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.

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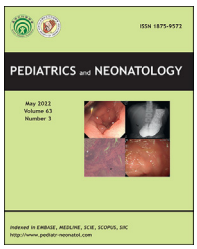

Letter to the Editor

Transient severe neutropenia in an infant with SARS-CoV-2 infection

To the Editor:

COVID-19-associated neutropenia is uncommon, and the presence of neutropenia combined with ferritin and cytokine levels has not been reported previously.

A 55-day-old infant girl, with no significant medical history, was admitted to our hospital after testing positive for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) on a nasal swab 2 days before presentation. On admission, she was afebrile and had no obvious signs of disease. Her vital signs and oxygen saturation were normal, and no abnormalities were detected on physical examination. Hematology showed severe neutropenia (hemoglobin, 10.3 g/dL, leukocyte count, 10,000 cells/μL; neutrophil count, 150 cells/μL; lymphocyte count, 9250 cells/μL; platelet count, 321 $\times$ 10^3/μL), but no morphological abnormalities were observed in the peripheral blood smears. Blood biochemistry showed increased ferritin and interleukin-18 (IL-18) levels (548 ng/mL and 769 pg/mL, respectively) and normal C-reactive protein (CRP) and interleukin-6 (IL-6) levels (<0.06 mg/dL and 3 pg/mL, respectively). Chest radiography did not reveal any abnormality. The results of the antigen tests for influenza virus, respiratory syncytial virus, human metapneumovirus, and adenovirus were negative. Epstein—Barr virus and cytomegalovirus serology showed patterns suggestive of previous infection. The neutrophil count spontaneously improved to 840 cells/μL, 7 days after admission, and the serum ferritin levels decreased (Fig. 1). The infant showed no physical signs of disease during her hospitalization and was discharged on day 8. At a follow-up visit on day 28, her neutrophil count was normal (1947 cells/μL).

Lymphopenia is a common hematological finding among adult patients with COVID-19,[1] but is not frequently observed in pediatric patients.[2] In contrast, COVID-19-associated neutropenia is uncommon in both adults and children. Severe neutropenia has been reported among patients with COVID-19.[3] However, the presence of neutropenia combined with ferritin and cytokine levels has not been reported previously. The patient in this case had neutropenia combined with elevated ferritin and IL-18 levels and normal CRP and IL-6 levels. Slaats et al.[4] proposed two inflammatory response pathways, namely the IL-18/ferritin axis for viral infection, and the IL-6/CRP axis. Based on the patient's test results, we speculate that this case involved an IL-18/ferritin response to SARS-CoV-2 infection, which elicited no physical signs of the disease. Although no studies have confirmed a direct relationship between the IL-18/ferritin response and neutropenia, it has been proposed that IL-18 promotes neutrophil recruitment from the peripheral blood into inflammatory lesions[5]; therefore, neutropenia may have resulted from increased transmigration and extravasation of neutrophils. The association between IL-18 and neutropenia in this report is noteworthy and warrants further investigation.

There have been few reports of severe neutropenia associated with SARS-CoV-2 infection; however, neutropenia has been previously reported in two infants, aged 23 and 39 days old, with SARS-CoV-2 infection.[6] This suggests that neutropenia might be characteristic of SARS-CoV-2 infection during early infancy. Thus, young infants with SARS-CoV-2 infection need to be managed carefully, even if they show no signs of disease, due to the risk of serious secondary infections in neutropenic patients.

Ethical consideration

Informed consent for the publication of the case report was obtained from the patient's parents.

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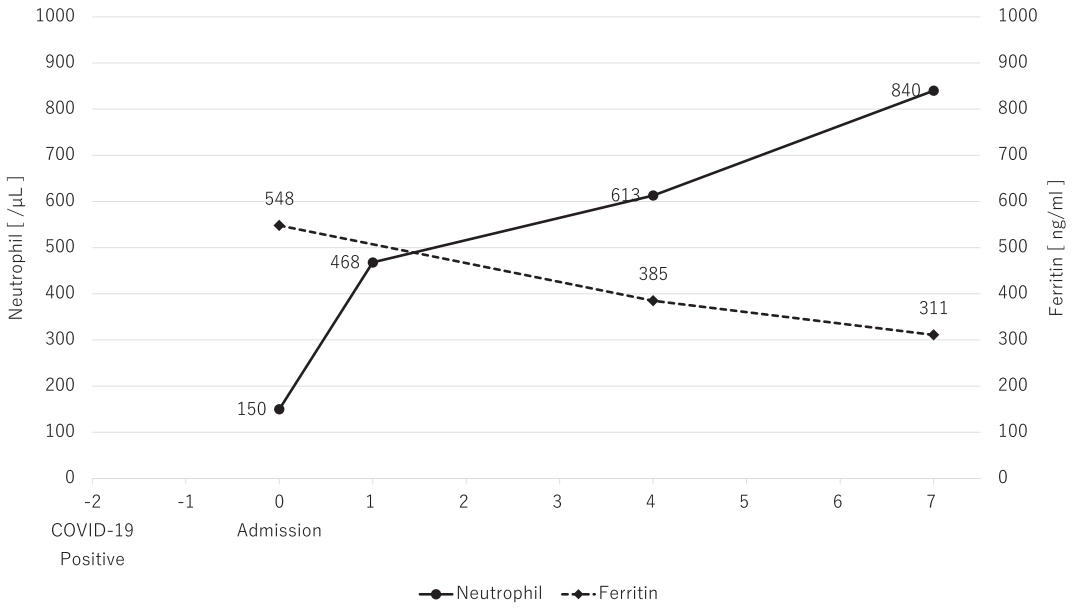

Figure. 1 Graph showing the changes in neutrophil counts and ferritin levels during the patient's hospitalization.

Declaration of competing interest

The authors declare no conflicts of interest.

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