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

High-dose chemotherapy in a patient with coronavirus disease (COVID-19)

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The coronavirus disease (COVID-19) pandemic caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is an unprecedented challenge [1]. High-dose chemotherapy (HDCT) with autologous stem cell transplantation (ASCT) represents a potentially curative option for testicular germ cell tumour (TGCT) [2]; however, to our knowledge, to date, there have been no reports on these regimens in patients with COVID-19.

On March 11th, 2020, a 33-year-old male smoker, weighting 55 kg, with metastatic TGCT was admitted to our institute to receive the third cycle of a multi-cycle HDCT TI-CE regimen (paclitaxel [T] plus ifosfamide [I] followed by high-dose carboplatin [C] plus etoposide [E] with stem-cell support) with ASCT [3]. He did not have other comorbidities. At diagnosis, on January 2005, he had a metastatic disease with an intermediate prognosis, according to International Germ Cell Cancer Collaborative Group (IGCCCG) classification with retroperitoneal metastases and alpha-fetoprotein (AFP) = 8000 U/mL and human chorionic gonadotrophin (HCG) = 7000 U/mL [4]. The orchiectomy revealed a TGCT with yolk sac tumour and teratoma; then he received four cycles of bleomycin, etoposide and cisplatin, followed by retroperitoneal lymph node dissection of the residual mass, showing mature teratoma. The patient remained disease free until May 2019, when he experienced a lower right mediastinal mass with AFP = 25 U/mL suggesting a mediastinal relapse of the TGCT rather than a new mediastinal primary TGCT. He received four cycles of ifosfamide, etoposide and cisplatin, with radiological partial response, but residual disease was judged as inoperable. After 3 months, he experienced further mediastinal progression and came to our institute to receive HDCT. On December 2019, at the beginning of HDCT, AFP was 321 U/mL but decreased to 58 U/mL after two cycles of HDCT (lactate dehydrogenase and HCG were maintained normal). On March 14th, he started the third HDCT cycle with carboplatin area under the concentration-time curve (AUC) 7 plus 400 mg/sqm of etoposide for three days followed by ASCT supported by G-CSF and levofloxacin. Six days after ASCT, the patient developed febrile neutropenia (38.6 °C) associated with moderate diarrhoea and abdominal pain. Physical examination revealed blood pressure of 100/60 mmHg, heart rate of 112 beats per minute and oxygen saturation of 100% while breathing ambient air. We performed blood culture, stool culture, interrupted levoxacin and started 4.5 g of piperacillin and tazobactam intravenously four times per day. Paracetamol of 1000 mg intravenously every 8 h was used in case of fever >38 °C. Furthermore,

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the patient was maintained in the fasted state and supported with total parenteral nutrition. In the same days, the residence town of the patient saw a cluster of cases of COVID-19. On March 24th, based on the clinical and epidemiologic history, according to national indications at that time, a nasopharyngeal swab was performed with a positive result for SARS-CoV-2 on real-time reverse transcriptase polymerase chain reaction assay (RT-PCR). Blood tests showed increased level of C-reactive protein (CRP = 191.6 mg/dL) and severe pancytopenia due to recent HDCT. The chest and abdomen computed tomography (CT) scan did not show pneumonia neither abdominal complications. Immediately, the patient started antiviral treatment with ritonavir (100 mg orally once per day), darunavir (800 mg orally once per day) and hydroxychloroquine (200 mg orally twice per day) with a gradual improvement of clinical conditions; fever disappeared after 4 days. Blood tests showed a progressive reduction of CRP (15.9 mg/dL) and the resolution of leukopenia. After 1 week, the RT-PCR test for SARS-CoV-2 was still positive, whereas CT confirmed absence of chest abnormalities. Antiviral therapy was interrupted because of the resolution of symptoms. On April 1st, the qSARS-CoV-2 IgG/IgM Rapid Test documented an initial development of an immune-specific response against the virus [5]. Clinic conditions allowed us to discharge the patient on April 3rd with a reduction of AFP to 15.6 U/mL versus 58 U/mL before the third cycle of HDCT. Discharge weight was stable. On April 11th, the patient was declared cured, due to the negativization of the RT-PCR test for SARS-CoV-2.

Liang *et al.* [6] demonstrated that patients with cancer are at increased risk of severe COVID-19.

To the best of our knowledge, we report the first case of a patient with TGCT infected by SARS-CoV-2 treated with HDCT. The symptoms reported, in particular fever and diarrhoea, were not specific for this infection, in fact also chemotherapy could determine diarrhoea and febrile neutropenia, even if after starting antiretroviral therapy patient rapidly obtained a resolution of symptoms. Despite the high risk of complications derived from SARS-CoV-2, our patient experienced not only a control of the COVID-19 disease but also the development of an efficient immune response able to bring him to healing after nineteen days, despite the immunosuppression condition. Our case also suggests that, if CT may be a sensitive modality to detect COVID-19 in asymptomatic individuals [7], probably in immunosuppressed patients this is not true, due to the lack of an inflammatory response against the virus which caused pneumonia. The rapid beginning of antiviral and antibacterial treatment, combined with symptomatic therapy, most likely contributed to a better outcome of COVID-19.

In light of this, despite the outbreak of COVID-19, a potentially curative multi-HDCT should not be stopped in COVID-19–positive patients without interstitial pneumonia with the support of antiretroviral therapy.

Conflict of interest statement

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