Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active.
Case Reports and Series

Hyperinflammation with COVID-19: The key to patient deterioration?☆☆

Kathryn Haigh a,*, Zoe Joanna Syrimi a, Sharon Irvine a, Tom J. Blanchard a, Muhammad Sajid Pervaiz b, Arpad G. Toth b, Libuse Ratcliffe a

a Tropical and Infectious Diseases Unit, Royal Liverpool University Hospital, Prescot Street, Liverpool, L7 8XP, United Kingdom
b Department of Haematology, Royal Liverpool University Hospital, Prescot Street, Liverpool L7 8XP, United Kingdom

ARTICLE INFO

Article history:
Received 25 April 2020
Received in revised form 8 May 2020
Accepted 18 May 2020

Keywords:
Communicable diseases
Hemophagocytic lymphohistiocytosis
Coronavirus infections

ABSTRACT

Background: The potential risk of cytokine storm in patients with coronavirus disease 2019 (COVID-19) has been described [1]; we write to share our experience treating a 17-year-old male with haemophagocytic lymphohistiocytosis (HLH) secondary to COVID-19 infection.

Case report: This patient presented with cough, sore throat, anorexia and pyrexia. On examination, he had gross cervical lymphadenopathy and palpable splenomegaly. Nose and throat swab for SARS-CoV-2 was positive and blood tests revealed pancytopenia with very high ferritin, triglyceride and d-dimer levels. The patient’s H-Score [2] was calculated at 220, suggesting probability of HLH of 93–96%. Considering Russell and colleagues’ [3] comments about potential harm of corticosteroid use in patients with COVID-19 infection, the patient was commenced on treatment with the selective IL-1 receptor antagonist drug, Anakinra, and a two-day course of intravenous immunoglobulin.

Results: The patient responded rapidly to treatment, becoming afebrile after 24 h. His lymph nodes and spleen began to normalise after the first 48 h, at which time point the ferritin also started to decrease. He was discharged after 11 days feeling fit and well.

Conclusion: This case certainly illustrates the importance of hyperinflammation syndromes in COVID-19. It also raises the question – is the severe pneumonitis seen in patients with COVID-19 an immunological phenomenon? We know that the viral load of patients with COVID-19 seems to peak in the early stages of illness [4,5]; however, patients deteriorate later in the disease course, at around days 10–14. This patient, who had risk factors for deterioration (male, pancytopenic), did not develop an oxygen requirement and clinically and biochemically improved rapidly on Anakinra with no adverse events. We might suggest Anakinra to the scientific community as a treatment option in COVID-19 infection.

© 2020 The Author(s). Published by Elsevier Ltd on behalf of British Infection Association. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

Introduction

The potential risk of cytokine storm in patients with coronavirus disease 2019 (COVID-19) has been described [1]; we write to share our experience treating a 17-year-old male with haemophagocytic lymphohistiocytosis (HLH) secondary to COVID-19.

Case

The patient had no past medical history and no regular medications. He was a non-smoker with no alcohol intake and a normal body mass index. He lived with his parents, and there was no family history of inflammatory disorders.

This patient presented with a six-day history of cough, sore throat, anorexia and pyrexia (recorded at 39.1 °C). On examination, he had gross cervical lymphadenopathy with submandibular nodes more than 10 cm in diameter. There was palpable splenomegaly.

Investigations revealed pancytopenia, hyponatraemia, hypocalcaemia and elevated alanine aminotransferase, lactate and C-reactive protein. Ferritin was 8197 μg/l, triglycerides 5.1 mmol/l, LDH 586 u/l, d-dimer 3758 ng/ml, fibrinogen 1.73 g/l and reticulocytes 13%. Further investigations revealed negative HIV, hepatitis B and C and toxoplasma screening. EBV and CMV IgG were both positive, but IgM and PCR negative. Serum immunoglobulins and electrophoresis were normal. Blood cultures were negative. Admission chest x-ray and...
Graph 1. Ferritin values during admission.

Graph 2. Neutrophil count during admission.

Graph 3. Platelet count during admission.
seasonal respiratory viral PCR panel (including, but not limited to, influenza A and B, rhinovirus and adenovirus) was negative. SARS-CoV-2 nose and throat swab taken on the day of admission and run using VIASURE by BioTec SARS-CoV-2 with QiaSymphony virus DSP extraction, returned positive on day two of admission with a cycle threshold value of 28.7. Graphs 1–4 show the pattern of change of ferritin, neutrophils, platelets and d-dimer blood parameters during admission.

On day two of admission there was ongoing pancytopenia and an increasing ferritin level. Bone marrow aspirate showed reactive marrow with no evidence of malignant infiltration. A bone marrow trephine could not be tolerated. The patient’s H-Score [2] was calculated to 220, suggesting a probability of HLH of 93–96%. Considering Russell and colleagues’ [3] comments about the potential harm of corticosteroid use in patients with COVID-19 infection, the patient was commenced on treatment with the selective IL-1 receptor antagonist drug, Anakinra to the scientific community as a treatment option in COVID-19 infection, and we understand a clinical trial is indeed in progress [6].

Once his ferritin had fallen to less than 1000 μg/l and almost normal clotting and liver function tests. Outpatient follow up was arranged to allow for clinical and biochemical review.

The patient responded rapidly to treatment, becoming afebrile after 24 h of Anakinra. His lymph nodes and spleen began to reduce in size after the first 48 h, at which time point the ferritin also started to decrease. Liver function tests worsened over the first five days, with alanine aminotransferase peaking at 771 u/l, but reduced thereafter. Once his ferritin had fallen to less than 1000 μg/l, on day nine, Anakinra was discontinued. The patient was kept in hospital for a further three days to ensure that his ferritin continued to decrease following treatment. He was discharged on day 11 feeling well, with a ferritin of 766 μg/l and almost normal clotting and liver function tests. Outpatient follow up was arranged to allow for clinical and biochemical review.

Conclusion

This case certainly illustrates the importance of hyperinflammation syndromes in COVID-19. It also raises the question – is the severe pneumonitis seen in patients with COVID-19 an immunological phenomenon? We know that the viral load of patients with COVID-19 seems to peak in the early stages of illness [4,5], however patients deteriorate later in the disease course, at around days 10–14. This patient, who had risk factors for deterioration (male, pancytopena), did not develop an oxygen requirement and clinically and biochemically improved rapidly on Anakinra with no adverse events. We might suggest Anakinra to the scientific community as a treatment option in COVID-19 infection, and we understand a clinical trial is indeed in progress [6].

Funding source

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Credit authorship contribution statement

Kathryn Haigh:Conceptualization, Formal analysis, Investigation, Writing - original draft. Zoe Joanna Syrimi:Investigation. Sharon Irvin:Formal analysis, Writing - review & editing. Tom J. Blanchard:Conceptualization, Formal analysis, Writing - review & editing. Supervision. Muhammad Sajid Pervaiz:Formal analysis, Investigation. Libuse Ratcliffe:Writing - review & editing.

References

1. Mehta P, McAuley DF, Brown M, Sanchez E, Tattersall RS, Manson JJ, et al. COVID-19: consider cytokine storm syndromes and immunosuppression. Lancet. 2020;395(10229):1033–4. https://doi.org/10.1016/S0140-6736(20)30628-0.
2. Fardet L, Galicier L, Lambotte O, Marzac C, Aumont C, Chahwan D, et al. Development and validation of the HScore, a score for the diagnosis of reactive hemophagocytic syndrome. Arthritis Rheumatol. 2014;66:2613–20. https://doi.org/10.1002/art.38690.
3. Russell CD, Millar JE, Bailie JK. Clinical evidence does not support corticosteroid treatment for 2019-nCoV lung injury. Lancet. 2020;395(10223):473–5.
4. Pan Y, Zhang D, Yang P, Poon LLM, Wang Q. Viral load of SARS-CoV-2 in clinical samples. Lancet Infect Dis. 2020;20(4):411–2. https://doi.org/10.1016/S1473-3099(20)30113-4.
5. Zou L, Ruan F, Huang M, Liang L, Huang H, Hong Z, et al. SARS-CoV-2 viral load in upper respiratory specimens of infected patients. N Engl J Med. 2020;382:1177–8. https://doi.org/10.1056/NEJMoa2001737.
6. ClinicalTrials.gov. [Internet]. U.S National Library of medicine [updated 2020 April 9, cited 2020 April 25]. Available from: . https://clinicaltrials.gov/ct2/show/NCT04324021.