients.
with autoimmune disease while these mechanisms are also prominent abnormality in most patients with CVID. True idiopathic aneurysms are the least common and less than a dozen reports of multiple idiopathic aneurysms have been published until now. If we consider this rare type of aortic aneurysm, the possibility of aneurysm in our patient with CVID might be accidental.

Despite extensive investigations, no unique single genetic defect identified in CVID and the reasons for the widely differing clinical manifestations are unknown. Meanwhile there are some evidences that mutation in the genes encoding transforming growth factor β receptor type II (TGFBR2) and smooth muscle alpha-actin (ACTA2) are responsible for reported syndromes with aortic dilatation. Therefore it could be hypothesized that the histological abnormalities of the aorta such as fibrosis and elastic tissue due to secretion of various inflammatory cytokines in CVID could be related to some mutations/polymorphisms in these genes. However, further genetic studies are needed to identify the genes encodes thoracic aortic aneurysm or the direct role of TGF-β activity in CVID patients.

To the best of our knowledge, this report is the first case of CVID associated with giant aortic aneurysm. The possibility of the patient’s aneurysm could be related to an undetermined recurrent infection. Early recognition and adequate immunoglobulin replacement could reduce the infection rate and consequently avoid further complications. It could be suggested that the respiratory and cardiovascular systems of immunodeficient patient with lung involvement should be carefully monitored.

REFERENCES