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LETTER TO THE EDITOR

Clinical-scientific note

SARS-CoV-2 infection in autologous stem cell transplantation

Patients with pre-existing immunosuppressive comorbidities, including haematological malignancies and solid-organ transplant recipients, have a higher risk of morbidity and mortality when infected with SARS-CoV-2.[1] We report the first case of an individual with human immunodeficiency virus (HIV) experiencing asymptomatic COVID-19 in the early period following autologous stem cell transplant (ASCT), potentially resulting in poor graft function (PGF).

A 51-year-old man underwent an ASCT for stage IIIB refractory Hodgkin lymphoma in the context of well controlled HIV infection. Complete remission had been achieved with standard salvage chemotherapy prior to conditioning with lomustine, cytarabine, cyclophosphamide and etoposide. His pre-ASCT CD4 count was 331, viral load 51 copies/mL and he continued on anti-retroviral therapy with tenofovir alafenamide, emtricitabine and raltegravir throughout.

On day 0, a dose of 8.4×10^6/kg CD34+ cells were infused. Neutropenic fever developed on day +5, septic workup was negative including PCR for respiratory viruses on a nasopharyngeal swab. He was empirically treated with piperacillin/tazobactam, defervesced within 24 h and was discharged day +14 when neutrophils rose to 7.64 ($\times 10^9$/L) following a dose of filgrastim.

After discharge, count recovery was unexpectedly delayed, with sustained neutrophil engraftment ($\geq 0.5 \times 10^9$/L for three consecutive results) on day +31 and platelet engraftment ($\geq 20 \times 10^9$/L for three consecutive results, unsupported) on day +52. He remains red cell transfusion dependent, meeting criteria for PGF.[2] Cytomegalovirus, Epstein–Barr virus, HIV and parvovirus polymerase chain reaction (PCR) on blood were all undetectable.

On day +52 post-transplant, when attending for transfusion support, the patient reported a painful palate, attributed to burning his mouth with food. Testing for SARS-CoV-2 by PCR was performed and returned positive. We retrospectively performed SARS-CoV-2 testing on his day +5 PCR sample, also returning positive, suggesting he had had SARS-CoV-2 for 48 days without symptoms. His SARS-CoV-2 cycle threshold value was 17.5 on day +5 and 25.32 on day +52, comparatively, and his PCR test remained positive until day +95. A bone marrow biopsy on day +69 suggested increased peripheral destruction as the cause for the patient's cytopenia.

While the predominant manifestation of COVID-19 is respiratory tract infection, SARS-CoV-2 appears to demonstrate tropism for many organ systems, including the haematological system, with reported cases of lymphopenia and coagulopathy.[3] Pancytopenia, particularly PGF, in recipients of ASCT, has not been reported.

While there is a recent report commenting on asymptomatic COVID-19 infection in bone marrow transplant recipients,[4] the present case appears novel, in that he experienced prolonged cytopenias in the absence of clinical features of COVID-19 infection. The impaired T-lymphocyte responses related to his recent ASCT and long-standing HIV may have contributed to a lack of a SARS-CoV-2 inflammatory response in our patient, as being implicated in the severity of COVID-19 in solid-organ transplant recipients.[5]

Graft failure, more common in allogeneic transplantation recipients, is relatively rare following ASCT.[2] PGF, defined as two or more cytopenias 28+ days post-transplant, has been primarily linked to poor stem cell dose, which was not an issue in the present case. Some viruses such as influenza may be associated with cytopenias, but this is invariably in the setting of severe, not asymptomatic, cases.[6] It would appear plausible that SARS-CoV-2 could be implicated in PGF following ASCT, even without symptoms. This has potential implications for investigation of prolonged cytopenias in immunocompromised patients during the current COVID-19 pandemic.

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References

1 Malard F, Genthon A, Brissot E, van de Wyngaert Z, Marjanovic Z, Ikhlef S *et al*. COVID-19 outcomes in patients with hematologic disease. *Bone Marrow Transplant* 2020; **55**: 2180–4.

2 Valcárcel D, Sureda A. Graft failure. In: Carreras E, Dufour C, Mohty M, Kröger N, eds. *The EBMT Handbook: Hematopoietic Stem Cell Transplantation and Cellular Therapies*. Cham: Springer International Publishing; 2019; 307–13. https://doi.org/10.1007/978-3-030-02278-5_41.

3 Zhang Y, Xiao M, Zhang S, Xia P, Cao W, Jiang W *et al*. Coagulopathy and antiphospholipid antibodies in patients with Covid-19. *N Engl J Med* 2020; **382**: e38.

4 Kanellopoulos A, Ahmed MZ, Kishore B, Lovell R, Horgan C, Paneesha S *et al*. COVID-19 in bone marrow transplant recipients: reflecting on a single centre experience. *Br J Haematol* 2020; **190**: 2019–21.

5 Antonio R, Silvia M. Immunosuppression drug-related and clinical manifestation of coronavirus disease 2019: a therapeutical hypothesis. *Am J Transplant* 2020; **20**: 1947–8.

6 Lalueza A, Trujillo H, Laureiro J, Ayuso B, Hernandez-Jimenez P, Castillo C *et al*. Impact of severe hematological abnormalities in the outcome of hospitalized patients with influenza virus infection. *Eur J Clin Microbiol Infect Dis* 2017; **36**: 1827–37.