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Good's syndrome unmasked by prolonged SARS-CoV-2 infection: A case report

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Abstract

Good's Syndrome (GS) is a rare adult-onset combined immunodeficiency characterized by thymoma, hypogammaglobulinaemia and B- cell depletion. Patients with GS are predisposed to recurrent infections. Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) infections have been scarcely reported in patients with GS. Here in, we describe a case of 49 year old, previously healthy patient who had GS newly diagnosed during prolonged and severe SARS-CoV-2 infection. She recovered after immunoglobulin replacement therapy, antivirals and dexamethasone.

Keywords: Good's syndrome; Immune deficiency; COVID-19; SARS-CoV-2; Case report.

Case description

A 49-years old lady in Hong Kong who enjoyed good past health and was not vaccinated against Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-COV-2) presented to a tertiary hospital in Hong Kong in April, 2022 with cough, fever and shortness of breath. She tested positive for SAR-CoV-2 by Rapid Antigen Test (RAT) on nasal swab sampling 20 days ago after close contact with a person with Coronavirus Disease 2019 (COVID-19).

On presentation, she was afebrile with oxygen saturation of 96% on 1 L/minute nasal cannula oxygen. Her chest X-ray showed multilobar pulmonary infiltrates. Her throat saliva's SARS-CoV-2 Ribonucleic Acid (RNA) Reverse Transcription-Polymerase Chain Reaction (RT-PCR) Cycle Threshold (Ct) value was 27.9. Blood tests showed lymphopenia and elevated inflammatory markers (Table 1A). She was started on intravenous amoxicillin-clavulanate and a 9-day course of oral dexamethasone. Remdesivir was not given initially as she was at day 20 of infection and had Ct value >25. The first day of infection was defined as the day of initial positive SARS-CoV-2 RAT.

Twenty-five days after infection, she developed spiking fever and persistent shortness of breath. Repeated sputum sample grew acinetobacterbaumanii, computer tomography of the thorax revealed multilobarperipheral ground glass opacities, consolidation and collapse over bilateral lower lobes, non-occlusive pulmonary embolism in left lower lobe segmental pulmonary artery and a thymic mass (Figure 1). She exhibited no features of myasthenia gravis and her anticholinesterase antibodies level was normal. Intravenous meropenem and subcutaneous low molecular weight heparin were started.

Thirty-six days after infection, her hypoxaemia worsened with PaO_2/FiO_2 of 124 mmHg on 10 L/minute face mask oxygen. She was admitted to the intensive care unit for high flow nasal cannula oxygen therapy. Repeat chest X-ray showed persistent diffuse ground glass infiltrates, CRP was 279.9 mg/L and ferritin was 7429 pmol/L. Bronchoalveolar lavage detected cytomegalovirus nucleic acids and found alveolar macrophages and inflammatory cells on cytology but did not detect other organisms. Autoimmune screen, myositis panel and human immunodeficiency virus serology were negative. Of note, repeat

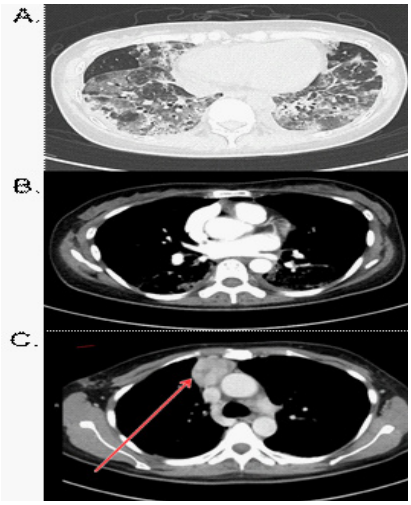

Figure 1: Contrast thorax computer tomography showing: A. bilateral ground glass opacities; B. Left lower lobe segmental pulmonary arterial embolism; C. Thymic mass (red arrow).

SARS-CoV-2 nasopharyngeal aspirate RT-PCR Ct value was 18 and serum SARS-CoV-2 IgG remained negative on day 36 after initial SARS-CoV-2 infection. Thus persistent COVID-19 infection with underlying immune compromised status was suspected. Serum immunoglobulin pattern showed hypogammaglobulinaemia (Table 1B). Lymphocyte subset study showed absent B cells, low CD4 cellsand low CD4/CD8 ratio (Table 1C). Lymphocyte Proliferation Assay (LPA) was normal (Table 1D). Fine needle aspiration biopsy of the thymic mass showed histological features compatible with type A thymoma. Good's Syndrome (GS) was diagnosed and Intravenous Immunoglobulin (IVIG) 0.4 g per kg was started. Co-trimoxazole and acyclovir prophylaxis was given to prevent further opportunistic infections. In view of persistently high SARS-CoV-2 viral load and clinical deterioration, she was given tocilizumab, repeated courses of dexamethasone and remdesivir. Antivirals targeting cytomegalovirus infection were not given in view of clinical improvement after IVIG and treatment of COVID-19. Following COVID-19 treatment and 2 days after commencement of IVIG, her PaO_2/FiO_2 improved to 576.56 mmHg on 3 L/minute nasal cannula oxygen. She was discharged home 51 days after admission and was able to be weaned off oxygen entirely. Immunoglobulin replacement was arranged monthly in the haematology clinic

Discussion

We described the first case of COVID-19 occurring in a patient with GS in Asia and the third case to our knowledge in which prolonged SARS-CoV-2 infection was the index presentation leading to the diagnosis of GS in a patient without any history of preceding infections or thymoma [1,2].

GS is a rare adult-onset combined immunodeficiency characterized by thymoma, hypogammaglobulinaemia and Bcell depletion [3]. Patients with GS are predisposed to recurrent infections, particularly from encapsulated organisms and opportunistic organisms such as cytomegalovirus, candida and pneumocystis carinii. The main findings on immunological investigation are hypogammaglobulinaemia, low or absent B cells, variable defects in cell mediated immunity such as CD4+ T cell lymphopenia and reduced T cell mitogen proliferative responses [3].

Table 1: Immunological and haematological parameters of the patient.

	Patient	Normal range/ Healthy control
A. Haematological parameters and inflammatory markers on admission		
Haemoglobin	7.6 g/dL	11.2 – 13.8 g/dL
Platelet	411 x 10^9/L	163 – 356 x 10^9/L
Leucocyte count	8.9 x 10^9/L	4.2 – 9.6 x 10^9/L
Lymphocyte count	0.8 x 10^9/L (0.8%)	1.1 – 3.1 x 10^9/L (17.4 – 44.5%)
Granulocyte count	7.8 x 10^9/L (88%)	2.2 – 6.4 x 10^9/L (42.6 – 72.3%)
Monocyte count	0.4 x 10^9/L (4%)	0.3 – 0.8 x 10^9/L (4.7-11.8%)
C-reactive protein	159.9 mg/L	<9.9 mg/L
Ferritin	167 P mol/L	29 – 337 pmol/L
D-dimer	1458	<500 ng/ml
Lactate dehydrogenase	669 U/L	103 – 199 U/L
B. Serum immunoglobulin pattern		
IgM	0.07 g/L	0.33 – 2.93 g/L
IgA	0.80 g/L	0.65 – 4.2 g/L
IgG	4.94 g/L	5.52 – 16.3 g/L
C. Immunophenotypic analysis of lymphocytes		
Leucocyte count	5.9 x 10^9/L	4.2 – 9.6 x 10^9/L
Lymphocyte count	1.17 x 10^9/L (20%)	1.1 – 3.1 x 10^9/L (17-44.5%)
Granulocyte count	4.22 x 10^9/L (72%)	2.2 – 6.4 x 10^9/L (42.6-72.3%)
Monocyte count	0.47 x 10^9/L (8%)	0.3 – 0.8 x 10^9/L (4.7-11.8%)
Total Tcells (CD3)	1.03 x 10^9/L (87.7%)	
Thelper cells (CD4)	0.3 x 10^9/L (25.7%)	
Tsuppressor cells (CD8)	0.66 x 10^9/L (56.1%)	
Total B cells (CD19)	0	
Natural Killer cells (CD56)	0.14 x 10^9/L (11.9%)	
CD4/CD8 ratio	0.46	
D. Lymphocyte proliferation assay		
Unstimulated	3153 cpm/10^6 cells	3300 cpm/10^6 cells
PHA	248880 cpm/10^6cells	355447 cpm/10^6 cells
Con A	157787 cpm/10^6cells	250793 cpm/10^6 cells
PWM	58787 cpm/10^6 cells	73027 cpm/10^6 cells

Abbreviations: PHA: phytohemagglutinin; Con A: concanavalin A; PWM: Pokeweed mitogen; CPM: Counts per minute.

In the context of SARS-COV-2 infection, Bcell alymphocytosis is linked to poorer prognosis [4]. Studies of B cell depleted patients with COVID-19 have found delayed clearance of SARS-CoV-2 and hyperactivation of myeloid immune response possibly leading to persistent infection and hyperinflammatory syndromes [5]. Our patient's immunological evaluation showed absent B cells but normal LPA indicating preserved T cell function, further demonstrating the important role of B cells in immune response against SARS-CoV-2.

Treatment of GS involves immunoglobulin replacement and resection of thymoma, although immune defects may persistent despite resection of thymoma [3]. Our patient was successfully treated with steroids, antiviral therapy and IVIG with clinical improvement and survival to hospital discharge. Convalescent plasma had also been used in another GS case with COVID-19 successfully [1].

Our case highlighted the importance of maintaining a high index of suspicion for underlying immunodeficiency in patients with persistent SARS-CoV-2 infection, as COVID-19 may be the first presentation of the immune deficiency. GS should be suspected in the context of thymoma even without known history of recurrent infections. Lymphopenia, being a common feature of COVID-19 infection [6], may become a red herring leading to under-recognition of underlying immunodeficiency. Timely diagnosis of GS by lymphocyte subset analysis, LPA and treatment with immunoglobulin replacements may improve outcomes and prevent future infections.

Declarations

Ethics: The patient was treated in accordance to the Declaration of Helsinki. The patient's written consent for the case report has been obtained.

Conflicts of interests: The authors have no conflicts of interests to declare.

Author contributions:

Concept or design: M Hau, L Ling, WH Yip

Acquisition of data: M Hau, WH Yip

Analysis or interpretation of data: M Hau, EKY Chiu

Drafting of the manuscript: M Hau

Critical revision of the manuscript for important intellectual content: EKY Chiu, L Ling, WH Yip

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