

Case Report

Diagnosis of Good Syndrome following Recurrent Coronavirus Disease-2019 Infections

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Keywords

Good syndrome · Thymoma · Hypogammaglobulinemia · COVID-19 · Intravenous immunoglobulin

Abstract

Background: Good syndrome is defined as the co-occurrence of a thymoma and hypogammaglobulinemia. **Case:** In this case report, we present a patient who was diagnosed with Good syndrome following recurrent infections with SARS-CoV-2. Of particular note was the patient's repeated presentation despite receiving outpatient treatment with nirmatrelvir-ritonavir. We describe the patient's presentation, diagnosis, and treatment – including robotic thymectomy and passive immunization with IVIG – and report the benefit to quality of life that the patient experienced. **Conclusion:** This case highlights the importance of quantitative testing of immunoglobulins in patients with known thymomas who present with recurrent infections of SARS-CoV-2.

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Introduction

Good's syndrome (GS), first described by Dr. R.A. Good in 1954, is a rare immunodeficiency, which is characterized by the presence of both a thymic mass and hypogammaglobulinemia [1]. This adult onset syndrome is typically associated with individuals between 40 and 60 years of age, has an estimated global incidence of 1.5 per 1,000,000 [2], and occurs at comparable frequencies in male and female patients [1]. The majority of data on GS is gleaned from case reports or small case series, and despite recent studies highlighting the near absence of B cells in most patients with GS, no underlying pathogenesis of the disease has been definitively

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elucidated [3]. Additionally, the genetic analyses conducted to date have yet to identify evidence of disease-driving genetic variance [2].

In addition to its rarity, GS is sometimes missed, or its diagnosis delayed stemming from the heterogeneity in clinical presentations among these patients. According to a study performed on a database of GS patients from the UK, it is most common for the thymoma and hypogammaglobulinemia to be diagnosed concurrently; however, up to 25% of their cohort had years separating the recognition of these two clinical features [4]. Patients with GS generally come to the attention of the medical system due to recurrent infections prompting either thoracic imaging showing a thymic mass or an immunodeficiency workup, which reveals their hypogammaglobulinemia. These recurrent infections are classically associated encapsulated bacterial organisms, opportunistic infections such as *Candida* or *Pneumocystis jirovecii*, and viruses such as *Cytomegalovirus* and varicella zoster [1, 5].

Management of GS has two major components. First is treatment of the immunodeficiency, which is accomplished through regular intravenous immunoglobulin (IVIG) infusions and antimicrobial coverage of infections. The second prong of the treatment strategy is resection of the thymoma. Historically, the most common approach involved a median sternotomy; however, several minimally invasive techniques including video-assisted thoracoscopic and robotic surgery have recently become more widely adopted and have shown good safety and efficacy [6, 7]. Robotic-assisted thoracoscopic surgery has advantages of allowing fine dissection in a confined space while maintaining minimal incision sites.

Staging as well as histologic typing of the thymoma are both good prognostic tools [8, 9]. While there is a recent move toward adopting a modified TNM staging system, most of the literature to date has utilized the Masaoka staging system. This system stratifies thymomas based on both the macro- and microscopic extent of the tumor tissue [10, 11]. The 5-year survival rates following surgical removal of stage I thymoma vary between 80% and 100%, with an average rate of 91% [7]. For histologic typing, the most commonly used system is the WHO, which stratifies tumors based on the relative abundance of type A, oval cells, which purport a better prognosis, and type B, round cells, which purport a worse prognosis. The more benign tumors, types A and AB, in this classification are expected to be invasive in less than 5% of cases and are associated with greater than 95% 10-year disease-free survival [8].

Irrespective of classification and stage, thymectomy is associated with improved prognosis in cases of thymoma generally; however, this benefit has not been shown in GS specifically [1, 12]. Unfortunately, it also does not appear that removal of the thymoma in patients with GS corrects the hypogammaglobulinemia [3].

In the last few years, publications have begun reporting about patients with GS experiencing infections of SARS-CoV-2. These reports describe the clinical features, radiographic findings, and hospital courses of coronavirus disease-2019 (COVID-19) in these patients [2, 13–15]. In this case report, we add to the growing association between recurrent COVID-19 and GS by describing a patient who was diagnosed with GS after requiring hospital admission for COVID-19 despite having recently received outpatient treatment for the same infection.

Case Presentation

A 60-year-old man with a history of obesity, hypertension, obstructive sleep apnea, and atrial fibrillation presented to the NYU Langone emergency room for fevers, shortness of breath, and near syncope in the setting of a positive home COVID-19 test. Of note, 3 weeks prior to presentation, the patient had completed a course of nirmatrelvir/ritonavir (Paxlovid®) that he received in the outpatient setting after experiencing fevers, coughs, and body aches for 2 days.

Upon presentation, the patient was hypoxic, despite non-rebreather, and was admitted for management of acute hypoxemic respiratory failure. He required noninvasive mechanical ventilation with bilevel positive airway pressure and underwent a diagnostic workup for additional causes of hypoxemia. Computed tomography of the thorax performed to rule out pulmonary embolism revealed a 10 cm mediastinal mass (see Fig. 1). Surgical resection was planned for the outpatient setting after the patient's infection and respiratory failure were expected to have resolved. However, this procedure was repeatedly delayed due to multiple subsequent hospitalizations requiring antibiotics and steroids for treatment of cryptogenic organizing pneumonia, cellulitis, thrush, and herpes. During this extended period, immunoglobulin levels were measured (see Table 1) and were significant for immunoglobulin deficiency. The patient thus met both criteria and was diagnosed with GS. Additionally, lymphocyte subsets were analyzed, which revealed 0 cells with expression of cluster of differentiation 19 (CD19), indicating significant deficiency of circulating B cells (see Table 2), another hallmark of GS.

The patient underwent robotic resection of a 9.2 cm, Masaoka stage 1, type AB thymoma with negative margins. He was also started on IVIG infusions. Consistent with the course of GS previously described in the literature, the patient's B-cell counts did not appear to improve following resection of the thymoma (see Table 2). Additionally, though they partially improved with IVIG, his immunoglobulin levels remained low, so he continues to receive monthly IVIG treatments. One and a half years after the thymectomy, there was a brief period when he was unable to receive infusions due to complications with the patient's insurance. Repeat laboratories were drawn after this period, which showed a decline in IgG (see Table 1). He was ultimately able to restart infusions. With this passive immunity, the number of infections the patient now experiences are significantly decreased from prior to his diagnosis. He has had one admission in the NYU system since initiation of IVIG for community-acquired pneumonia; however, he has notably not tested positive for COVID-19 during this time period. The patient reports that despite requiring monthly IVIG infusions, the decrease in infections since his diagnosis has contributed positively to his quality of life.

Discussion

Across the GS literature, authors recommend measuring immunoglobulin levels in patients with known thymomas and hospital presentations for specific infections classically associated with GS [1, 16, 17]. The growing number of publications describing the coincidence of GS and COVID-19 are hinting at the importance of considering SARS-CoV-2 in the list of pathogens that should raise suspicion for GS. While COVID-19 is perhaps too prevalent to merit this association in all cases, hospitalizations due to COVID-19 occurs in fewer than 1% of patients with mild-moderate symptoms who are treated with Paxlovid [18, 19]. As such, patients with imaging evidence of a thymoma who require hospitalization for COVID-19 despite Paxlovid treatment should raise suspicion for GS. It is also interesting to note the complex interplay between immunosuppression or immunodeficiency and COVID-19. While immunosuppression likely makes patients more susceptible to infection with SARS-CoV-2 [15], there is potentially a protective element in preventing severe disease mediated by overstimulation of the immune system [13, 20]. The patient in this case did require noninvasive ventilation for hypoxemia indicating his illness was likely severe. It would be interesting to see how severity of COVID-19 differs in patients who are immunodeficient due to GS compared to the general population.

The staging and histologic typing of this stage I and type AB tumor portend a very good prognosis and very low likelihood of disease recurrence with regard to the thymoma itself. Nonetheless, consistent with the clinical course of GS described in the literature wherein the

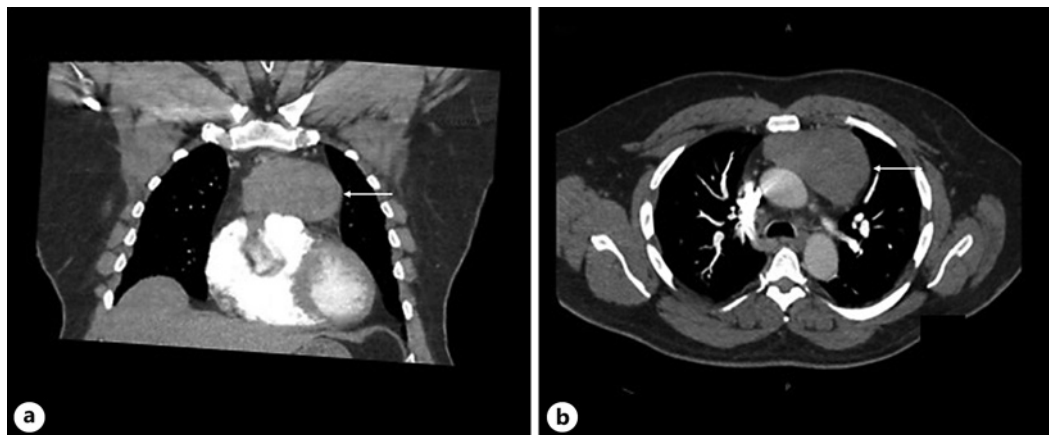


Fig. 1. Computed tomography (CT) scan of patient's thorax from his initial presentation showing evidence of a mediastinal mass. **a** Coronal slice. **b** Axial slice. White arrows point to the thymoma in both panels.

Table 1. Immunoglobulin levels (mg/dL) during patient's treatment course

	Pre-thymectomy	2 months after IVIG initiation	9 months of IVIG	After 2-month lapse in IVIG	Reference ranges
IgA	51	52	54	47	68–408
IgG	190	655	791	490	768–1,632
IgM	<14	<14	<14	<14	35–263

Table 2. Lymphocyte subgroup analysis before and after thymectomy

	Before thymectomy	2 months after thymectomy	1.5 years after thymectomy	Reference range
CD3 (polyclonal)	619	700	1,283	656–1,903 cells/ μ L
CD3+ percent	87	82	81	53–87%
CD3+/CD4+ absolute count	361	378	764	359–1,439 cells/ μ L
CD3+/CD4+ percent	49	43	49	29–59%
CD3+/CD8+ absolute count	279	338	486	145–725 cells/ μ L
CD3+/CD8+ percent	38	38	31	11–33%
CD4/CD8 ratio	1.29	1.12	1.57	0.70–4.50
CD19+ percent	0	0	0	2–26%
CD19+ absolute count	0	0	4	4–624 cells/ μ L
CD16+56+ percent	12	17	17	4–28%
CD16+56+ absolute count	85	142	265	73–421 cells/ μ L

hypogammaglobulinemia does not improve despite thymectomy [3], the patient continues to require IVIG and has not shown signs of B-cell reconstitution. Finally, this case additionally highlights the potential quality of life benefit of diagnosing and treating GS in patients who suffer from recurrent infections.

Conclusion

This case emphasizes the value of teaching about GS and keeping it on the differential for patients with thymomas, so providers will have a lower threshold to measure immunoglobulin levels in the appropriate patients. Diagnosis and treatment with passive immunity can significantly improve these patients' quality of life.

Acknowledgment

We would like to thank the patient for encouraging the publication of this report.

Statement of Ethics

Written informed consent was obtained from the described patient for publication of the details of their medical case and any accompanying images. Ethical approval is not required for this study in accordance with local or national guidelines since it meets the following description: "The activity is a case report involving the observation of a single patient whose novel condition or response to treatment was guided by the care provider's judgment regarding the best interest of the individual."

Conflict of Interest Statement

M.B. has no conflicts of interest. J.K.S. has advisory roles in AstraZeneca, Genentech, Janssen, Pfizer, Regeneron, Sanofi Genzyme, Takeda, and Mirati Therapeutics.

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Author Contributions

M.B. was responsible for writing and reviewing. J.K.S. was responsible for conceptualization and supervision.

Data Availability Statement

There are no pertinent data beyond those which are published in the body of the article. Further inquiries can be directed to the corresponding author. The CARE Checklist has been completed by the authors for this case report, attached as online supplementary material (for all online supplementary material, see <https://doi.org/10.1159/000542928>).

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