Good Syndrome, a Rare Cause of Refractory Chronic Diarrhea and Recurrent Pneumonia in a Chinese Patient after Thymectomy

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The diagnosis of Good syndrome is very difficult. It has various symptoms, and these symptoms can be present at different periods. In this report we present a patient with refractory chronic diarrhea, recurrent pneumonia, and dysgammaglobulinemia after thymectomy, who was finally then diagnosed with Good syndrome.

CASE REPORT

In June 2006, a 41-year-old man was admitted to a local hospital for watery diarrhea (about 10 bowel movements per day). A thymoma with a size of 10 × 8 cm was identified by computed tomography (CT), and then a thymectomy was performed. His bowel movement returned to normal after the surgery. Two months later, he was admitted to the hospital again with more-severe watery diarrhea (10 to 15 bowel movements per day). Escherichia coli was identified by stool culture, levofloxacin (0.4 g intravenously daily) was given, and he recovered after 5 days. From December 2006 to January 2011, he was repeatedly admitted to hospitals for recurrent diarrhea, chronic cough, and fever. Colonoscopy was normal. His condition improved after antibiotic therapy each time. In January 2011, he was admitted to our hospital for severe watery diarrhea (15 to 20 bowel movements per day, accompanied by urgency and incontinence), productive cough, and weakness.

On physical examination, the patient was malnourished. Diffuse rales were heard in the bilateral lower lung. A CT scan of the chest revealed several infiltrates on the lungs. Gastroscopy and capsule endoscopy showed chronic superficial gastritis and scattered congestion as well as swelling in the small intestine, respectively. Colonoscopy revealed focal hemorrhage in the transverse colon. Blood chemistry was normal except for a decreased serum albumin level of 31.8 g/liter (reference range, 35 to 55 g/liter). Dysgammaglobulinemia was noted with an IgG concentration of 6.93 g/liter (reference range, 8 to 15.5 g/liter), but the IgM and IgA concentrations were normal. Flow cytometry showed a CD4+ lymphocyte percentage of 13% and an inverted CD4+/CD8+ ratio of 0.16. Tests for IgM antibodies to cytomegalovirus (CMV) and herpes simplex virus were positive. Quantitative PCR testing of CMV DNA was also positive at 18,200 copies per milliliter. Sputum culture showed Escherichia coli and Haemophilus influenzae infection. Multiple stool cultures were negative. Repeated HIV serology was negative. Bone marrow aspiration and biopsy showed no obvious abnormalities. Good syndrome (GS) was diagnosed.

Piperacillin sodium-sulbactam sodium (3 g every 12 h) and acyclovir (5 mg/kg of body weight every 8 h) were given. Monthly intravenous immunoglobulin (IVIG) was scheduled. Two weeks later, his gastrointestinal (GI) and respiratory conditions improved. His bowel movement was one to two times per day, and daily stool weight was about 300 g. He recovered with a good appetite and gained weight. A CT scan showed that the infiltrates in the lung were significantly reduced. He continued with IVIG monthly after being discharged. To date, the patient’s bowel movement has remained normal.

Good syndrome was first described in 1954; it is a rare association of thymoma and adult-onset immunodeficiency (1). The incidence is not clear yet. It has a worldwide distribution, but most cases have been described in Europe. To date, only 17 cases have been reported in China. The immunodeficiency in GS is characterized by reduced or absent B cells in peripheral blood, dysgammaglobulinemia, and T-cell immunodeficiency. The clinical manifestations of GS include thymoma, opportunistic infections, diarrhea, and autoimmune manifestations, such as myasthenia gravis, pure red cell aplasia (PRCA), and aplastic anemia (2).

Although up to 31.8% of patients with GS can have diarrhea, the cause of diarrhea is still not clear. Many factors may be related to the cause of diarrhea, such as infections and malabsorption. Immunodeficiency can increase the risk of opportunistic infections in the GI tract. Many pathogens have been identified, including CMV, Campylobacter spp., and Giardia lambia, etc. (3–6), among which Salmonella spp. were the most common one. Hypogammaglobulinemia and mucosal lesions resembling villous atrophy can also lead to malabsorption (7, 8). Other causes of diarrhea may include bacterial overgrowth (9) and immune-mediated colitis (10). Ulcerative colitis also has been reported and may be an explanation for the diarrhea in many patients. Although we could not identify definite pathogens in this patient’s stool, his diarrhea still was alleviated by antibacterial treatment, which suggested that his diarrhea may be caused by infection by an unusual pathogen.

Sinopulmonary infection is the most commonly described infection in GS (2). The pathogens identified included Haemophilus
influenza and Streptococcus pneumoniae, etc. Tuberculosis also has been reported. CMV is the most commonly described viral infection in GS (2). About 21.1% of patients with GS presented with CMV infection. The clinical manifestations of CMV infection in GS include pneumonia and colitis, etc. (2). In our patient, Escherichia coli, Haemophilus influenza, CMV, and herpes simplex virus were identified at the same time. To our knowledge, this is the first report of two kinds of bacterial and viral infections in one patient with GS. We believe that the recurrent infection was related to his humoral immunity deficiency and his low CD4/CD8 ratio.

The pathogenesis of immunodeficiency in GS remains unknown. The thymus is an organ that mediates important immune functions. In thymoma, derangement of the microenvironment of the medullary and cortical compartments in the thymus may lead to loss of self-tolerance (11), impaired immune surveillance, and various autoimmune phenomena (12).

The standard treatment of thymoma is surgical removal or debulking of the tumor (13); however, the clinical outcomes of thymectomy differ. For some patients, symptoms improved (12), for some symptoms became aggravated (14), and for the others there was no change (15, 16). Our patient’s symptoms became worse after the surgery. The mechanism is not fully understood. In almost all cases, thymectomy does not restore immune function. The thymus plays a central role in the generation and maintenance of peripheral T-cell populations. Thymectomy was not able to change the number of peripheral T cells, which may be related to thymectomy extending the half-life of immature T cells; in fact, thymectomy can reduce the number of T₄₁ cells (17), which may lead to a reduction in the number of activated B cells. The mechanism of chronic diarrhea in GS is a complex mechanism, with multiple factors involved and thymoma itself may be one of the factors.

In conclusion, in a patient with thymoma and recurrent opportunistic infection, Good syndrome should be considered, and the immunological parameters should be checked. Currently, there is no satisfactory treatment. Thymectomy can prevent locally invasive growth and metastasis of thymoma, but it does not reverse dysimmunity (18). Gammaglobulin replacement was recommended to suppress infections associated with GS. A recent report showed that the use of IL-7 or IL-5 cytokines might be able to rebuild immunity in patients with GS (19).

REFERENCES

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