**CASE SERIES**
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# Thymoma-associated Immunodeficiency (Good's Syndrome): A Case Series and Comprehensive Literature Review

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## ABSTRACT

Good's syndrome (GS) is a rare immunodeficiency disorder associated with thymoma, characterized by hypogammaglobulinemia and impaired cellular immunity. Due to its variable clinical presentation and lack of clear diagnostic criteria, GS is often underrecognized or diagnosed with delay.

We report 7 patients diagnosed with GS, including 2 previously reported cases and 5 new cases. Clinical, immunological, and radiological data were analyzed to characterize the spectrum of disease manifestations and outcomes.

The study comprised 6 men and 1 woman, with a mean age of 48 years at thymoma diagnosis and 50 years at immunodeficiency detection. Two patients were diagnosed with thymoma and immunodeficiency simultaneously, while in 5 patients thymoma preceded GS diagnosis by 1 to 2.5 years. Common clinical features included recurrent sinopulmonary infections and autoimmune manifestations, such as myasthenia gravis and lichen planus. Opportunistic infections, including cytomegalovirus and mycobacterial infections were observed. Immunological profiles demonstrated hypogammaglobulinemia, reduced B-cell markers (CD19, CD20), and variable T-cell subsets. Intravenous immunoglobulin replacement therapy led to clinical improvement in most cases. Two patients succumbed to complications related to severe infections.

GS presents with diverse clinical and immunological features, necessitating a high index of suspicion in patients with thymoma and recurrent infections. Early recognition and individualized immunoglobulin replacement therapy are critical for improving outcomes. Our series highlights the need for ongoing monitoring and management of immunodeficiency in thymoma patients.

**Keywords:** Good's syndrome; Immunodefiency; Thymoma

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## INTRODUCTION

Good's syndrome (GS) is a rare immunodeficiency disorder occurring in adults, characterized by its association with thymoma and an unclear underlying cause, first described by Dr Robert Good and colleagues in 1954. It presents with a wide range of clinical features, including recurrent infections, autoimmune conditions, malignancies, and involvement of the hematologic, gastrointestinal, and respiratory systems.[1]

The diagnosis of GS is often delayed due to its diverse clinical presentation and the absence of well-defined diagnostic criteria. As one of the rarest and least explored immune deficiency syndromes, its pathophysiology remains unclear. Initially thought to be a thymoma-associated variant of primary antibody deficiency—marked by a diminished or absent population of mature B cells—it has since been recognized that profound impairments in T cell-mediated immunity are primarily responsible for the occurrence of opportunistic infections.[2]

Recent investigations in immunology and molecular research established a new classification for GS as an indirect or acquired phenocopy of inherited inborn errors of immunity (IEI). Phenocopy refers to a condition that has a clinical and immunologic phenotype that mimics a genetically determined primary immunodeficiency but is due to an acquired, nonheritable cause. The concept of immunological phenocopies is particularly relevant in the case of GS, in which thymoma-associated immune dysregulation causes combined defects in both humoral and cellular immunity, which resemble congenital combined immunodeficiency disorders. Unlike classical IEIs due to germline mutations, GS usually develops later in life following secondary mechanisms that produce immunological defects, such as thymic epithelial dysfunction, somatic mutations, and epigenetic changes, which affect lymphocyte development and immune homeostasis. Based on these findings, GS is now being classified as an acquired combined immunodeficiency, with overlapping characteristics of both antibody deficiency and T-cell dysfunction. This reclassification reflects the importance of viewing GS not merely as paraneoplastic complications of thymoma but as a model for acquired phenocopies of IEI, in which various tumor-driven or microenvironment factors may result in global failure of the immune system.[3,4]

Autoimmune involvement may affect the skin, nervous system, and hematopoietic tissues. Commonly reported autoimmune manifestations include oral lichen planus, pure red cell aplasia, graft-versus-host disease-like symptoms, enteropathy, myasthenia gravis, neutropenia, and inflammatory bowel disease. Immunologically, patients often show markedly reduced or absent peripheral B cells, leading to hypogammaglobulinemia, alongside variable T-cell abnormalities, including a reversed CD4/CD8 ratio, CD4 lymphopenia, and inconsistent proliferative responses to mitogens. At present, there is no curative treatment, and management primarily involves immunoglobulin replacement therapy to mitigate the risk of infections and complications.[1]

In the present study, we report a total of 7 patients diagnosed with GS, including 2 previously reported cases and 5 new cases, highlighting the clinical heterogeneity of this condition and reinforcing the importance of recognizing GS as an acquired phenocopy of IEI that requires a multidisciplinary diagnostic and therapeutic approach.

## CASE PRESENTATION

The median patient age across the 5 cases was 47 years old (39–58). Each patient presented with recurrent or opportunistic infections, including cytomegalovirus (CMV) pneumonia, fungal infection, bacterial pneumonias, and tuberculosis. Hematologic abnormalities were present in most patients, with 3 patients with mild to moderate anemia and 2 with mild lymphopenia, and no autoimmune cytopenia or eosinophilia was present. Immunologic evaluations demonstrated severe hypogammaglobulinemia, with markedly decreased or absent $CD19^+$ and $CD20^+$ B cells, and there were also variable T-cell subset abnormalities consistent with combined immunodeficiency. All 5 patients were human immunodeficiency virus (HIV)-negative.

### Case 1

A 55-year-old man with a history of diabetes mellitus and hypertension was admitted for evaluation of persistent cough, fever, night sweats, and a 22-kg weight loss over 6 months. On examination, his temperature was 38°C, blood pressure 100/80 mmHg, heart rate 100 beats/min, respiratory rate 20 breaths/min, and oxygen

saturation 95%. Auscultation revealed coarse crackles in the right lung. The patient had a history of recurrent sinopulmonary infections in recent years. Laboratory results showed hemoglobin 11.4 g/dL, WBC 5600/µL, and normal platelets. Chest computed tomography (CT) scan showed a large anterior mediastinal mass measuring 38 mm, consistent with thymoma, along with multiple bilateral patchy ground-glass opacities suggestive of bronchopneumonia (Figure 1).

Abdominal and neck CT scans were unremarkable. Bone marrow aspiration and biopsy showed no evidence of malignancy. Bronchoscopy with bronchoalveolar lavage (BAL) revealed no pathogenic microorganisms. HIV antibody testing was negative. CMV viral load was elevated at 3017 copies/mL.Immunologic evaluation demonstrated hypogammaglobulinemia with immunoglobulin levels of IgG 76 mg/dL, IgA 45 mg/dL, IgM 24 mg/dL, and IgE 10 mg/dL. Flow cytometry of peripheral lymphocytes showed a marked deficiency in B-cell populations, with CD20 at 0.08% and CD19 at 0.09%. T-cell subsets were within normal ranges: CD3 at 91%, CD4 at 21%, and CD8 at 67% ((Table 1). A CT-guided biopsy of the anterior mediastinal mass was performed, and histopathology confirmed a mixed (AB) type thymoma. These findings indicate an immunodeficiency characterized by impaired humoral immunity, confirming the diagnosis of GS. Intravenous immunoglobulin (IVIG) replacement therapy was administered, leading to notable clinical improvement.

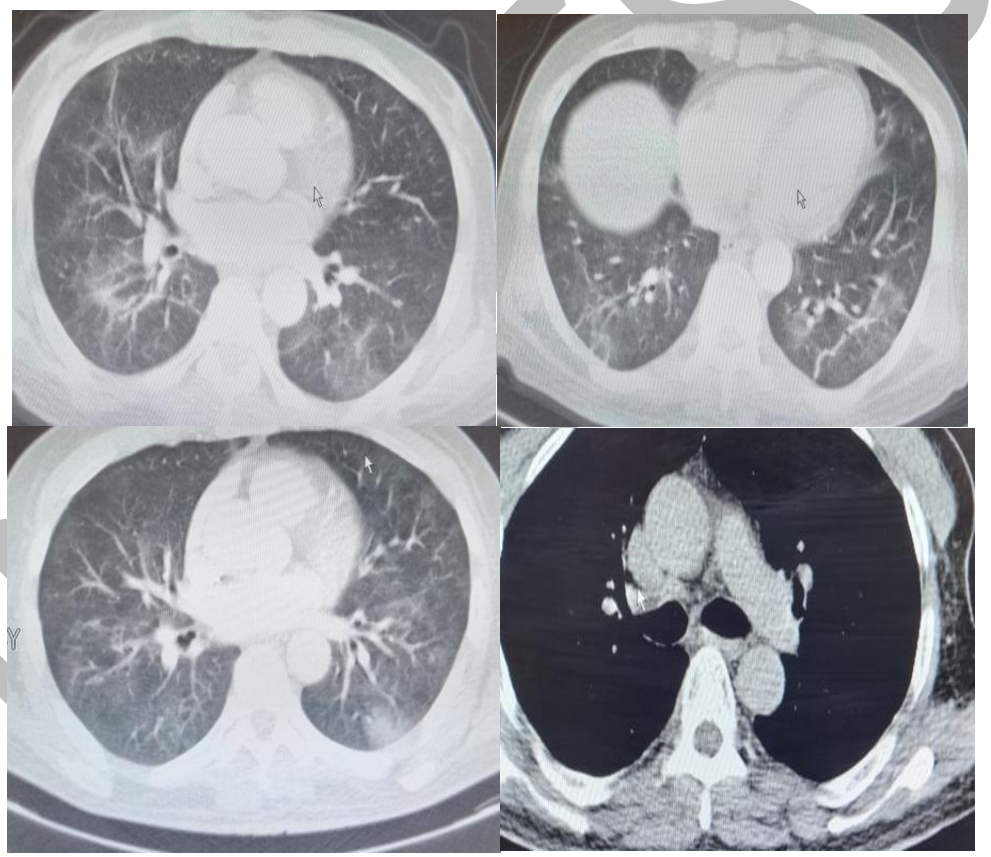

**Figure 1. Spiral chest CT showing a large anterior mediastinal mass (thymoma AB type) with bilateral patchy ground-glass opacities suggestive of bronchopneumonia.**

**Case 2**

A 39-year-old previously healthy woman was diagnosed with thymoma and myasthenia gravis 1 year ago. She underwent thymectomy 1 year prior and has been treated with prednisolone 42.5 mg daily and pyridostigmine 60 mg 4 times daily. She was admitted to the hospital presenting with a 1-month history of fever, cough, dyspnea (functional class II), muscle aches involving axillary, occipital, and femoral muscles, and progressive weakness.


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On physical examination, Glasgow Coma Scale was 15/15, blood pressure 95/60 mmHg, heart rate 87 beats/min, respiratory rate 21 breaths/min, temperature 36.5 °C, and oxygen saturation 93% on room air. Lung and heart auscultation were normal. A tender, mobile left axillary lymph node measuring 3 × 3 cm was incidentally noted. Muscle strength in the lower limbs was reduced (3/5).

COVID-19 and influenza polymerase chain reaction (PCR) tests were negative. Laboratory findings included WBC 4000/µL (80% polymorphonuclear cells, 15% lymphocytes), hemoglobin 10 g/dL, platelets 144 000/µL, BUN 23 mg/dL, creatinine 0.05 mg/dL. HIV, HBsAg, anti-HBs, and HCV serologies were negative. Blood and urine cultures were negative. Coagulation profile showed partial thromboplastin time (PTT) 45 seconds, prothrombin time (PT) 12 seconds, INR 1.45. Echocardiogram revealed an ejection fraction of 50% to 55%, pulmonary artery pressure of 25 mmHg, and mild tricuspid regurgitation.

Ultrasound of the left axillary region identified a large, oval lymph node measuring 18 × 38 mm with a preserved fatty hilum, suggestive of a reactive process. Venous Doppler ultrasound of the lower extremities showed patent popliteal, deep femoral, superficial femoral vein, and common femoral veins, all compressible with normal venous flow, no evidence of thrombosis or obstruction. Arterial Doppler ultrasound showed triphasic flow with normal peak systolic velocities in tibial arteries; no significant stenosis was detected.

An approximately 20 cc intramuscular mass without vascularity was noted in the left upper thigh, consistent with a hematoma. Screening for coagulation disorders and follow-up ultrasound were recommended. Chest CT scan demonstrated a cavitary lesion with collapse and consolidation of the left lung, accompanied by centrilobular nodules in the right middle lobe and a tree-in-bud pattern in the paratracheal region (Figure 2).

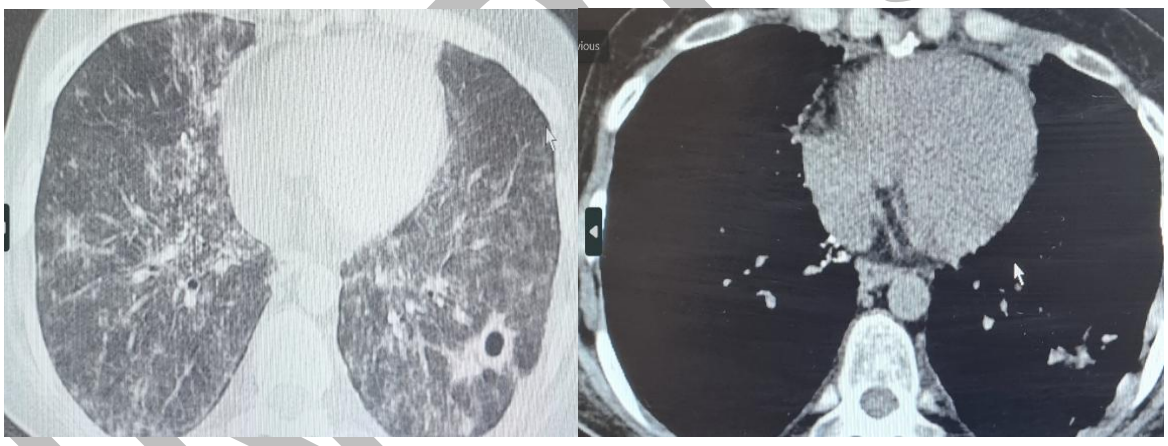

**Figure 2. Spiral thoracic CT (noncontrast, 3D reconstruction) demonstrating post-surgical changes, cavitary lesions in the left lung, centrilobular nodules, and tree-in-bud pattern in the right middle lobe.**

Excisional biopsy of the left axillary lymph node showed granulation tissue formation, patchy suppurative infiltration, and fibrocollagenization, without evidence of granulomas or neoplastic infiltration. Bronchoscopy with BAL revealed no signs of tuberculosis, fungal, bacterial infections, or malignancy; however, CMV was detected with a viral load of 85 700 IU/mL in the BAL fluid. The patient was treated with intravenous ganciclovir, resulting in undetectable CMV viral load after 3 weeks.

The thigh hematoma was surgically drained, with findings consistent solely with hematoma, and cultures of the drained fluid were negative. Immunological workup demonstrated hypogammaglobulinemia. Flow cytometry showed markedly reduced B-cell populations (CD19 0.5%, CD20 0.1%) with relatively preserved T-cell subsets in Table 1(CD4 25%, CD8 48%).

These findings indicated an immunodeficiency characterized primarily by humoral immune defects, while cellular immunity remained intact. Based on the history of thymoma, hypogammaglobulinemia, and myasthenia gravis, a diagnosis of GS was established. IVIG replacement therapy was initiated.

**Case 3**

A 58-year-old man with a history of diabetes mellitus, hypertension, and recurrent pneumonias presented with a 4-month history of progressive shortness of breath and reduced exercise tolerance, which had recently become associated with fever and productive cough. On admission, he was tachypneic and exhibited type 1 respiratory failure, with an oxygen saturation of 87% on room air. Laboratory investigations revealed Hb 12.1 g/dL, WBC 4800/µL, platelets 210 000/µL along with elevated C-reactive protein (CRP) level of 99.8 mg/dL and an erythrocyte sedimentation rate (ESR) of 81 mm/h.

A year prior, a chest CT scan with contrast was performed at another center for evaluation of recurrent pneumonias, which revealed diffuse ground-glass opacities (GGO) and an anterior mediastinal mass. The patient subsequently underwent thymectomy, and histopathological examination confirmed a diagnosis of thymoma. However, he was lost to follow-up and did not undergo further evaluation or treatment after surgery.

He now presents with worsening respiratory symptoms. A repeat high-resolution CT scan of the thorax was performed and compared with the previous study. The findings showed persistent and progressive pulmonary opacities (Figure 3). Differential diagnoses included immunotherapy-related transient lung opacities, drug-induced pneumonitis, organizing pneumonia, eosinophilic pneumonia, and pulmonary metastasis.

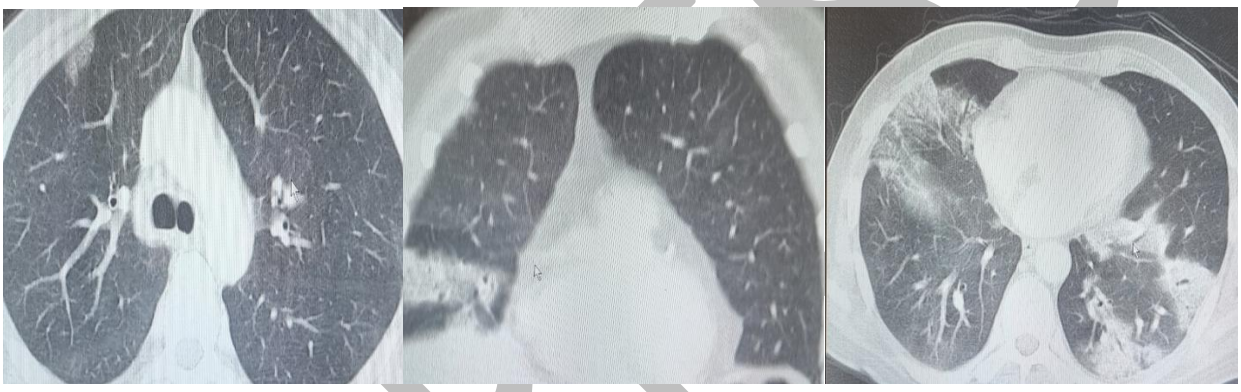

**Figure 3. Spiral thoracic CT showing persistent peri-broncho-vascular and subpleural ground-glass opacities with consolidations, suggestive of CMV pneumonia.**

Spiral CT scan of the thorax without intravenous contrast and with 3D reconstruction revealed no evidence of local recurrence or abnormal soft tissue mass in the anterior mediastinum. Multiple mediastinal lymph nodes were noted, with a short-axis diameter up to 10 mm, unchanged from the previous imaging. However, persistent peri-broncho-vascular and subpleural ground-glass opacities and consolidations were again observed. Compared to prior CT imaging, these opacities had increased in size and extent. Retrospective comparison also demonstrated dynamic changes in the shape, size, and distribution of pulmonary opacities, raising suspicion for transient lung opacities possibly related to immunotherapy. Differential diagnoses included drug-induced pneumonitis and organizing pneumonia; eosinophilic pneumonia and, less likely, pulmonary metastasis were also considered. The bony thorax and cardiac structures were unremarkable. No abnormal pleural nodularity or focal thickening was detected. Follow-up imaging and correlation with clinical findings were recommended.

Bronchoscopy with BAL was performed. BAL specimens were negative for acid-fast bacilli (AFB), bacterial, fungal, and mycobacterial cultures, as well as tuberculosis PCR. However, BAL CMV PCR was positive. Serum CMV PCR was also elevated at 3417 IU/mL. The patient was seronegative for HIV. Based on his clinical presentation, imaging findings, and background of thymoma, a diagnosis of bilateral CMV pneumonia was made. He was started on intravenous ganciclovir at a dose of 5 mg/kg twice daily.

Immunologic workup revealed profound hypogammaglobulinemia (IgG 315 mg/dL, IgA 16 mg/dL, IgM 25 mg/dL, IgE 10 mg/dL) and a near-complete absence of B cells (CD19 0.09%, CD20 0.08%). T-cell subsets were preserved in Table 1 (CD4 20%, CD8 54%). These findings confirmed a diagnosis of GS-characterized by thymoma-associated


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immunodeficiency with a defect in humoral immunity. The patient was initiated on IVIG replacement therapy at 0.4 g/kg monthly. Since the start of IVIG therapy, he has remained clinically stable without recurrence of infections.

**Case 4**

A 39-year-old man with a known history of myasthenia gravis and anterior mediastinal mass was diagnosed 2 years ago. He underwent thymectomy, and histopathological evaluation confirmed the presence of a thymoma. Postoperatively, he was maintained on Mestinon (pyridostigmine). One year after thymectomy, the patient was admitted to the hospital with complaints of a chronic productive cough, progressive dyspnea (NYHA functional class III), generalized weakness, and an unintentional weight loss of 10 kg over 3 months. On physical examination: blood pressure was 110/70 mm Hg, heart rate 80 beats/min, respiratory rate 20 breaths/min, temperature 37°C, and oxygen saturation was 92% on room air.

Laboratory findings included: WBC 10 000/µL, hemoglobin 13.2 g/dL, platelets 387 000/µL, BUN 30 mg/dL, and creatinine 1.3 mg/dL. COVID-19 PCR test was positive, while influenza PCR was negative. Blood cultures were sterile. HIV, HBV, and HCV serologies were also negative.

A spiral CT scan of the thorax revealed diffuse bronchiectasis and bronchiectasis predominantly affecting the middle and lower lobes, along with peribronchial wall thickening and centrilobular nodular infiltrates (Figure 4).

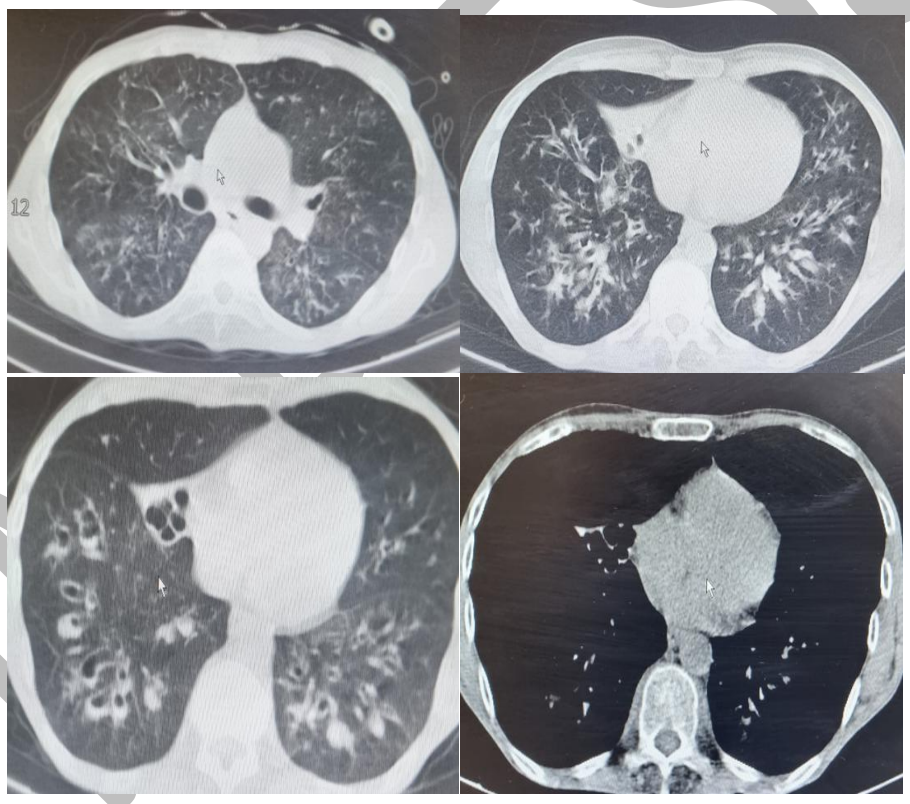

**Figure 4. Spiral CT of thorax demonstrating diffuse bronchiectasis, peri-bronchial wall thickening, and centrilobular nodular infiltrates.**

Based on the patient's persistent respiratory symptoms and characteristic lung findings on CT scan, treatment with remdesivir was initiated. Bronchoscopy with BAL was performed. BAL testing was negative for viral pathogens including SARS-CoV-2, influenza, and tuberculosis, and showed no evidence of malignancy. However, qualitative CMV DNA was detected in the BAL fluid. Concurrent plasma CMV PCR revealed a viral load of 7128 IU/mL. Immunologic evaluation revealed hypogammaglobulinemia with IgG 381 mg/dL, IgA 34 mg/dL, IgM 19 mg/dL, and IgE 3 IU/mL. Flow cytometry showed severely reduced B-cell counts

(CD19 1.1%, CD20 1.3%) with preserved T-cell populations in Table 1 (CD4 36%, CD8 40%).

Considering the elevated CMV viral load, the patient was treated with intravenous ganciclovir at a dose of 5 mg/kg every 12 hours for 2 weeks, which was subsequently discontinued after clinical improvement. The coexistence of thymoma, hypogammaglobulinemia, and B-cell lymphopenia confirmed the diagnosis of GS. IVIG replacement therapy was initiated.

However, 2 months later, the patient returned with a productive cough and was found to have persistently low serum IgG levels, attributed to nonadherence with IVIG therapy. Repeat thoracic CT imaging showed progression of central bronchiectasis and new patchy consolidations. Additionally, paranasal sinus CT demonstrated pansinusitis, further supporting recurrent sinopulmonary infection as a complication of the underlying immunodeficiency (Figure 5).

Bronchoscopy with BAL showed no evidence of infectious microorganisms or malignancy. The patient was started on IVIG replacement therapy along with antibiotics for management of sinopulmonary infection and was discharged with a prophylactic antibiotic regimen.

One month later, he was readmitted with pneumonia and a decreased serum IgG level. He received another course of IVIG therapy and antibiotics. For the fourth time, the patient was hospitalized due to recurrent episodes of cough and dyspnea. A spiral CT scan of the lungs revealed complete collapse of the right middle lobe (RML), a cavitary lesion in the left upper lobe, bilateral centrilobular ground-glass nodules, central bronchiectasis, patchy consolidations, and mediastinal lymphadenopathy (Figure 6). No pleural effusion was identified.

Paranasal sinus CT scan revealed normal anatomy with no evidence of sinusitis. Serum galactomannan (GM) was elevated at 0.83, suggestive of possible fungal infection. PCR testing for COVID-19 and influenza was negative. CMV plasma viral load was undetectable at this stage.

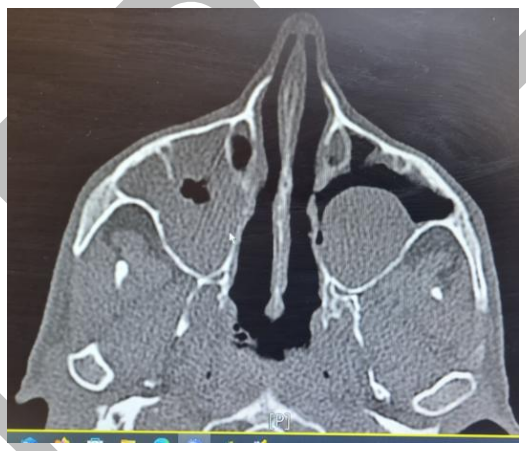

**Figure 5. Paranasal sinus CT demonstrating pansinusitis, consistent with recurrent sinopulmonary infection.**

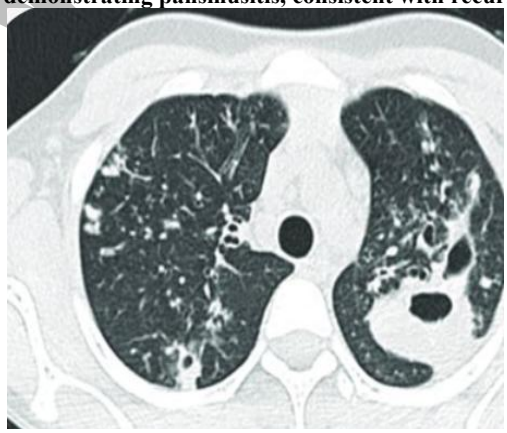

**Figure 6. Spiral CT of lungs showing complete collapse of the right middle lobe, cavitary lesion in the left upper lobe, central bronchiectasis, patchy consolidations, and mediastinal lymphadenopathy.**



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Given the positive serum GM and clinical suspicion for opportunistic infections, the patient was empirically started on antibiotics, voriconazole, and trimethoprim-sulfamethoxazole (TMP/SMX), targeting possible invasive aspergillosis and *Pneumocystis jirovecii* pneumonia (PCP). Bronchoscopy with BAL was performed. BAL PCR testing was negative for CMV, PCP, and *Aspergillus* species. BAL galactomannan was also negative. However, BAL PCR was positive for *Mycobacterium tuberculosis* (MTB). Additionally, 3 consecutive sputum samples were positive for *Mycobacterium tuberculosis* complex on smear and culture, confirmed by GeneXpert testing, which demonstrated sensitivity to rifampin.

Antituberculosis therapy was initiated with HRZE (isoniazid, rifampin, pyrazinamide, ethambutol), supplemented with vitamin B6. IVIG replacement therapy was continued. The patient's respiratory symptoms gradually improved following initiation of anti-TB treatment.

**Case 5**

A 43-year-old man with a medical history of diabetes mellitus, hypertension, ectopic Cushing's syndrome, and a prior *Pseudomonas* abscess in the left arm (2 years earlier) presented to our facility. He had undergone thymectomy 6 months prior at another institution, with histopathology confirming a type A thymoma.

Despite the thymoma diagnosis, he did not return for postoperative follow-up. Two months prior to the current presentation, he was admitted elsewhere with symptoms of headache, nausea, and vomiting. Neuroimaging revealed a brain abscess, for which he received appropriate medical management (Figure 7).

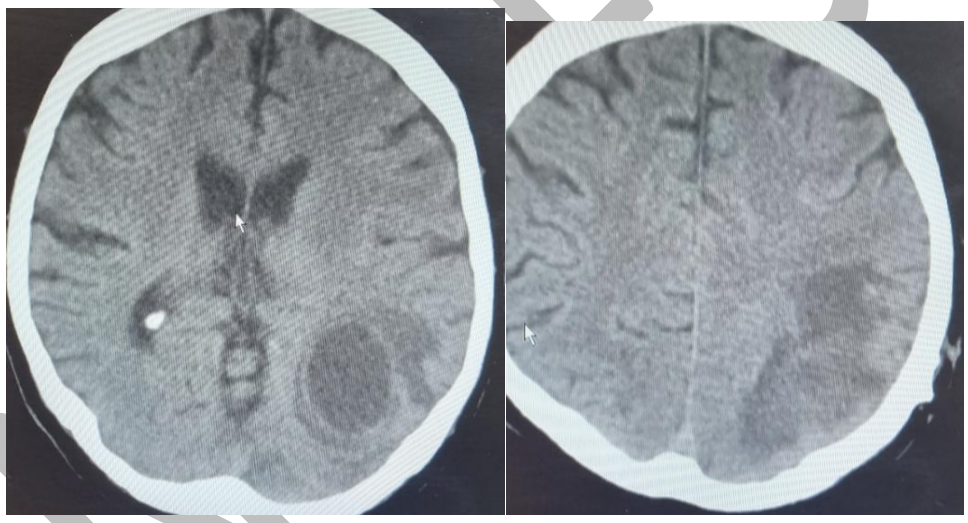

**Figure 7. Brain CT without contrast showing a well-circumscribed intra-axial hypodense lesion in the left parietal lobe with surrounding vasogenic edema, consistent with brain abscess.**

Post-craniotomy changes are evident in the left parietal lobe, including linear hyper densities consistent with hemorrhagic sequelae. Given the patient's history of thymoma and brain abscess, immunological evaluation was performed.

Laboratory results revealed Hb 11.2 g/dL, WBC 15 000/µL, platelets 294 000/µL, CRP 57 mg/L, ESR 60 mm/h and immunologic evaluations showed IgG 555 mg/dL, IgA 86 mg/dL, IgM 115 mg/dL, CD19 4.19%, CD20 4.18%, CD4 noted as preserved, and CD8 31.3% (Table 1). Results demonstrated hypogammaglobulinemia with markedly reduced B-cell populations (low CD19 and CD20 levels). These findings were consistent with GS. The patient was initiated on periodic IVIG therapy. Following treatment, symptoms improved, and he was discharged with instructions to continue regular IVIG infusions.

However, the patient did not adhere to the scheduled IVIG therapy and subsequently presented with generalized weakness and fatigue. On examination, vital signs were as follows: blood pressure 120/80 mm Hg, heart rate 118 beats/min, temperature 37.9°C, respiratory rate 20 breaths/min, and oxygen saturation of 93% on room air. Cardiopulmonary examination


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revealed normal heart and lung sounds. The recurrence of symptoms was attributed to the interruption of immunoglobulin replacement, underscoring the importance of consistent IVIG administration in managing GS (Figure 8).

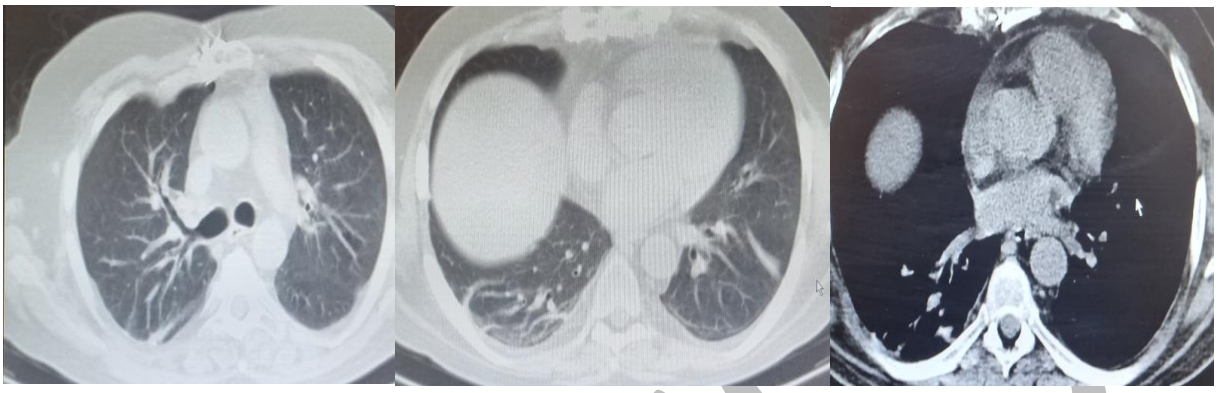

**Figure 8. Spiral thoracic computed tomography demonstrating atelectatic and subpleural curvilinear fibrotic bands in both lower lobes, likely sequelae from prior infections.**

Further evaluation revealed a urinary tract infection caused by carbapenem-resistant *Klebsiella* species. The patient was treated with ceftazidime-avibactam and resumed IVIG therapy. Following clinical improvement, he was discharged in stable condition with recommendations for continued monitoring and adherence to IVIG therapy.

Formal lymphocyte proliferation tests (eg, mitogen-induced proliferation to PHA or anti-CD3 stimulation) were not available for all cases. However, the combination of severe hypogammaglobulinemia, B-cell depletion, opportunistic infections, and abnormal CD4/CD8 ratios supports a diagnosis of 'GS.

**Table 1. Immunologic and hematologic profiles of the five cases**

| Case | Hb, g/dL | WBC, /µL | Lymphocytes, % | CD19, % | CD20, % | CD4, % | CD8, % | IgG, mg/dL | IgA, mg/dL | IgM, mg/dL | Key Findings |
|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | 11.4 | 5600 | 22 | 0.09 | 0.08 | 21 | 67 | 76 | 45 | 24 | CMV viremia, Thymoma AB |
| 2 | 10.0 | 4000 | 15 | 0.5 | 0.1 | 25 | 48 | ↓ | ↓ | ↓ | CMV pneumonia, Myasthenia |
| 3 | 12.1 | 4800 | 20 | 0.09 | 0.08 | 20 | 54 | 315 | 16 | 25 | CMV pneumonia, CID |
| 4 | 13.2 | 10 000 | 18 | 1.1 | 1.3 | 36 | 40 | 381 | 34 | 19 | TB, COVID, bronchiectasis |
| 5 | 11.2 | 15 000 | 24 | 4.19 | 4.18 | – | 31.3 | 555 | 86 | 115 | Brain abscess, UTI |

[a]↓: markedly decreased; CID: combined immunodeficiency; CMV: cytomegalovirus; Hb: hemoglobin; Ig: immunoglobulin; TB, tuberculosis; WBC: white blood cell.



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## DISCUSSION

We report a series of 7 patients with 'GS, emphasizing the diversity of clinical presentations, associated infectious complications, and autoimmune manifestations (Table 2). Recurrent respiratory infections, particularly sinopulmonary infections, such as pneumonia and sinusitis, were the most common clinical presentation. Opportunistic infections occurred in 3 patients, including CMV pneumonia and fungal etiology, and 1 patient developed tuberculosis. Two patients presented with persistent or relapsing symptoms of COVID-19 (ie, long COVID-19), which were contributory factors for the diagnosis of GS. Of the documented autoimmune manifestations, 2 patients exhibited myasthenia gravis, underscoring the overlap between thymoma-related autoimmunity and immunodeficiency.

These results are consistent with earlier investigations that identify recurrent respiratory tract infections as the most frequent presentation in patients with GS, often leading to diagnosis several years after the initial infections.[1,5,6] The recognized delay of GS diagnosis in adolescent and adult populations typically occurs years after thymoma resection or identification, highlighting the need for increased clinical awareness in adults who have thymoma and altered immunodeficiency.

All our patients had a thymoma diagnosis, but the temporal relationship to the onset of immune dysregulation varied, suggesting that immune dysregulation may sustain, or even progress, without tumor presence or treatment. This outcome supports the compelling possibility that GS is not merely a paraneoplastic phenomenon of thymoma but rather may be an acquired-combined immunodeficiency syndrome secondary to thymic epithelial dysfunction and potentially driven by epigenetic or post-thymic immune reorganization.[7]

The pathogenesis of GS remains incompletely understood. Approximately half of thymomas is associated with immune dysregulation,[5] although advanced thymoma is a malignant epithelial tumor. Thymic epithelial cells play a major role in T-cell education and tolerance; the neoplastic transformation can disrupt normal thymopoiesis, reduce proper B-cell maturation, and can lead to autoimmunity. As a result, GS is a distinct intersection of immunodeficiency and autoimmunity, and often presents with overlapping features, including myasthenia gravis, pure red cell aplasia, and oral lichen planus.

Our research supports the necessity of a full immunologic work-up, including lymphocyte subset phenotyping and immunoglobulin levels, even in cases without initial abnormalities on immune workup. In the cases we observed, CD19 and CD20 markers were notably low while CD4/CD8 ratios were generally reversed, indicative of global immune dysfunction. These laboratory abnormalities will not always be present at presentation, reinforcing the need for serial active immune monitoring, especially when new infectious or autoimmune phenomena present.

From a management perspective, all patients responded favorably to IVIG therapy, with respect to decreased infection risk and clinical stability. However, the clinical outcomes of patients were more associated with infectious complications over thymoma histopathology and surgical outcomes. The deaths of 2 patients due to COVID-19–related sickness underscore the need for heightened infectious watchfulness and early antiviral treatment of these medically complex patients.

In summary, our observation supports that GS should be considered in adults with thymoma and recurrent or unusual infections, even years after thymectomy. Early immunologic evaluation and initiation of IVIG replacement therapy into the treatment plan can vastly improve patients' outcomes. Future studies should investigate the genetic and molecular mechanisms of the disease, specifically focusing on contributions from changes to the thymic microenvironment and epigenetic changes that lead to acquired immune dysfunction.

**Table 2. Clinical, immunological, and laboratory features of seven patients with Good's syndrome**

| Feature | Case 1[8] | Case 2[9] | Case 3 | Case 4 | Case 5 | Case 6 | Case 7 |
|---|---|---|---|---|---|---|---|
| Age of initial symptoms | 46 | 63 | 55 | 39 | 58 | 39 | 43 |
| Interval to GS diagnosis | 46 | 63 | 7 months | 1 year | 6 months | 1 year | 6 months |
| Age at thymoma detection | 45 | 63 | 56 | 38 | 58 | 38 | 43 |
| Age at immunodeficiency detection | 46 | 63 | 56 | 39 | 58 | 38 | 43 |
| Presentation | Severe and long COVID-19 | Severe and COVID-19 | Recurrent sinopulmonary infections | Recurrent pneumonia | Recurrent pneumonia | Recurrent sinopulmonary infections | Brain abscess |
| Site of infection | Lungs | Lungs | Lungs and sinuses | Lungs | Lungs | Lungs and sinuses | Brain |
| Bronchiectasis | No | No | No | No | No | Yes | No |
| Autoimmune manifestation | No | Lichen planus | No | Myasthenia gravis | No | Myasthenia gravis | No |
| Malignancy | No | No | No | No | No | No | No |
| Death | Yes | Yes | No | No | No | No | No |
| IgG (NR: 700–1400), mg/dL | 445 | 415 | 76 | 269 | 315 | 381 | - |
| IgA (NR: 50–400), mg/dL | 17 | 54 | 45 | 19 | 16 | 49 | - |
| IgM (NR: 40–230), mg/dL | 22 | 17 | 24 | 41 | 20 | 19 | - |
| IgE (NR: <10), IU/mL | 1 | <10 | 10 | 10 | <10 | <10 | - |
| Opportunistic infection | COVID-19 | COVID-19, CMV | None | CMV | CMV | CMV, TB | Bacterial infection |
| HIV Ab | Negative | Negative | Negative | Negative | Negative | Negative | Negative |
| CD4% (NR: 20–65%) | 22% | 24% | 21% | 25% | 20% | 36% | 20% |
| CD8% (NR: 10–40%) | 42% | 28% | 67% | 48% | 54% | 40% | 31.3% |
| CD4/CD8 ratio (NR: 1–4) | 0.5 | 0.8 | 0.3 | 0.5 | 0.3 | 0.9 | 0.6 |
| CD19% (NR: 4–25%) | 1% | 0.01% | <1% | 0.5% | 0.09% | 1.1% | 4.19% |
| CD20% (NR: 4–25%) | 1% | 0.01% | <1% | 0.1% | 0.08% | 1.3% | 4.18% |

[a]Ab: antibody; CD: cluster of differentiation; CMV: cytomegalovirus; COVID-19: coronavirus disease 2019; GS: Good syndrome; HIV: human immunodeficiency virus; Ig: immunoglobulin; NR: normal range; TB: tuberculosis.

The underlying pathogenesis of GS is still not fully understood. Its diagnosis is often delayed due to the wide range of clinical presentations and the absence of clear diagnostic criteria. Identifying the associated immunodeficiency is crucial, as impaired immune defenses likely contribute to the syndrome's diverse manifestations. When thymoma is present alongside GS, early recognition and prompt management of complications are essential.

## STATEMENT OF ETHICS

This study was conducted in accordance with the principles of the Declaration of Helsinki. Written informed consent was obtained from all patients for publication of their clinical data and any accompanying images.

## FUNDING

Not applicable.

## CONFLICT OF INTEREST

The authors declare no conflicts of interest.

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Not applicable.

## DATA AVAILABILITY

Upon reasonable request (please contact corresponding author (Dr Payam Tabarsi) for any data request. Email: payamtabarsi@yahoo.com

## AI ASSISTANCE DISCLOSURE

Grammerly tool was used for editing the manuscript grammer and also plagiarism check.

In some part of the manuscript paraphrasing tools were used to avoid any plagiarism. At the end the manuscript was revised to humanize it by all authors.

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