Received: 16 February 2024 | Revised: 20 March 2024 | Accepted: 12 April 2024

DOI: 10.1002/ccr3.8962

CASE REPORT

Clinical Case Reports Open Access WILEY

Long COVID-19 leading to Good's syndrome diagnosis: A clinical case-report and literature review

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Key Clinical Message

Good's syndrome (GS) in conjunction with a severe COVID-19 infection, shedding light on the complexities of managing this rare condition that combines thymoma and immunodeficiency.

Abstract

This study delves into the clinical presentation and management of a 63-year-old male diagnosed with Good's syndrome (GS) amid a severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection. GS, an uncommon association between thymoma and immunodeficiency, remains a clinical mystery, necessitating increased awareness and understanding. Our patient's intricate clinical course, marked by recurrent COVID-19 symptoms and multiple hospitalizations, exemplifies the challenges posed by GS. Through a systematic review of GS cases globally, we highlight its worldwide distribution, with a substantial proportion reported in Europe. Notably, the diagnosis of thymoma often precedes immunodeficiency, emphasizing the importance of vigilance in clinical assessments.

KEYWORDS

COVID-19, Good's syndrome, long COVID-19, SARS-CoV-2

1 | INTRODUCTION

The global landscape has been significantly impacted by the COVID-19 pandemic, with its diverse clinical presentations and complications posing substantial challenges to healthcare systems worldwide.[1] Recognizing the distinctiveness of each patient's journey through the course of COVID-19 is vital in enhancing our understanding of the disease and refining therapeutic strategies.[2]

Epidemiologically, COVID-19 has manifested with varied intensity across populations, underscoring the importance of meticulous research and documentation. It has been presented differently from mild flu-like symptoms to severe neurological manifestations.[3,4] The intricacies of this viral infection extend beyond the acute phase, with emerging evidence highlighting long-term complications that demand thorough investigation.[5]

Good's syndrome (GS) is an acquired rare adult immunodeficiency characterized by thymoma, hypogammaglobulinemia, and recurrent infections due to a weak immune response. Its manifestation can vary from mild bacterial infections to severe malignancies.[6]

In this context, our study aims to delve into the nuanced clinical course of a patient's journey with COVID-19, emphasizing the significance of detailed case reports in unraveling the complexities of the disease. By exploring the

presentation, treatment modalities, and subsequent complications in our patients, we aspire to contribute to the evolving knowledge base surrounding COVID-19.

2 | CASE HISTORY/EXAMINATION

This study presents the case of a 63-year-old man, presenting with a chief complaint encompassing fever, chills, cough, sputum, and shortness of breath. Upon admission, a thorough examination of the patient's vital signs revealed a heart rate of 110, respiratory rate of 28, oxygen saturation level of 90% (with a normal value of above 95%), and an oral temperature of 39°C. On his lung auscultation, fine crackles were detected in the lower parts of the chest cavity. The clinical assessment, combined with a positive polymerase chain reaction (PCR) test for COVID-19, culminated in the diagnosis of SARS-CoV-2 infection. The patient's presentation was characterized by the involvement of multiple symptoms commonly associated with respiratory illness attributable to COVID-19. Notably, the severity of pulmonary involvement was accentuated by lung CT findings (Figure 1), highlighting the presence of ground-glass opacities, a distinctive radiological manifestation of COVID-19. The patient had received two doses of Sinopharm BIBP COVID-19 vaccine at the time of admission.

3 | METHODS

Upon the confirmation of the COVID-19 diagnosis, the patient underwent prompt medical intervention, inclusive of the administration of remdesivir and dexamethasone. Throughout the treatment trajectory, a gradual amelioration of the patient's symptoms ensued, resulting in a favorable clinical outcome. Subsequently, with the patient demonstrating significant recovery and resolution of symptoms, a decision was made to discharge him from the hospital.

The patient sought readmission due to recurrent symptoms, including cough, shortness of breath, and diminished blood oxygen levels, registering at 80% saturation 20 days after his first visit. This presentation was accompanied by pleuritic chest pain and fever. A positive polymerase chain reaction (PCR) test for COVID-19, along with a CT scan consistent with lung involvement and a C-reactive protein (CRP) level of 120 mg/dL (with a normal value of less than 0.3 mg/dL), affirmed the persistence of the SARS-CoV-2 infection. The therapeutic approach this time involved the administration of Remdesivir, ACTEMRA (Tocilizumab), and Dexamethasone.

Due to the worsened shortness of breath a CT angiography was performed to rule out pulmonary embolism. However, it revealed the presence of a mass in the right mediastinal area, prompting recommendations for a biopsy to further characterize the nature of the mass (Figure 2). Regrettably, the patient declined to provide consent for the sampling and biopsy of the mediastinal mass and was consequently discharged. Remarkably, despite the resolution of symptoms such as cough, fever, chills, shortness of breath, and chest pain upon discharge, the patient exhibited gradual weight loss post-discharge. This weight loss progressed, reaching 15 kg within 1 year after the initial discharge, raising concerns about the underlying cause and necessitating further investigation into the patient's clinical trajectory. Additionally, it is noteworthy that at the time of discharge, the PCR test results remained positive for the ongoing presence of the coronavirus infection.

Despite repeated medical recommendations for the patient to undergo further investigations, particularly the sampling of the mediastinal mass, the patient consistently declines any diagnostic interventions. Approximately 2 years after the first visit, the patient was readmitted, presenting with recurrent symptoms of fever, chills, cough, shortness of breath, delirium, and hypotension. Confirmatory testing indicated a positive COVID-19 polymerase chain reaction (PCR), prompting the initiation of previous treatments.

During this hospitalization, the patient again refused consent for the assessment of the mediastinal mass. Despite experiencing persistent shortness of breath and incomplete symptom resolution, the patient opted for discharge, expressing personal satisfaction with the care provided. After discharge, the patient attempted to enhance symptom management by procuring an oxygen machine for home use. However, a noticeable decline in muscle strength ensued, resulting in considerable difficulty navigating stairs, reflecting a reduction in overall mobility.

Simultaneously, the patient developed red maculopapular lesions on the extensor surfaces of the upper and lower limbs. This dermatological manifestation, coupled with ongoing respiratory distress and declining physical function, introduces additional complexities to the patient's clinical presentation.

4 | CONCLUSION AND RESULTS

Two and a half years after his first visit, the patient represented with exacerbated symptoms, including heightened fever, chills, cough, and shortness of breath. Notably, the patient's vital signs exhibited a blood pressure of 110/70 mmHg, heart rate of 108 bpm, oral temperature of 38°C, and oxygen saturation of 86%. The results of the

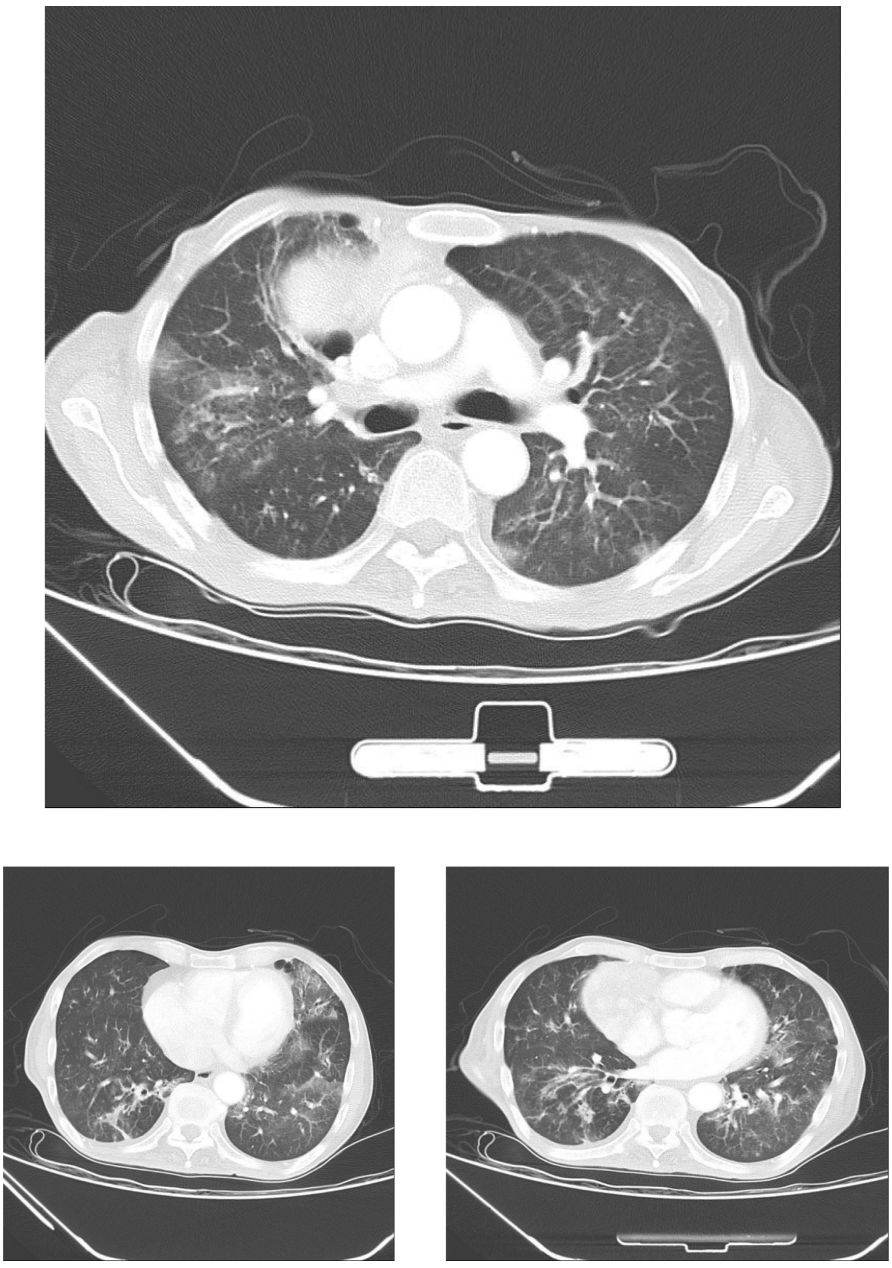

FIGURE 1 Multifocal ground glass opacities revealed in distinct CT sections of the patient's pulmonary landscape.

patient's tests during this visit are detailed in Table 1. A subsequent CT scan identified an 85 mm mediastinal mass, consistent with thymoma. A biopsy of the mass was performed, yielding a diagnosis of Spindle cell thymoma type A1. Concurrently, a biopsy of the skin lesion revealed characteristics indicative of lichen planus; however, it is an uncommon complication of GS.[7] Neurological consultation attributed the patient's muscle weakness to myasthenia gravis.

Considering these findings, the patient was diagnosed with Good's syndrome. The evaluation of the patient's immunoglobulin levels, as detailed in Table 2, revealed hypogammaglobulinemia. Subsequent flow cytometry, outlined in the same table, confirmed the diagnosis of Good's syndrome due to a decline in immunoglobulins and B cells. To address the hypogammaglobulinemia associated with Good syndrome, the patient underwent intravenous immunoglobulin (IVIG) therapy. Concurrently, steroid administration persisted, contributing to the amelioration of symptoms. Following clinical improvement, the patient was discharged.

A couple of months later, the patient was readmitted presenting with fever, delirium, shortness of breath, and fluctuations in blood pressure. The severity of the clinical condition led to the necessity of intubation due to loss of consciousness and respiratory compromise. In light of the suspected diagnosis of sepsis, comprehensive cultures, including blood, urine, and tracheal

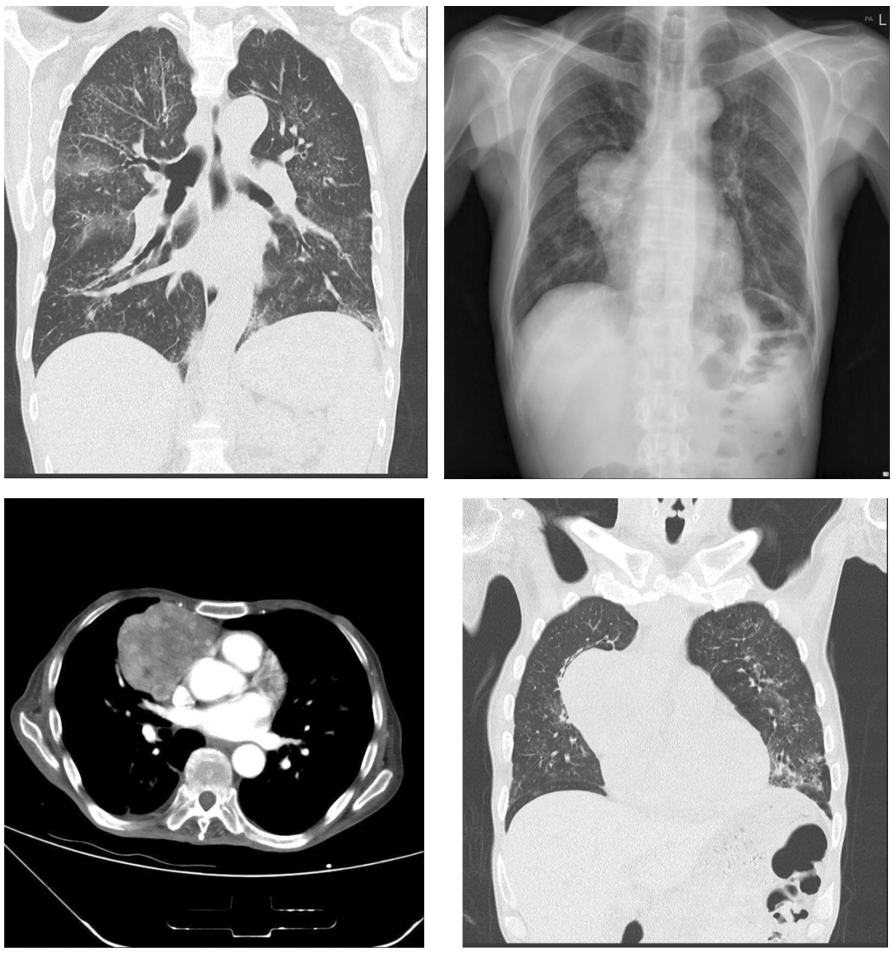

FIGURE 2 Right mediastinal mass. Coronal CT and anteroposterior radiography views.

RT-PCR for SARS-CoV-2		Fasting blood sugar	109 mg/dL
N gene	24	Urea	44 mg/dL
RdRp gene	23	Creatinine	0.7 mg/dL
RT-PCR for influenza	Negative	LDH	421 U/L
Cell blood counts		Sodium	141 mEq/L
WBC	6000/L	Potassium	4.5 mEq/L
Neutrophil	42%	AST	16 U/L
Lymphocyte	55%	ALT	36 U/L
Monocyte	5.0%	Alkaline phosphatase	102 U/L
Eosinophil	5.6%	Bilirubin total	0.8 mg/dL
Hemoglobulin	12.6 g/dL	Bilirubin direct	0.2 mg/dL
MCV	80 FL	Ferritin	364 ng/mL
Platelet	119,000/L	D-dimer	245 mg/L
Urine culture	Negative	ESR	60 mm/h
Blood culture	Negative	CRP	57 mg/dL

TABLE 1 General laboratory results of the patient.

Abbreviations: ALT, alanine Aminotransferase; AST, aspartate transferase; LDH, lactate dehydrogenase; MCV, mean corpuscular volume; WBC, weight blood cell.

samples, were collected for analysis. Simultaneously, blood cytomegalovirus (CMV) polymerase chain reaction (PCR) testing was conducted due to observed pancytopenia.

The results of the diagnostic investigations revealed significant findings. Blood culture demonstrated *Escherichia coli* sensitivity to carbapenem, while tracheal culture identified multidrug-resistant (MDR) Klebsiella

TABLE 2 Immunology and flow cytometry laboratory results of the patient.

Factor		Value	Normal range
IgG total		415 mg/dL	700–1400 mg/dL
IgM total		17 mg/dL	40–230 mg/dL
IgA total		54 mg/dL	50–400 mg/dL
IgE total		<10 mg/dL	<10 mg/dL
Flow cytometry			
CD19	0.01%	CD20	0.01%
CD6	24%	CD8	27%
CD56	8%		

organisms. Additionally, the patient's procalcitonin level was noted to be elevated at 25 ng/mL (with a normal value of less than 0.1 ng/mL), CRP was substantially elevated at 260 mg/dL, and CMV PCR indicated a significant viral load of 930 Gr/mL. To address the infectious and inflammatory components of the patient's condition, a therapeutic regimen was initiated, incorporating ganciclovir for CMV infection, colistin for MDR Klebsiella (based on the antibiogram results), meropenem for *E. coli* (produced extended-spectrum beta-lactamase (ESBL)), and continued steroid administration. Despite the comprehensive treatment approach, the patient's clinical status continued to deteriorate, culminating in an unfortunate and untimely demise.

5 | DISCUSSION

The presented case involves a 63-year-old man who initially sought medical attention with classical COVID-19 symptoms, subsequently developing a complex clinical trajectory involving recurrent hospitalizations and a constellation of symptoms. The patient's journey underscores the challenges in managing COVID-19, particularly when complicated by underlying conditions.

A systematic review provides a comprehensive review of Good syndrome, a rare condition characterized by the association of thymoma and immunodeficiency. Despite being documented over 50 years ago, GS remains a clinical enigma. The systematic analysis of 152 cases reveals a global distribution, with nearly half reported in Europe.[8] Interestingly, the diagnosis of thymoma often precedes the identification of hypogammaglobulinemia, infection, or diarrhea.[9] The study underscores the significant mortality rate associated with GS, emphasizing the need for enhanced clinical awareness and understanding of its diverse clinical and immunological features. The findings advocate for improved early recognition through astute clinical acumen, aiming to prevent mortality. The article concludes by highlighting the imperative for further research to unravel the complexities surrounding this perplexing clinical entity.

This study sheds light on the rarity of Good's syndrome, a condition with a nuanced clinical presentation that can be easily overlooked. Early diagnosis is paramount, as this syndrome, although infrequent, can lead to severe and potentially fatal infections. By detailing the patient's case, we emphasize the importance of heightened clinical suspicion and comprehensive diagnostic evaluations when encountering patients with persistent or recurrent symptoms, ensuring timely intervention to prevent dire consequences.

In comparing our case with the one reported by Pozzi et al., both instances highlight the rare and challenging nature of Good's syndrome, particularly when compounded by SARS-CoV-2 infection.[10] In Pozzi et al.'s case, unfortunately, the patient experienced a fatal outcome, underscoring the potential severity of the syndrome in the context of COVID-19. Both cases emphasize the limited understanding of Good's syndrome's pathophysiology, with a likely bone marrow defect contributing to T and B cell maturation inhibitors.[11] The thymoma-associated hypogammaglobulinemia observed in both cases aligns with the classic diagnostic criteria. However, our case, with its unique clinical course and extended complications, contributes to the evolving understanding of Good's syndrome in the context of COVID-19, offering valuable insights into the varied presentations and outcomes associated with this rare immunodeficiency disorder. Additionally, both cases underscore the importance of early diagnosis and comprehensive management strategies to improve outcomes in this challenging clinical scenario, where replacement treatment with immunoglobulins is recommended to mitigate the poor prognosis associated with Good's syndrome.

Notably, this study marks a significant milestone in medical literature as the first reported case of Long COVID-19 in Good's syndrome in Iran. This unique contribution adds to the global understanding of the syndrome's prevalence and clinical manifestations. The absence of prior documented cases in Iran accentuates the need for increased awareness among healthcare professionals, emphasizing the importance of considering immunodeficiency in patients presenting with recurrent COVID-19 symptoms, especially in regions where such cases might be underreported or underrecognized. Other similar cases worldwide are summarized in Table 3.

Agarwal et al reported other cases of Good's syndrome which is comparable with our cases. In contrast to Case 1 of their reports, which involved a 51-year-old woman presenting with gastrointestinal symptoms, our case featured

TABLE 3 GS cases alongside COVID-19 infection.

Year	Authors	Age	Gender	Presentation	Outcome	Reference
2022	Lawek Berzenji et al.	55	Male	Oral lichen planus and cutaneous lesions	Alive	[12]
2022	Edwin Daniel Maldonado-Domínguez et al.	51	Male	Myalgia, arthralgia, anosmia, and dysgeusia	Dead	[13]
2022	Maria Lourdes Cos Esquius et al.	79	Female	Asymptomatic (admitted to perform a lymph node biopsy)	Alive	[10]
2021	Maria Duarte et al.	70	Female	Cough, dyspnea, fever, and myalgia	Alive	[14]
2020	Maria Rosa Pozzi et al.	51	Male	Low-grade fever, myalgias, and asthenia	Dead	[11]

a 63-year-old male primarily exhibiting classical COVID-19 symptoms, emphasizing the varied clinical presentations of Good's syndrome.[15] While Case 1 experienced COVID-19-associated pancytopenia and revealed babesiosis on peripheral blood smear as a rare COVID-19 complication, our case navigated through recurrent COVID-19 symptoms and a thymoma-associated immunodeficiency.[16,17] Notably, our patient's clinical trajectory involved repeated hospitalizations and complications, highlighting the heterogeneity of Good syndrome presentations.

Furthermore, the article underscores a critical public health consideration. In cases of recurrent COVID-19 symptoms coupled with persistent positive PCR results, clinicians should broaden their diagnostic approach to include the evaluation of primary and secondary immune deficiencies.[18] This expanded perspective is crucial to identify individuals at risk for opportunistic infections, allowing for timely diagnosis and the implementation of necessary treatments.[19]

In conclusion, the presented long COVID-19 case and the broader review of GS underscore the rarity and intricate nature of this thymoma-associated immunodeficiency disorder. The unique clinical trajectory observed in our case contributes to the growing body of knowledge surrounding GS, particularly in the context of SARS-CoV-2 infection. The global distribution of GS, as highlighted in the literature, emphasizes the need for increased awareness among clinicians worldwide. The high mortality rate associated with GS underscores the urgency for early recognition and intervention. By shedding light on the clinical and immunological intricacies of GS, this study adds valuable insights to the existing literature. Continued research and collaborative efforts are imperative to enhance our understanding of GS, paving the way for improved diagnostic strategies and therapeutic interventions to mitigate the challenges associated with this complex syndrome.

AUTHOR CONTRIBUTIONS

Payam Tabarsi: Conceptualization; data curation; formal analysis; investigation; methodology; project administration; supervision. **Marjan Hemmatian:** Investigation; supervision; writing – original draft; writing – review and editing. **Maryam Moradi:** Writing – review and editing.

FUNDING INFORMATION

None.

CONFLICT OF INTEREST STATEMENT

None.

DATA AVAILABILITY STATEMENT

The authors confirm that the data supporting the findings of this study are available within the article.

ETHICS STATEMENT

The manuscript adheres to the CARE guidelines. Written informed consent was obtained from the patient for publication. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

CONSENT

Written informed consent was obtained from the patient to publish this report in accordance with the journal's patient consent policy.

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How to cite this article: Tabarsi P, Hemmatian M, Moradi M. Long COVID-19 leading to Good's syndrome diagnosis: A clinical case-report and literature review. *Clin Case Rep*. 2024;12:e8962. doi:10.1002/ccr3.8962