Good's Syndrome Presenting with Cytomegalovirus Pneumonia
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Abstract

A 61-year-old woman who had undergone an operation for thymoma 17 years previously suddenly became dyspneic and showed bilateral pulmonary infiltrates on a chest radiograph. In the bronchoalveolar lavage fluid cells contained characteristic cytomegalic inclusion bodies, as well as cytomegalovirus DNA demonstrated by a polymerase chain reaction. Immunological findings included hypogammaglobulinemia, deficient numbers of circulating B cells, and impaired blast transformation of peripheral blood T cells in response to mitogens in vitro. Considering all of the findings, the patient was diagnosed with Good's syndrome presenting with cytomegalovirus pneumonia.

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Key words: hypogammaglobulinemia, thymoma, immunodeficiency

Introduction

It has become increasingly clear that primary immunodeficiencies are as common in adults as in children. Various forms of hypogammaglobulinemia are known to occur in adults, and are commonly complicated by recurrent, sometimes severe, episodes of bacterial infections including pneumonia, sinusitis, and otitis media. We treated an adult patient with Good’s syndrome, an acquired immunodeficiency characterized by hypogammaglobulinemia and thymoma, presenting with cytomegalovirus (CMV) pneumonia without any medical history of recurrent bacterial infection.

Case Report

A 61-year-old woman was transferred to Kurume University Hospital because of pneumonia unresponsive to treatment with antibiotics including a carbapenem, a macrolide, and a fluoroquinolone. She had been well until 2 weeks prior to transfer when she developed a sore throat. One week later she suddenly experienced dyspnea while gardening. Diagnosed with pneumonia she was admitted to another hospital and received antibiotic treatment as stated above. The patient had been taking medications for ischemic heart disease regularly for several years, and 10 mg of prednisolone daily to relieve pain in the soles of her foot for 1 month. She had undergone surgery for a thymoma 17 years previously and for a myoma uteri 15 years previously. Acute distress was apparent on admission. The pulse rate was 120/min; respiration rate, 40 minutes; blood pressure, 90/48 mmHg; body temperature, 37.4°C. Coarse crackles were audible over both lungs. A chest radiograph (Fig. 1) and computed tomography of the chest disclosed diffuse ground-glass opacities in both lung fields. Blood gas determination in an arterial sample obtained while the patient was receiving 10 l/min of oxygen by mask indicated a pH of 7.52; PaCO₂, 28 torr; and PaO₂, 61 torr. A complete blood count was as follows: white blood cells, 4,200/µL including 70% neutrophils, 1% eosinophils, 22% lymphocytes, and 5% monocytes; red blood cells, 358×10⁶/µL; hemoglobin, 10.2 g/dL; hematocrit, 32.1%; platelets, 26.0×10⁹/µL. The serum total protein concentration was 5.3 g/dL (66.8% albumin, 5.5% alpha 1 globulin, 12.3% alpha 2 globulin, 8.1% beta globulin, and 7.3% gamma globulin). Serum immunoglobulin concentrations were IgA, 45 mg/dL; IgM, 24 mg/dL; IgG, 220 mg/dL. A tuberculin test was negative, tests for human immunodeficiency virus (HIV) antibody and human T cell lymphotropic virus 1 (HTLV-1) were negative, and bacterial culture of sputum was negative. Bronchoalveolar lavage (BAL) was performed to identify the cause of pneumonia. Cytospin samples from these washings showed characteristic inclusion-bearing cells (Fig. 1). Polymerase chain reaction amplifications of DNA extracted from cells in the washings were positive for CMV, and negative for Legionella pneumophila, mycobacteria, or Pneumocystis carinii. No bacterial pathogen was cultured from the washings. Enzyme immunoassays for CMV antibodies in serum detected elevated IgM, 2.87 M index; reference value, <0.8 and IgG, 16.9 G index; reference value, <2.0 (Mitsubishi Kagaku Bio-Clinical Laboratories, Tokyo). Furthermore, an assay for CMV antigenemia that detects pp65 antigen in peripheral blood leukocytes was positive (Mitsubishi Kagaku Bio-Clinical Laboratories).

The patient initially was given 500 mg of methylprednisolone to treat respiratory distress. To treat the hypogamma-
Good’s Syndrome with CMV Pneumonia

Figure 1. (A) A chest radiograph on admission presenting diffuse ground-glass opacities in both lung fields. (B) A representative cell recovered by bronchoalveolar lavage with a deeply basophilic round nuclear inclusion that is surrounded by a clear halo (original magnification: x400).

Table 1. The Results of Flow Cytometric Analysis of Peripheral Blood

<table>
<thead>
<tr>
<th>Marker</th>
<th>% (Range)</th>
<th>/μl (Range)</th>
</tr>
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<tbody>
<tr>
<td>CD2</td>
<td>84 (64–93)</td>
<td>693 (630–2,914)</td>
</tr>
<tr>
<td>CD3</td>
<td>84 (51–87)</td>
<td>485 (525–2,881)</td>
</tr>
<tr>
<td>CD4</td>
<td>43 (25–56)</td>
<td>268 (238–1,513)</td>
</tr>
<tr>
<td>CD5</td>
<td>82 (53–88)</td>
<td>474 (539–2,914)</td>
</tr>
<tr>
<td>CD7</td>
<td>71 (56–84)</td>
<td>410 (490–2,782)</td>
</tr>
<tr>
<td>CD8</td>
<td>35 (17–44)</td>
<td>218 (217–1,247)</td>
</tr>
<tr>
<td>CD20</td>
<td>1 (9–34)</td>
<td>8 (70–752)</td>
</tr>
<tr>
<td>CD21</td>
<td>0 (4–22)</td>
<td>0 (69–591)</td>
</tr>
<tr>
<td>CD57</td>
<td>36 (6–43)</td>
<td>225 (89–9,861)</td>
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</tbody>
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*Parentheses indicate reference ranges.

globulinemia and CMV pneumonia, intravenous gamma globulin and ganciclovir were administered. Further immunological studies indicated normal concentrations of complement components, intact oxygen-radical releasing as well as phagocytic capability of peripheral blood neutrophils (Mitsubishi Kagaku Bio-Clinical Laboratories), intact natural killer cell activity of peripheral blood (Mitsubishi Kagaku Bio-Clinical Laboratories), and impaired blast transformation reactions in response to mitogens for peripheral blood lymphocytes (15,822 cpm in response to phytohemagglutinin and 13,046 cpm in response to concanavalin A. Table 1 shows the results of flow cytometric analysis of peripheral blood leukocytes 1 month after the admission.

After 3 months of treatment the pulmonary infiltrates had mostly cleared, and CMV antigenemia was no longer demonstrable. The patient was discharged home with supplemental oxygen, necessitated by the development of pulmonary fibrosis. No significant improvements in immunological dysfunction were evident.

Discussion

Good’s syndrome, an acquired immunodeficiency state characterized by hypogammaglobulinemia associated with thymoma (1), accounts for 7% to 13% of adult-onset cases of hypogammaglobulinemia (2). Patients with hypogammaglobulinemia commonly have multiple and sometimes severe episodes of respiratory infections, typically caused by encapsulated pyogenic bacteria such as *Streptococcus pneumoniae* and *Haemophilus influenzae*, these infections result in development of chronic sinusitis and bronchiectasis (1, 3). The present patient lacked this characteristic medical history and had been asymptomatic with unrestricted daily activity until pneumonia developed. No radiological evidence of chronic sinusitis or bronchiectasis was present. Although this patient had significantly reduced amounts of gamma globulin, antibody production against CMV infection was evident. This limited but significant antibody-producing response presumably was sufficient to prevent recurrent bacterial infections. Elevations of CMV antibodies showed little change over 2 months.

The vast majority of cases of community-acquired pneumonia are caused by a limited number of microbes including mainly bacteria (*S. pneumoniae*, *H. influenzae*, and *Staphylococcus aureus*) and atypical pathogens such as *Chlamydia*,
Mycoplasma, and Legionella (4). Viral pathogens, mainly respiratory viruses such as influenza virus, parainfluenza virus, and adenovirus (4), account for 2% to 15% of cases of community-acquired pneumonia. CMV, on the other hand, becomes pathogenic only in immunocompromised hosts such as developing fetuses, transplant recipients and individuals with HIV (5). Cell-mediated immunity is considered the primary defense against CMV infection, and has been demonstrated in human patients and in experimental animals (5–7). Nonetheless, humoral immunity against CMV appears to play a vital role.

Patients with hypogammaglobulinemia have been demonstrated to have subclinical lower respiratory tract infections with viruses including CMV (8). Furthermore, patients in whom severe CMV infection has developed fail to mount a significant antibody response (9), and intravenous immunoglobulin administration can decrease the severity of CMV infection (10). While CMV identified in BAL fluid from immunocompromised patients can be clinically insignificant (11), CMV infection in the present case was considered the causative agent of pneumonia, since cells from the fluid revealed cytomegalic inclusion bodies as well as CMV DNA. Demonstration of CMV antigenemia also was consistent with CMV pneumonia. To our knowledge, this is the first reported case of Good’s syndrome to present with CMV pneumonia.

In the present case the number of circulating B cells (Table 1) and production of immunoglobulins were both decreased. In addition to impaired humoral immunity, cell-mediated immunity appeared deficient given by a negative tuberculin skin test as well as blunted blast transformation of peripheral lymphocytes in response to mitogens in vitro. Previous oral administration of prednisolone may have further suppressed the patient’s immunity and predisposed her to the development of CMV pneumonia.

References