

Case
Report

A Case of Good's Syndrome: A Rare Acquired Immunodeficiency Associated with Thymoma

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The patient was a 76-year-old man who had a prior history of recurrent pneumonia and severe, chronic sinusitis. Computed tomography showed a thymoma, and laboratory results revealed hypogammaglobulinemia. Therefore, Good's Syndrome (GS, rare adult-onset immunodeficiency with thymoma) was diagnosed. To treat his sinusitis, we started the patient on long-term clarithromycin therapy, preoperatively. A thymothymectomy was performed, but the immunological disorder was not resolved. Although standard gamma globulin replacement was not given, his sinusitis symptoms were ameliorated, and he has not had pneumonia since the operation. Long-term macrolide therapy probably plays some role in managing sino-pulmonary infections associated with GS.

Key words: thymoma, immunodeficiency, Good's syndrome, macrolide, sino-pulmonary infection

Introduction

Good's Syndrome (GS), an adult-onset immunodeficiency associated with thymoma, is quite rare in Japan, as it occurs in only 0.2–0.3% of thymoma patients. In typical GS, hypogammaglobulinemia and B-cell depletion are observed.^{1–2)} Preventing infection improves the prognosis of GS and, to date, cyclical gamma globulin replacement therapy is considered necessary. Here, we describe a case of GS for which the long-term administration of clarithromycin appeared to be effective, both for preventing pneumonia and ameliorating sinusitis without the need for gamma globulin replacement therapy.

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Received: September 24, 2009; Accepted: November 9, 2009
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Case

The patient was a 76-year-old man who had been referred to the division of respiratory medicine of Fukui Red Cross Hospital in 2006 for recurrent pneumonia. In December 2005, he had pneumonia of the left lung, which was treated by his family physician. At presentation, a chest roentgenogram and computed tomography showed infiltrative shadows (pneumonia) in the bilateral lower lobes, and an anterior mediastinal mass was noted (**Fig. 1**). After successful treatment of the pneumonia with ciprofloxacin, he was referred to the division of thoracic surgery for resection of the anterior mediastinal mass, which was suspicious for thymoma.

At the time of referral to our division, severe chronic sinusitis was evident, which was the probable cause of the recurring episodes of pneumonia. Clarithromycin at 400 mg/day was administered to treat his sinusitis. After the sinusitis symptoms improved, he was admitted for surgical removal of the tumor.

Laboratory results on admission showed hypogammaglobulinemia: IgM = 22 mg/dl (normal, 57–288 mg/dl), IgA = 1 mg/dl (normal, 84–438 mg/dl), IgG = 214 mg/dl (normal, 680–1620 mg/dl) and B cell depletion (only 1 % of

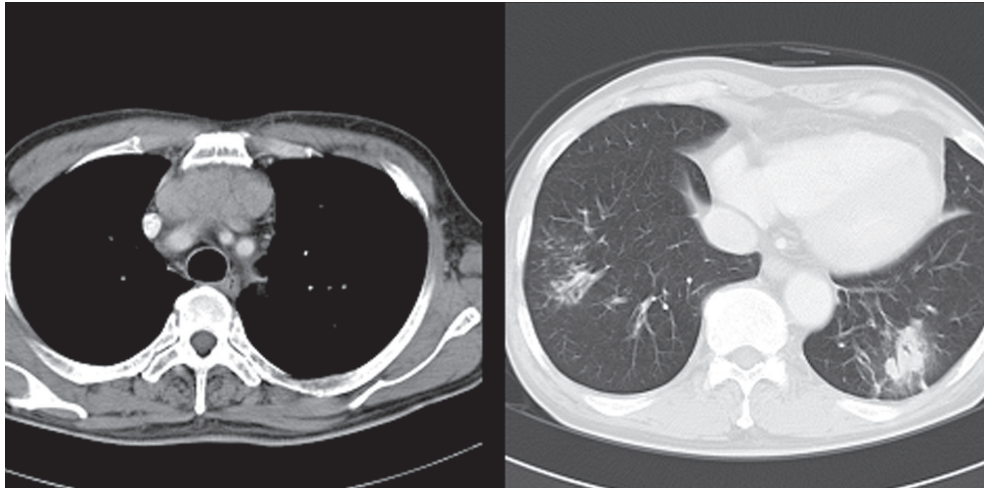


Fig. 1 Computed tomography showing an anterior mediastinal mass and infiltrative shadows of the bilateral lungs.

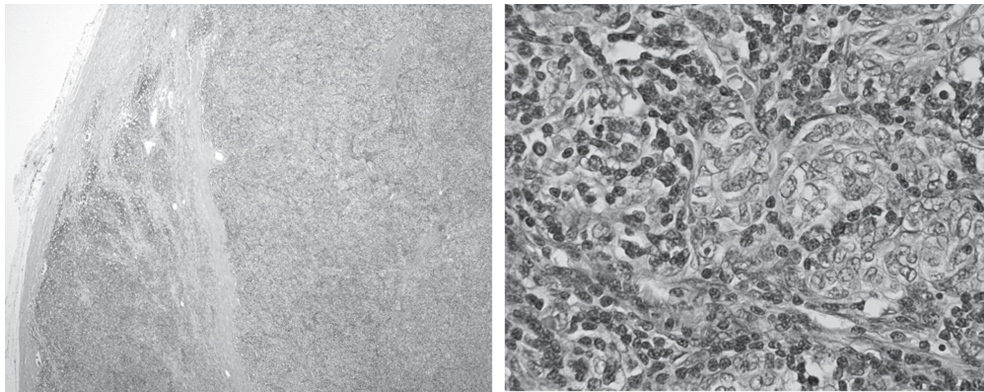


Fig. 2 Microscopically, the tumor was encapsulated and loculated by fibrous connective tissue (left, Hematoxylin and Eosin (HE) stain, $\times 20$); round or spindle-shaped epithelial tumor cells with infiltrations of abundant lymphocytes (right, HE stain, $\times 400$).

total lymphocytes). From these results, we diagnosed GS.

The patient continued to take clarithromycin, and gamma globulin replacement therapy was administered just before surgery. The tumor was resected via median sternotomy. Pathologically, the tumor was diagnosed as a type AB thymoma according to the World Health Organization classification (**Fig. 2**). Several months after the operation, the clarithromycin dose was reduced to 200 mg/day, resulting in the recurrence of sinusitis. Therefore, the dose was returned to 400 mg/day to relieve the sinusitis. On follow-up, while continuing with clarithromycin at 400 mg/day, but without gamma globulin replacement, he has had no episodes of pneumonia or any other severe infections for more than 2 years after the operation. However, his immune function remains abnormal.

Discussion

Good's Syndrome (GS) is an acquired, primary immunodeficiency disease associated with thymoma. GS occurs in 5–10% of thymoma patients in Western countries, but it only occurs in 0.2%–0.3% of thymoma patients in Japan.³⁾ GS most often occurs during the fourth to sixth decades of life and affects both sexes equally. Although this association was first reported by Good et al. in 1954, the pathogenesis of this syndrome is poorly understood.

GS is characterized by hypogammaglobulinemia, B cell depletion and variable defects in cell mediated immunity, such as CD4⁺ T cell lymphopenia and reduced T cell mitogen proliferative responses. The clinical char-

acteristics of GS are increased susceptibility to bacterial infections with encapsulated organisms and opportunistic viral and fungal infections.¹⁻²⁾ The most common infections are recurrent respiratory infections by encapsulated organisms, such as *Haemophilus influenzae*, *Streptococcus pneumoniae* and others, which reflects deficient humoral immunity. Another common complication in GS patients is chronic diarrhea. In the majority of cases, the pathogen inducing chronic diarrhea is unclear. Opportunistic infections associated with disorders of cell mediated immunity commonly occur in GS. The most frequently observed infections include mucocutaneous candidiasis, herpes zoster, herpes simplex virus infection, *Pneumocystis jiroveci* pneumonia and cytomegalovirus infection. For reasons that are not clear, mycobacterial infections are rare.

The prognosis for GS is believed to be poorer than that for X linked agammaglobulinemia and common variable immune deficiency. In a single center review, the 5-year and 10-year survival rates for patients with GS were 70% and 33%, respectively.⁴⁾

With regard to treatment, thymothymectomy should be performed to avoid local invasion, dissemination and metastatic spread of thymoma. However, thymothymectomy does not restore immune function in almost all cases.¹⁻²⁾ By consensus, standard immunoglobulin replacement is useful for hypogammaglobulinemia.¹⁻²⁾

A retrospective review of the efficacy of immunoglobulin replacement for GS showed that 23 of 30 patients had favorable responses during their follow-up periods.¹⁾ However, there are no other established treatment options to suppress infections, and it is important to find a new management options. Macrolides have proven efficacy for the management of chronic respiratory infections. Over the past decade, there has been increasing interest in these agents as tissue modifying, anti-inflammatory agents. There is accumulating evidence that confirms their clinical effects for numerous inflammatory sino-pulmonary disorders, including diffuse panbronchiolitis, chronic sinusitis, cystic fibrosis and non-cystic fibrosis bronchiectasis.⁵⁾ Anecdotally, there have been 2 reports from Japan regarding the efficacy of long-term macrolides for the treatment of sino-pulmonary infection in GS.^{3, 6)} In one case, treatment with an oral erythromycin at 600 mg/day for 6 months improved the symptoms of sinusitis and pulmonary infection.⁶⁾ For another case, treatment with macrolides for 2 months also improved sino-pulmonary infection.³⁾

In the case reported here, thymothymectomy did not

normalize the immunological disorder for the patient, as we had expected. However, clarithromycin prescribed for the treatment of severe sinusitis, before the diagnosis of GS was established, ameliorated the sinusitis symptoms and unexpectedly prevented the recurrence of pneumonia. Therefore, this is the third case showing the efficacy of macrolides for controlling sino-pulmonary infections in GS.

Conclusion

We have reported a case of GS, a rare adult-onset immunodeficiency associated with thymoma. There is currently no established treatment, other than standard gamma globulin replacement therapy, to suppress infections associated with Good's syndrome. Although thymothymectomy did not resolve the immunological disorder of the patient, long-term clarithromycin therapy prevented the recurrence of pneumonia and suppressed the sinusitis. We believe that long-term macrolide therapy plays some role in controlling sino-pulmonary infection of GS, as in cases with other chronic sino-pulmonary diseases. Investigations with larger numbers of cases are required to confirm this hypothesis.

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