Good's syndrome complicated with bronchiectasis with pulmonary hypertension

Chun Fei Yap, MRCP[1], Keen Tien Boey, MD[2], Yi Fan Goh, MD[1], Say Thin Chu, MRCP[1], Jiunn Sheng Chin, MRCP[1]

[1]Department of Internal Medicine, Hospital Duchess of Kent, [2]Department of Internal Medicine, Hospital Putrajaya

SUMMARY

Good's syndrome (GS) is a rare but important adult-onset immunodeficiency characterized by the coexistence of thymoma and hypogammaglobulinemia in adults. Diagnosis is often delayed because of the wide interval between the appearance of thymoma and the onset of immunodeficiency-related infections. Clinicians should maintain a high index of suspicion in adults with thymoma and recurrent or unusual infections, particularly respiratory infections, and routinely assess serum immunoglobulin levels. Early recognition and initiation of immunoglobulin replacement therapy are essential for reducing infectious complications and improving outcomes. Thymectomy, while necessary for tumor control, does not reverse immune dysfunction. This case report of GS aims to raise awareness among healthcare workers for patients with thymoma who present with recurrent or unusual infections and further workup for this group of patients. We herein report a case of a young female patient with underlying type AB thymoma but defaulted follow-up, history of bacteremia, and presented with recurrent pulmonary infections complicated with pulmonary hypertension who was found to have hypogammaglobulinemia leading to a diagnosis of GS. She was treated with intravenous immunoglobulin (IVIG) and was subsequently planned for long-term immunoglobulin replacement therapy.

INTRODUCTION

GS, an adult-onset immunodeficiency associated with thymoma, leads to immune system dysfunction and increased susceptibility to severe infections due to encapsulated bacteria, viruses, and fungi.[1-2] Both males and females are equally affected, commonly in their 4th or 5th decade of life, although it can rarely occur in younger patients.[1-2] It is challenging to recognize the disease because of its complexity, frequently leading to diagnostic delays.[2-3] Treatment mainly involves immunoglobulin replacement, treatment of infections, and removal of thymoma.[3-4] The prognosis is believed to be worse than that of other adult immunodeficiency conditions.[5]

CASE PRESENTATION

A 33-year-old single, nulliparous, non-smoker woman with a history of childhood asthma and recurrent pulmonary infections, including Salmonella non-typhi bacteremia, and recurrent admission for pulmonary infections presented with a 6-month history of productive cough without hemoptysis. She reported significant unintentional weight loss and reduced appetite over the same duration, along with a 2-week history of progressive shortness of breath.

Physical examination revealed bilateral generalized rhonchi accompanied by crepitations across both lung fields. Initial blood gas analysis showed type II respiratory failure, with a full blood count showing leukocytosis and elevated C-reactive protein levels of 58 × 10^3/µL (neutrophil predominance) and 74 mg/L. Chest radiography revealed consolidation with cavitation in the bilateral upper lung zones. She was initially intubated for 1 week for respiratory failure, requiring intensive care unit (ICU) admission for 9 days before transfer to the general medical ward for further treatment. She was treated for community-acquired pneumonia (CAP) with a 1-week course of intravenous Meropenem in ICU. Although she improved and was transferred to a general medical ward, her condition deteriorated and she developed desaturation five days later. She was then treated for Pseudomonas aeruginosa pneumonia, as evidenced by a positive sputum culture, with a total of one month of anti-Pseudomonas antibiotics. Computed tomography pulmonary angiography was performed due to the patient's difficulty in oxygen weaning, and it showed no pulmonary embolism.

Serial infective workups showed negative blood, fungal, urine, and Mycobacterium tuberculosis cultures. Connective tissue workup showed normal C3/C4 values with negative antinuclear antibodies (ANA) and anti-neutrophil cytoplasmic antibodies, while the immunoglobulin test showed hypogammaglobulinemia with IgA, IgG, and IgM values of 0.3 g/L, 4.02 g/L, and <0.25 g/L, respectively, with a raised ESR value of 21 mm/h. Contrast-enhanced computed tomography (CECT) of the thorax showed features consistent with organizing pneumonia with bilateral upper lung lobe fibrosis and bronchiectasis changes, as well as an anterior mediastinal mass representing thymoma. Further history revealed that the patient had a thymoma previously, for which thymectomy was not performed as she defaulted to follow-up. Echocardiography was also performed to look for complications of bronchiectasis and showed pulmonary hypertension.

In view of the collective evidence of recurrent pulmonary infection, presence of thymoma type AB, and hypogammaglobulinemia, a diagnosis of GS was made. The patient was discharged after 3 months of hospitalization, and two courses of IVIG were administered during admission. Following a second course of IVIG one month after the first,

This article was accepted: 22 June 2026
Corresponding Author: Chun Fei Yap
Email: yapchunfei@moh.gov.my

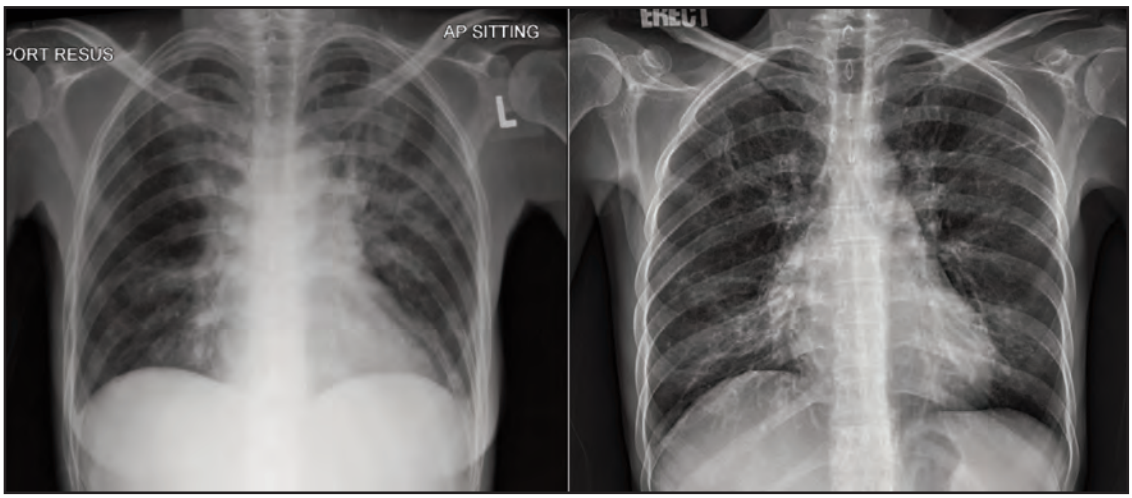

Fig. 1: Left - Chest radiograph upon arrival at the emergency department with pneumonia changes seen over the bilateral upper lobe; Right - Chest radiograph after two courses of antibiotics and one course of IVIG showing resolution of pneumonia

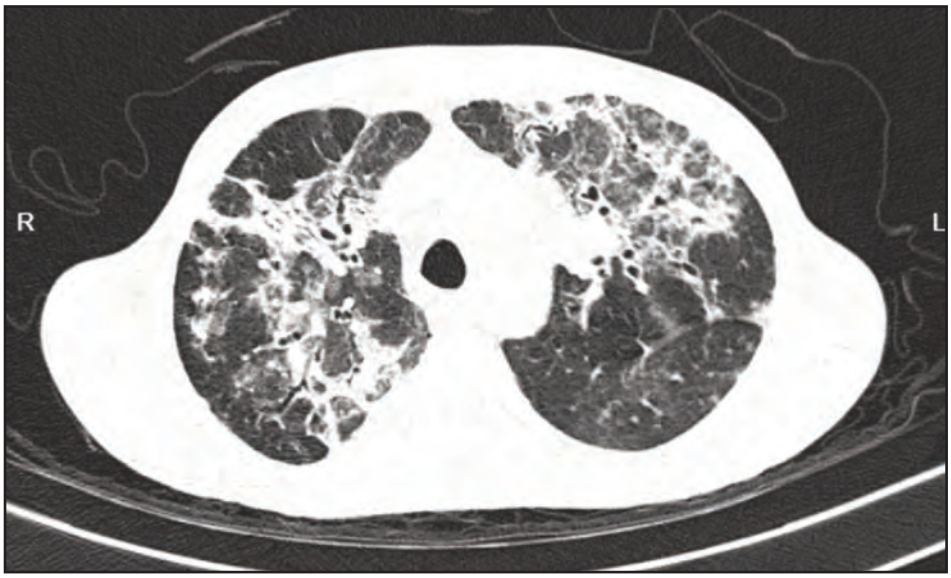

Fig. 2: Bronchiectasis changes from the CECT thorax

immunological reassessment showed IgG improvement from 4.02 g/L to 6.44 g/L after the second course. The post-treatment CD4 and CD8 levels were 404 cells/µL and 603 cells/µL, respectively, resulting in an inverted CD4/CD8 ratio of 0.67.

DISCUSSION

GS, a rare adult-onset immunodeficiency associated with thymoma, was first identified in 1954 by Dr. Robert Good, who described a case of thymoma and hypogammaglobulinemia in an adult patient.[6] The condition has an estimated incidence of 0.15 cases per 100,000 population annually. Hypogammaglobulinemia occurs in approximately 6–11% of patients with thymoma. GS typically presents between the ages of 40 and 60 years, with a prevalence of approximately 1 in 700,000 adults.[1] To our knowledge, based on a comprehensive review of the literature, no prior cases of GS have been reported from Sabah, making this the first documented case in this Malaysian state; however, there could be a possibility of prior unreported cases.

The pathogenesis of immunodeficiency in GS remains unknown, and there are no formal diagnostic criteria for this disorder. There is some evidence that the basic defect may be in the bone marrow, as suggested by the presence of B- and T-cell lymphopenia, pre-B-cell arrest, impaired maturation of erythroid and myeloid precursors, pure red cell aplasia (PRCA), neutropenia, and eosinophilia.[2] Although the principal feature of GS is humoral immunodeficiency, cell-mediated immunity is also impaired. Another proposed mechanism is that B cell dysfunction may be caused by autoimmune destruction, likely due to the presence of autoantibodies associated with thymomas, as observed in other paraneoplastic disorders.[7] T-cells from thymomas can

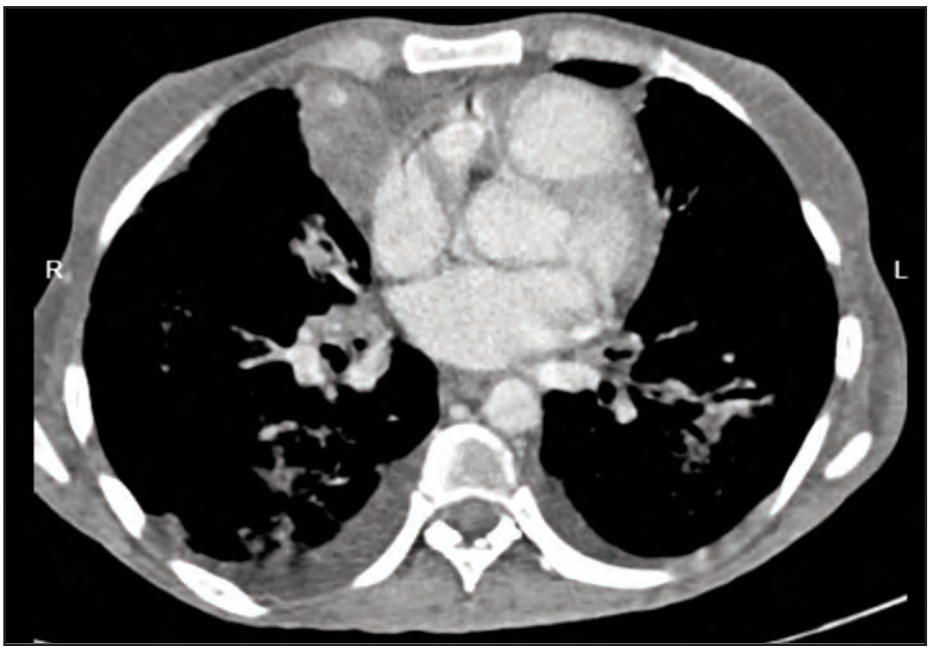

Fig. 3: Thymoma from CECT thorax

also impair the growth of B-cells and their immunoglobulin production. To date, it has been classified as a distinct entity by the expert committee of the World Health Organization/International Union of Immunological Societies on primary immunodeficiencies. Most of the literature reviews used the simultaneous presence of thymoma and hypogammaglobulinemia as the minimal diagnostic criteria for a diagnosis of GS, which in our case fulfilled these minimal diagnostic criteria.[8]

The clinical presentation of GS is highly variable and typically reflects the site of infection. Lower respiratory tract infections are the most frequently reported cases, but patients may also present with upper respiratory, gastrointestinal, skin and soft tissue, urinary tract, systemic, or central nervous system infections. Complications of this recurrent sinopulmonary infection, such as bronchiectasis, necrotizing pneumonia with lung abscess, and empyema, have also been noted in the literature by Tarr et al. and other authors. (2) With regard to causative micro-organisms, bacterial infections account for 80% of the cases, followed by viral and fungal infections.[5]

This patient's history of recurrent pulmonary infections led to bronchiectasis and type 2 respiratory failure. Furthermore, the patient developed group 3 pulmonary hypertension secondary to bronchiectasis. Due to the delayed diagnosis, the combination of pulmonary hypertension and type 2 respiratory failure necessitated long-term oxygen therapy.

Patients with GS usually present in the 4th or 5th decade of life. In a literature review of 51 patients with GS, the mean age of the patients was 56 years (range, 29 – 75 years) at the time of the 1st presentation (infection, thymoma, or hypogammaglobulinemia).[2] Diagnosis of thymoma preceded the diagnosis of hypogammaglobulinemia, infection, or diarrhea in 18 patients in the above literature with an interval of 3 months to 23 years, and in the remaining 29 patients, thymoma was diagnosed after the documentation of infection or hypogammaglobulinemia with an interval of 3 months to 20 years. Of the remaining four patients, two were diagnosed within two months of each other, and in the other two patients, thymoma was only diagnosed at autopsy. These results indicate that thymoma and hypogammaglobulinemia as the minimal diagnostic criteria can be fulfilled as short as within 2 months but can take up to 23 years, which can lead to a delay in diagnosis and treatment.[2] Another systematic review of 152 patients also reported that the diagnosis of thymoma preceded hypogammaglobulinemia or vice versa can be diagnosed within 2 months but can also take a longer period of up to 18 years.[3]

In this case, the patient was first diagnosed with an anterior mediastinal mass at the age of 29 years as an incidental finding when a CECT thorax was performed as part of the investigation for chronic cough. A biopsy of the anterior mediastinal mass was performed, and the histopathological features were in favor of thymoma type AB. Although the patient was not in the 4th or 5th decade of life, her first presentation was still within the range.[2] The patient was diagnosed with Good Syndrome only 4 years after the diagnosis of thymoma, as evidenced by hypogammaglobulinemia. Zaman et al reported in their article on 78 United Kingdom patients with GS that patients with AB-type thymomas were more likely to have bronchiectasis. Another systematic review by Dong et al. reported that type AB is the most common histologic type of thymoma in Chinese patients with GS, which is similar to the findings in our case.[8-9]

Prior to the diagnosis of Good syndrome, our patient experienced multiple episodes of respiratory infections, including several admissions for CAP. During her first

presentation, no pathogens were isolated from sputum or blood cultures, and the tuberculosis workup was negative; however, she had marked leukocytosis (white cell counts - WCC 59 × 10^3/μL) and elevated C-reactive protein (155 mg/L), which normalized after antibiotic treatment. A few years after her first encounter, she presented with a milder episode managed with outpatient antibiotics, again with negative cultures and a peak WCC of 17 × 10^3/μL. During her third encounter, she was admitted for CAP with non-typhoidal Salmonella isolated from blood despite no gastrointestinal symptoms. Subsequent stool and urine cultures were negative, and WCC peaked at 15.3 × 10^3/μL without significant leukocytosis. Another admission for pneumonia showed significant leukocytosis (WCC 70.3 × 10^3/μL), with Pseudomonas aeruginosa isolated from sputum. Although pulmonary tuberculosis remains a high-burden disease in Sabah, it is rarely associated with GS and was consistently ruled out during all admissions. Peripheral blood films consistently showed no evidence of hematological malignancy.

The principal immunological findings in GS are hypogammaglobulinemia, few or absent B cells, an abnormal CD4+:CD8+ T-cell ratio, CD4 + T-cell lymphopenia, and impaired T-cell mitogenic response. Almost all patients have reduced serum IgG, IgA, and IgM levels, but there are very limited data on the prevalence of reduced specific antibody levels. GS should be suspected in patients aged > 40 years with a history of recurrent sinopulmonary infections or opportunistic infections such as cytomegalovirus or mucocutaneous candidiasis, and further workup such as CECT thorax scan should be performed to look for any mediastinal mass. Conversely, serum immunoglobulins should be considered as part of routine diagnostic investigations for patients with anterior mediastinal masses. If the immunologic test results are normal, testing should be performed periodically if GS is suspected, because there can be an interval between the diagnosis of immunodeficiency and/or thymoma and the development of infection.[10]

The management of GS mainly consists of thymectomy for thymoma and gamma globulin replacement. The treatment of thymoma involves surgical intervention, either removal or debulking of the tumor, and the most important indicator of long-term prognosis is the completeness of tumor resection. Thymectomy can prevent locally invasive growth and metastasis of thymomas and usually has a favorable effect on associated conditions, such as myasthenia gravis and PRCA; however, it does not usually reverse the immunological abnormalities in GS.[4] Lifelong immunoglobulin replacement therapy to maintain adequate trough IgG levels has been reported to improve infection control, reduce hospitalization, and decrease the use of antibiotics. In one study, 23 of 30 patients (76%) had a reduction in the number of bacterial sinopulmonary infections, while another study reported that approximately 38% of patients with GS had a reduced incidence of infections after treatment with gamma globulin.[2-3] Thus, IVIG is recommended to maintain appropriate immunoglobulin levels in all these patients. Hizantra, a subcutaneous immunoglobulin, has been FDA-approved for use in immunodeficiency since 2010 and is commonly being transitioned from IVIG, especially in patients who require long-term immunoglobulin replacement. Subcutaneous immunoglobulin is reported to be much more convenient and easier to use, achieving a similar result compared to IVIG, with tolerable minimal side effects.

The patient is scheduled for lifelong monthly IVIG infusions with regular reassessment of immunoglobulin levels while awaiting approval for subcutaneous administration of immunoglobulin. After two courses of IVIG, her IgG levels improved, and she remained free of admission at the time of this report. The patient was enrolled in a regular pneumococcal and influenza vaccination program. She is currently under cardiothoracic review for thymoma, with ongoing discussions regarding thymectomy as part of her management.

In conclusion, this case highlights the importance of clinical awareness and knowledge of GS in patients with thymoma, as delayed recognition can lead to repeated hospital admissions and missed opportunities for timely diagnosis and management of GS. Patients with thymoma should undergo routine assessments of serum immunoglobulin levels to facilitate the early detection of GS. Immunoglobulin replacement is an effective therapy for managing immunodeficiency-related complications.

REFERENCES

1. Kabir A, Alizadehfar R, Tsoukas CM. Good's Syndrome: Time to Move on From Reviewing The Past. Frontiers In Immunology. 2021; 12: 815710.
2. Tarr PE, Sneller MC, Mechanic LJ, Economides A, Eger CM, Strober W, et al. Infections in patients with immunodeficiency with thymoma (Good syndrome). Report of 5 cases and review of the literature. Medicine 2001; 80(2): 123-33.
3. Kelesidis T, Yang O. Good's Syndrome Remains A Mystery After 55 Years: A Systematic Review of The Scientific Evidence. Clinical Immunology (Orlando, Fla) 2010; 135(3): 347-63.
4. Souadjian JV, Enriquez P, Silverstein MN, Pépin JM. The Spectrum of Diseases Associated with Thymoma. Coincidence or Syndrome? Archives of Internal Medicine 1974; 134(2): 374-9.
5. Jansen A, van Deuren M, Miller J, Litzman J, de Gracia J, Sáenz-Cuesta M, et al. Prognosis of Good Syndrome: Mortality and Morbidity of Thymoma Associated Immunodeficiency In Perspective. Clinical Immunology (Orlando, Fla). 2016;171:12-7.
6. Good R. A gammaglobulinemia-A provocative experiment of nature. Bulletin University Minnesota Hospitals and Minnesota Medical Foundation 1954; 26:1 .
7. Charles RJ, Sabo KM, Kidd PG, Abkowitz JL. The pathophysiology of pure red cell aplasia: implications for therapy. Blood 1996; 87(11): 4831-8.
8. Zaman M, Huissoon A, Buckland M, Patel S, Alachkar H, Edgar JD, et al. Clinical and Laboratory Features of Seventy-eight UK Patients with Good's Syndrome (Thymoma and Hypogammaglobulinaemia). Clinical and Experimental Immunology 2019; 195(1): 132-8.
9. Dong JP, Gao W, Teng GG, Tian Y, Wang HH. Characteristics of Good's Syndrome In China: A Systematic Review. Chinese Medical Journal 2017; 130(13): 1604-9.
10. Velde KT, Huber J, van der Slikke LB. Primary Acquired Hypogammaglobulinemia, Myasthenia, and Thymoma. Annals of Internal Medicine 1966; 65(3): 554-9.