Peer Review File

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Reviewer A

The authors mainly evaluated the relation between Good syndrome and COVID-19 infection. The study is well written; however, some improvement will be required. I suggest several issues that should be revised.

<Major Comments>

Comment 1

What did you newly show in this article? There are already some reports of COVID infection in patients with Good syndrome.

Reply 1

In this case report, our patient had persistent COVID-19 shedding, which has not been described in previous reports as of yet. Furthermore, although there are a few reports of COVID-19 infections in patients with Good's syndrome, data on these patients is very scarce. The authors chose to write this case report to shed more light on the rare simultaneous occurrence of these two entities.

Comment 2

You said that patients with Good syndrome are less likely to become severe COVID-19 infection in order to prevent hyperinflammatory conditions. What is the basis for this? Please explain in details.

Reply 2

Several authors have hypothesized that some types of immunodeficiences could, paradoxically, be protective against developing hyperinflammation due to COVID-19 as these patients lack the ability to form a cytokine storm, which is often one of the main aggravators of severe COVID-19 infections. However, these hypotheses are mainly based on small case series of patients with different types of immunodeficiencies. These findings have not been corroborated by large, prospective trials.

Changes in the text 2:

We elaborated on this point in our text as well (Page 5 lines 172-175)

Comment 3

What does the long-term emission of COVID-19 from sputum mean?

Reply 3:

This indicates that the patient either is still shedding infectious, replication-competent virus or shedding residual RNA and not infectious virus. Clinically, the patient did not have any symptoms related to the prolonged shedding. However,

careful follow-up is warranted to prevent the patient of developing possible severe symptoms.

Reviewer B

Case reports of Good's Syndrome have value as it is a very rare syndrome and information on patients with concomitant COVID-19 has importance. As noted the patient had severe stress relating to having COVID and an immune deficiency. For this reason it is my opinion that the report be published but only if more details are provided.

Although Good's Syndrome is an immune deficiency, this patient "had no relevant past medical history". There is no mention of any infections other than with Sars-Cov-2. Data on past vaccination responses would be helpful. The diagnosis of immune deficiency appears to only be based on having hypogammaglobulinemia (HGG). Corticosteroids can be a cause of HGG.

Reply:
The patient had received all standard vaccinations that are part of the national vaccination campaign in Belgium. There were no indications that the patient had a lack of response to these previous vaccinations. However, no specific tests were performed with regards to these previous vaccinations. Furthermore, the diagnosis of Good's syndrome was based on the combination of the symptoms of oral lichen planus, HGG, the thymoma, a low B cell count and a low CD4/CD8 ratio.

The authors state that the patient received corticosteroids without providing the doses and time frame with respect to the initial finding of HGG. This puts in question if these treatments significantly contributed to the HGG. The authors should provide a time frame, specifying the time course of treatments and laboratory findings.

Reply:
Prolonged corticosteroids can indeed contribute to the development of HGG. The patient received methylprednisolone on several occasions by the dermatologist for his symptoms of oral lichen planus which had developed approximately 1 year before. Previous reports on the exact duration and dose of the corticosteroid treatments could not be found as the initial treatment was initiated by the patient's private dermatologist. However, during the first consultation at our hospital, the patient was still treated with 2 mg of methylprednisolone every 2 days.

Changes in the text:
We elaborated on this point in our text as well (Page 3 lines 100-103)

Although immune phenotyping was conducted on peripheral blood, there is no mention of any phenotyping of the thymoma nor of the HGG levels at that time. At what IgG level was treatment started. Was the IgG replacement given intravenously or by subcutaneous injection? At what dose and did the patient achieve target levels. The IgG replacement was not likely to impact on the development of COVID-19, however it could have helped in preventing concurrent respiratory bacterial infections.

Reply:
A core needle biopsy was performed, which showed spindle-shaped cells and lymphoid cells. Additional tests showed terminal deoxynucleotidyl transferase (TdT), cluster of differentiation 3 (CD3), and CD5 positivity in the lymphoid cells. Furthermore, pancytokeratin (CKpan) was positive in the spindle-shaped cells. Treatment was started at an IgG level of 2.45 g/L (table 2) and was given intravenously at a dose of 25 g every 4 weeks. The patient achieved a level of 9.04 g/L after 5 months.

Changes in the text:
This data was added in the text as well (Page 4, lines 110-119)

Please state the interval between chemotherapy cycles and the impact on lymphocyte numbers. Did the patient develop severe lymphopenia with Sars-Cov-2?
It is stated (line 165) that the infection was not severe. Was this based on the clinical presentation? Despite this he was given Remdesivir. Did the patient also receive corticosteroids? If so, please comment on the possible impact on viral shedding.

Reply:
The interval between the first and second chemotherapy cycles was 21 days. No overall lymphopenia was noted in the lab results of our patient during the chemotherapy treatments. The severity of the infection was mild to moderate, mainly based on clinical symptoms. The patient was indeed administered Remdesivir as this was the guideline at that time for patients with immunodeficiencies. The patient already received a low dose of methylprednisolone (4 mg/day). Additional treatment with corticosteroids was not started.

Changes in the text:
Page 4, lines 129-132.

The patient was vaccinated with 2 doses of an mRNA vaccine without any evidence of an anti body response. What anti bodies were assessed and was it

only to the spike protein? Was the patent vaccinated to other agents such as Pneumococcus, Hemophilus, Tetanus or Influenza? What were the responses to the other vaccines?

Reply:
Antibodies to the Spike protein were indeed tested at that time, which showed a response of <1U/mL. No other tests were available to us at that time. The patient was indeed vaccinated against other agents including Pneumococcus, Hemophilus, Tetanus and Influenza. Unfortunately, the response to these vaccines had not been tested. However, the patient was also vaccinated against Hepatitis B, for which response was evaluated. Indeed, similar to the SARS-CoV-2 vaccination, the patient was a non-responder to the Hepatitis B vaccination as well.

The patient received IgG replacement every 4 weeks following discharge. Please indicate the dose on a per Kg basis.

Reply:
The dose was between 350-400 mg/kg every 4 weeks.

Changes in the text:
Text added (Page 4, lines 141-142)