

Thymoma and hypogammaglobulinemia (Good's syndrome): a case report

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Good's syndrome is extremely rare and refers to an acquired B and T cell immunodeficiency in thymoma patients. We report a 51-year-old female thymoma patient who presented with recurrent herpes zoster, pneumonia, diarrhea and opportunistic infections. She was found to have acquired hypogammaglobulinemia with absent B cells. Despite repeat intravenous immunoglobulin replacement and antibiotic therapy, she died of bacterial pneumonia-induced acute respiratory distress syndrome. Clinicians should look for evidence of immunologic dysfunction in thymoma patients presenting with recurrent infections.

Key words: Thymoma, hypogammaglobulinemia

Good's syndrome (GS) was first reported by Robert Good in 1954, and is commonly referred to as a rare constellation of thymoma and hypogammaglobulinemia [1]. The estimated incidence showed that about 3-6% of patients with thymoma may develop hypogammaglobulinemia [2]. The clinical manifestations of GS are thymoma with increased susceptibility to opportunistic infections and hypogammaglobulinemia with reduced or absent B cells [3]. Herein, we describe an unusual thymoma patient, who presented with acquired hypogammaglobulinemia and recurrent herpes zoster, pneumonia and diarrhea. After intravenous immunoglobulin (IVIG) supplement, acyclovir and antibiotics, she died eventually of bacterial pneumonia with acute respiratory distress syndrome. To the best of our knowledge, this is the first reported case of GS in Taiwan.

Case Report

A 51-year-old woman was previously healthy when, in 1990, a mediastinal mass was discovered on a chest X-ray when she underwent right hip replacement due to femoral neck fracture at a local clinic. Thymoma was confirmed by biopsy but she refused thymectomy. In

1998, she had a clinical episode of herpes zoster over S2-S3 dermatomes and was regularly followed up at a dermatology clinic. In January 2001 and February 2001, she was admitted to a local clinic due to 2 episodes of pneumonia, and persistent leukopenia, oral candidiasis, and diarrhea. She underwent bone marrow aspiration but no specific finding was found. The pneumonia responded to granulocyte monocyte colony-stimulating factor and antibiotic treatments but persistent watery diarrhea and body weight loss were noted.

In March 2001, worsening diarrhea, fever, and weight loss of about 5 kg were noted and she was admitted to our hospital. A recurrent herpes zoster outbreak over the buttock was found on physical examination. Laboratory studies disclosed the following findings: hemoglobin 7.7 g/dL; white blood cell count 1.8×10^3 cells/mm³ (58% polymorphonuclear leukocytes, 16.3% lymphocytes and 24.9% monocytes); erythrocyte sedimentation rate 19 mm/h; C-reactive protein 143 mg/L; C3 102 mg/dL; C4 33.9 mg/dL; albumin 3.0 g/dL. Blood and stool cultures showed no growth. She was found to be hypogammaglobulinemic at this time, with low levels of immunoglobulin G (IgG) [150 mg/dL; reference range, >760 mg/dL], immunoglobulin A (43 mg/dL; reference range, >99 mg/dL), and immunoglobulin M (4 mg/dL; reference range, >38 mg/dL). The CD4⁺ T cell count was 189/μL with an inverted CD4/CD8 ratio of 0.30, and peripheral B cells were absent (Table 1). Human immunodeficiency virus serology test and antinuclear

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Table 1. Immune profile of the patient

Antinuclear antibodies	Negative
Human immunodeficiency virus	Negative
Lymphocyte subpopulations	
CD4	23% (189/ μ L)
CD8	73% (630/ μ L)
CD4/CD8	0.30
CD19	0% (0/ μ L)
Serum immunoglobulins	
Immunoglobulin G	150 mg/dL
Immunoglobulin A	43 mg/dL
Immunoglobulin M	4 mg/dL

antibodies were negative. Chest films revealed a bulging mass in medial aspect of right hemithorax (Fig. 1A). Repeated chest computed tomography revealed a big lobulated soft tissue mass ($10 \times 9 \times 7$ cm) with multiple nodular and well-enhanced structures, and thymoma was considered (Fig. 1B). Monthly IVIG supplementation (400 mg/kg) and appropriate antibiotics with acyclovir were prescribed to reduce the frequency of infection.

In March 2002, she was readmitted due to fever, persistent diarrhea, cough, oral candidiasis and cachexia. *Pseudomonas aeruginosa* and *Staphylococcus aureus* were cultured from the sputum. She did not respond to antibiotics and then developed respiratory failure. She died of acute respiratory distress syndrome with multiple organ failure.

Discussion

GS is defined as thymoma in patients with adult-onset immunodeficiency that is characterized by

hypogammaglobulinemia, low or absent B cells, variable defects in cell-mediated immunity with CD4⁺ T lymphopenia and reduced T cell mitogen proliferative responses [4,5]. Common variable immunodeficiency (CVID) is a heterogeneous group of acquired hypogammaglobulinemia with cellular immune defects that resemble GS. However, the reduced number of peripheral blood B cells that is typical of GS is not a feature of CVID [6].

The pathogenesis of immunodeficiency in patients with GS remains unknown, although there are some connections with bone marrow defects and pre-B cell lymphopenia [7], and frequent coexistence of eosinopenia [8]. Anemia was present in over half of the GS patients [4]. Occasionally, GS patients with pure red cell aplasia may respond to glucocorticosteroids, suggesting autoimmune pathogenesis which directly or indirectly inhibits erythropoiesis; however, the immunologic abnormalities do not improve following treatment [4,9]. Another possible explanation for the immune deficiency in patients with GS was that T cells isolated from thymoma patients inhibited immunoglobulin production by B cells and pre-B cell growth in healthy control subjects [10,11]; however, further investigations is warranted.

The most common infectious characteristic of patients with GS was recurrent sinopulmonary infection with encapsulated bacteria [4]. This likely reflects the deficiency of humoral immunity, specifically the low serum levels of IgG [3]. Patients with GS appear to develop opportunistic viral and fungal infections frequently, which suggests severe defects in cell-mediated

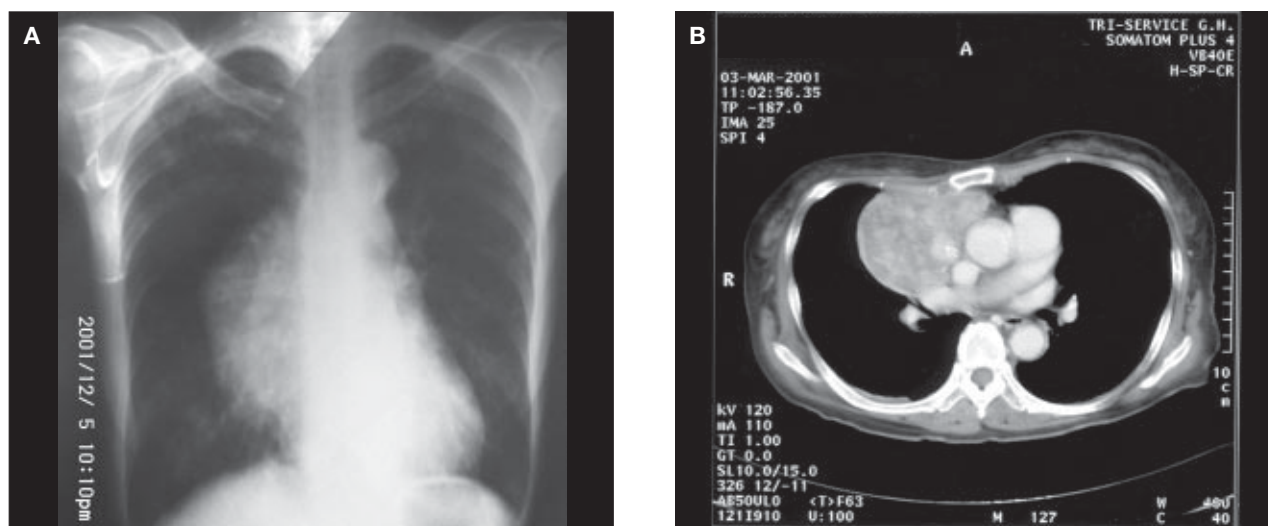


Fig. 1. (A) A bulging mass in medial aspect of right hemithorax. (B) Chest computed tomography scan revealed a large lobulated soft tissue mass ($10 \times 9 \times 7$ cm) with multiple nodular and well-enhanced structures.

immunity. This is supported by results of in vitro studies showing defects in T lymphocyte proliferation and/or interleukin-2 production [5]. In addition, the function of phagocytes was essentially normal in patients with GS [4].

The most frequently observed opportunistic infections included mucocutaneous candidiasis, *Pneumocystis carinii* pneumonia, herpes zoster [12], and recurrent herpes simplex infections [13]. Another common complication in patients with GS was chronic diarrhea. Most of the patients with diarrhea had no definite pathogens identified; however, gastrointestinal pathogens, such as *Giardia lamblia*, non-typhoidal *Salmonella*, or cytomegalovirus were found occasionally [4]. It would be wise to assess the risks of opportunistic infections in GS patients and perform appropriate microbiologic investigations and consider prophylactic antibiotics to prevent infections.

Most resected thymoma in patients with GS were found to be noninvasive, well-encapsulated tumors and 75% of thymoma were spindle cell type [3]. There was no consistent relationship between the microscopic appearance of thymomas and their clinical behavior. In addition, there is an absence of any reports of resolution of the immunodeficiency in patients with GS that were related to thymectomy [3,4].

The mortality rate was even higher in patients with GS than patients with X-linked agammaglobulinemia or CVID [14]. The major causes of death of patients with GS were infection, autoimmune disease and hematologic complications [3,4]. Despite repeat IVIG replacement and prophylactic antibiotic therapy, our patient died of bacterial pneumonia. In conclusion, further immunologic studies about the number of peripheral B cells, and CD4⁺ and CD8⁺ T cell ratios using flow cytometry and quantitative serum immunoglobulin subclasses should be considered in all patients presenting with recurrent infection and thymoma. In addition, IVIG had the clinical benefits of improved infection control, reduced hospitalization rates and decreased use of antibiotics [4], and we recommend that it be given to all GS patients in order to maintain appropriate IgG values.

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