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CASE REPORT

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# Successful restart of chemotherapy in a patient with primary mediastinal nonseminomatous germ cell tumor after COVID-19 infection

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**Abstract**

Cancer patients are considered highly susceptible to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection. However, it is not well known when chemotherapy can be safely restarted in cancer patients after coronavirus disease 2019 (COVID-19). Here, we describe the case of an 18-year-old man diagnosed with primary mediastinal nonseminomatous germ cell tumor (PMNSGCT) in which chemotherapy could be safely restarted after COVID-19. On day 11 of the third cycle of bleomycin, etoposide, plus cisplatin (BEP), he was diagnosed with mild COVID-19. On day 16 after the onset of COVID-19 (day 26 of third cycle of BEP), chemotherapy for his PMNSGCT was restarted. He received surgery after the fourth cycle of BEP without recurrence of COVID-19. Chemotherapy could be restarted and followed by surgery in this post-COVID-19 patient who had experienced mild illness after the discharge criteria were met and all symptoms had disappeared. We report this case with a review of the literature on restarting chemotherapy after SARS-CoV2 infection.

**KEYWORDS**

chemotherapy, COVID-19, PMNSGCTs, post-COVID-19, primary mediastinal nonseminomatous germ cell tumors

## INTRODUCTION

The outbreak of coronavirus disease 2019 (COVID-19) has led to a global pandemic. COVID-19 is the respiratory infection caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Cancer patients are considered highly susceptible to SARS-CoV-2 infection. Several reports have described that cancer patients might have an increased risk of severe response to infection by the virus and COVID-19-related complications.[1–4] However, when chemotherapy should be restarted in cancer patients with COVID-19 is not well known.

Although the majority of nonseminomatous germ cell tumors (NSGCTs) develop in the gonads, 5%–10% originate in an extragonadal site. Testicular NSGCTs are treated with cisplatin-based chemotherapy regimens followed by surgical resection of residual disease, which is regarded as the most successful therapy, with >80% overall long-term survival. It has been well established that primary mediastinal (PM) NSGCTs are a distinct subtype of NSGCTs, with a 40%–50% overall survival at 5 years, which positions PMNSGCTs in a poor risk category.[5–9] Therefore, even if there is a delay in the chemotherapy due to complication such as COVID-19 infection, it is desirable to restart the treatment as soon as possible in order to complete the chemotherapy and follow it by surgical resection. Here, we describe a case of PMNSGCT in which we were able to restart chemotherapy followed by surgery after COVID-19 without recurrence.

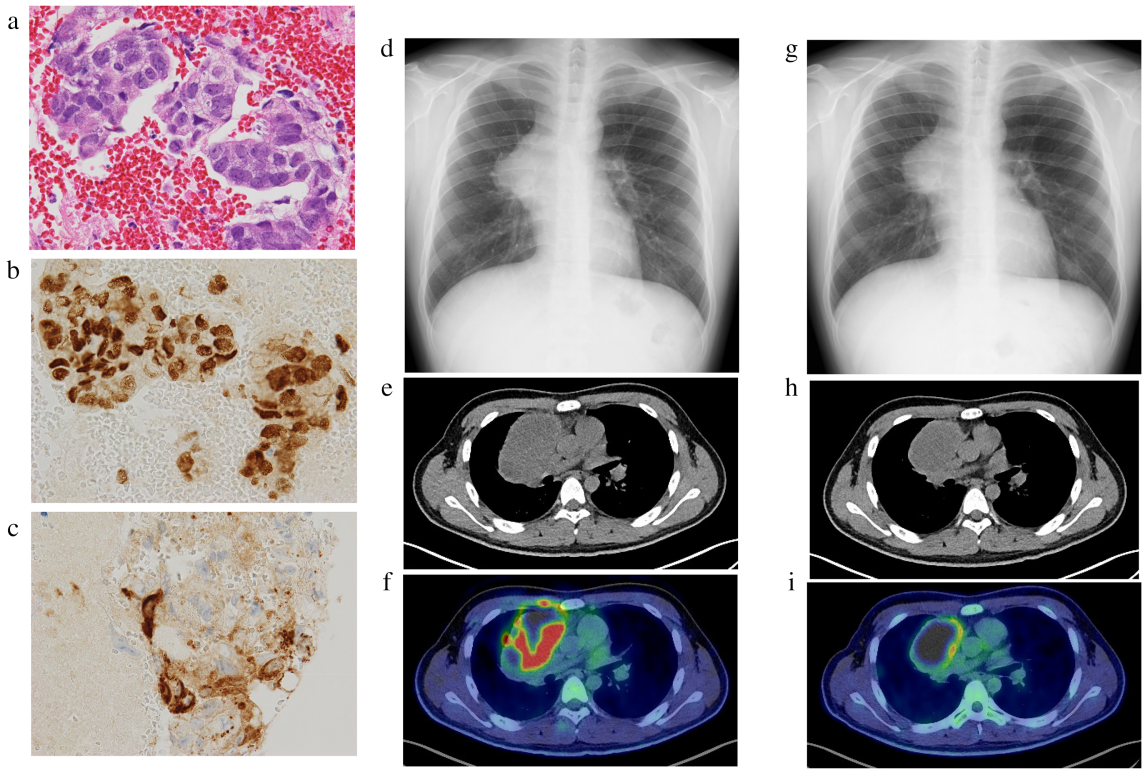


**FIGURE 1** (a–c) The pathological findings at the time of diagnosis as PMNSGCTs. A small number of atypical cells with marked necrosis are observed, in which the nuclei are enlarged in a circular shape and the chromatin is aggregated and shows epithelial connectivity. (a) H&E 400× magnification, (b) Sall4 400× magnification, (c) AFP 400× magnification, (d–f) before BEP for PMNSGCTs, and (g–i) two cycles after BEP, the evaluation of chemotherapy was partial response (PR). BEP, cisplatin, etoposide, and bleomycin; PMNSGCTs, primary mediastinal nonseminomatous germ cell tumors

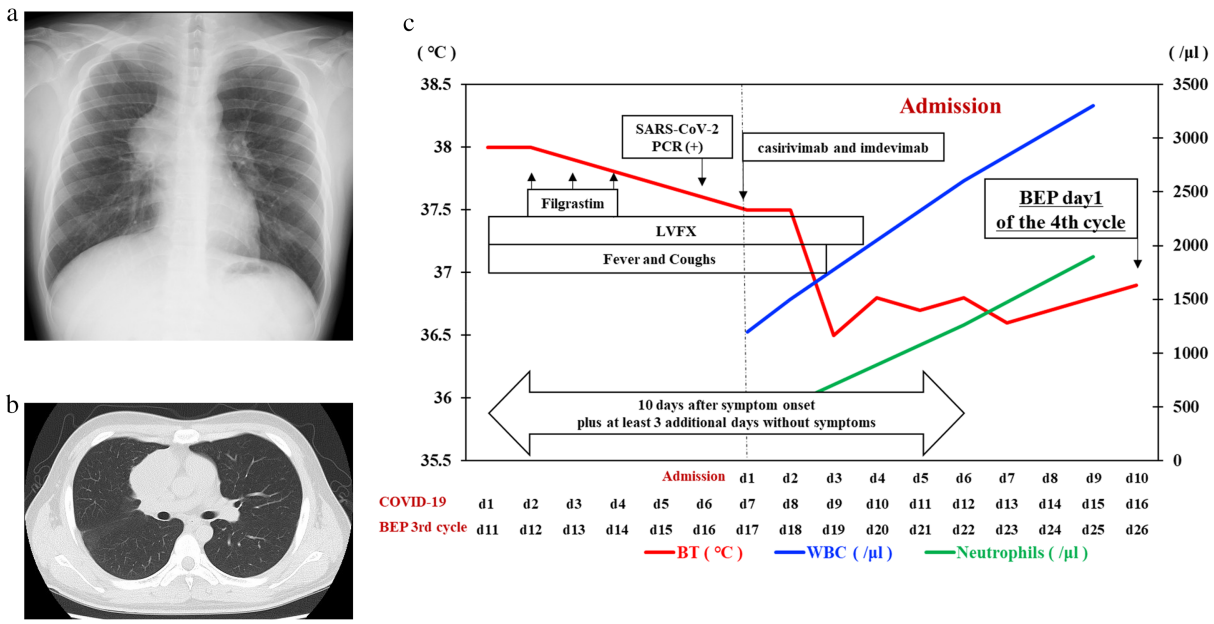


**FIGURE 2** (a, b) Onset of COVID-19, without ground-glass opacity or consolidation suggesting COVID-19. (c) Timeline after the onset of COVID-19. BT, body temperature; WBC, white blood cell; LVFX, levofloxacin; PCR, polymerase chain reaction

## CASE REPORT

The patient was an 18-year-old man without a significant medical history. He was diagnosed with PMNSGCT in July 2021 (Figure 1a–f) and started to receive the chemotherapy, BEP (cisplatin 20 mg/m$^2$ days 1–5, etoposide 100 mg/m$^2$ days 1–5, bleomycin 30 mg/bodyweight days 2, 9, 16; every 3 weeks). Although this regimen was effective against his

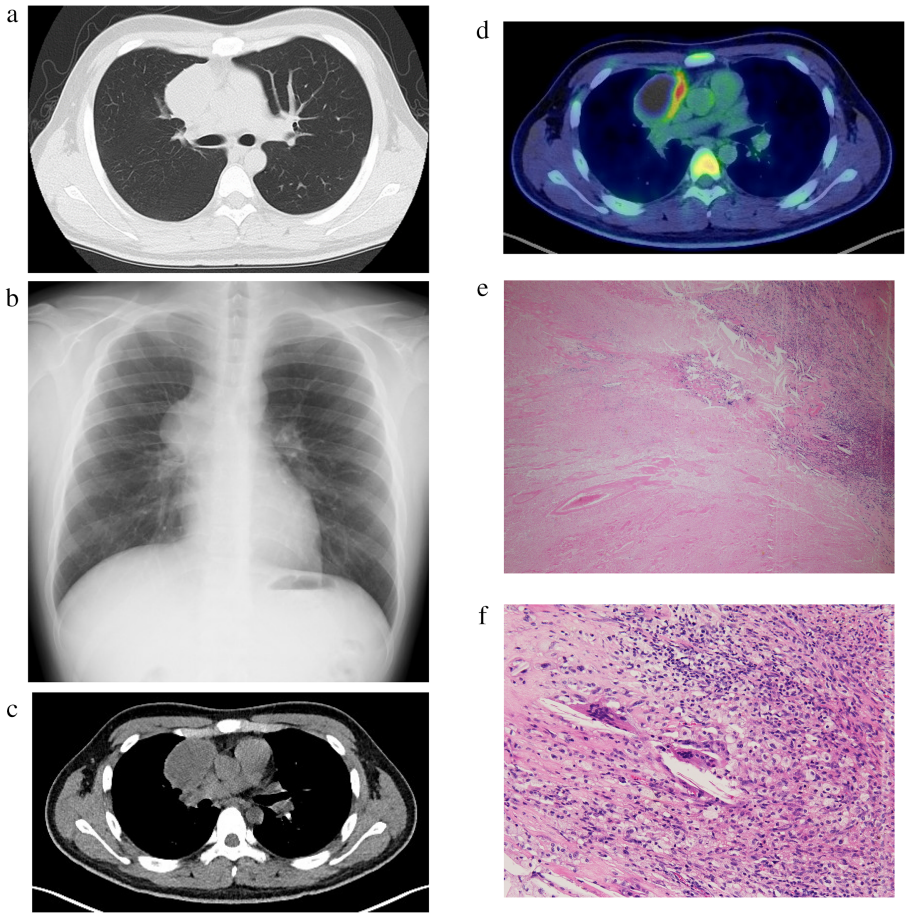


**FIGURE 3** (a) CT findings without recurrence of COVID-19. (b–d) The evaluation of chemotherapy was PR after four cycles of BEP and before surgery. (e, f) The resected specimen. Most of the tumor is in necrosis. The margins show aggregations of histiocytes and multinucleated giant cells, as well as fibrosis. The tumor cells are degenerated, and there are no residual viable tumor cells. (e) H&E 40× magnification, (f) H&E 200× magnification. BEP, cisplatin, etoposide, and bleomycin; CT, computed tomography; PR, partial response

tumors (Figure 1g–i), he showed a fever and cough on day 11 of the third cycle. SARS-CoV-2 test by reverse transcription polymerase chain reaction (RT-PCR) was performed on day 16 of the third cycle, and the result was positive. No signs were observed in his chest examination. A laboratory test revealed the following findings: white blood cell count, 1200/μl with 31.0% neutrophils, 57.0% lymphocytes, 9.0% monocytes, and 2.5% eosinophils; hemoglobin, 13.1 g/dl; platelet count 111 000/μl; and C-reactive protein 1.35 mg/dl. Chest computed tomography (CT) showed no ground-glass opacity or consolidation suggesting COVID-19 (Figure 2a,b). The severity of COVID-19 was mild illness. He was treated with casirivimab and imdevimab for COVID-19, and antibiotic therapy (oral levofloxacin 500 mg every 24 h) and filgrastim (50 μg/m$^2$ SC, every 24 h for 3 days) were also administered. His symptoms improved on the following day (Figure 2c) and he did not show any further symptoms. As it was ideal for the cure of his PMNSGCT to restart fourth cycle of BEP followed by surgery as soon as possible, we decided to restart chemotherapy after he and his family were adequately informed of the risks and benefits. The fourth cycle of BEP was restarted on day 26 of the third cycle, excluding bleomycin, which causes lung toxicity. Four cycles of BEP were completed without recurrence of COVID-19 (Figure 3a) and the evaluation after the fourth cycle of chemotherapy was partial response (PR) (Figure 3b–d). Complete resection of the residual mass was established on day 33 of the fourth cycle. The resected specimen had no viable tumor cells, and therefore additional chemotherapy was not needed (Figure 3e,f).

## DISCUSSION

We present the first case report of a PMNSGCT patient with COVID-19 in which the chemotherapy was successfully restarted without recurrence of the COVID-19. At present, there are no criteria on restarting chemotherapy after COVID-19, and there have only been a few case reports describing restart of chemotherapy in post-COVID-19 patients (Table 1).[10–12] Tang et al. reported that the decision on postponing or continuing anticancer treatment depends on the risk of disease progression in the patient with malignancy and COVID-19.[13] In our case, chemotherapy should have been restarted immediately because in the consensus report of the European Germ Cell Cancer Consensus Group (EGCCCG), BEP should be given at 22-day intervals for four cycles and postponing treatment should rarely be considered to improve the outcome of the patients of PMNSGCT with poor prognosis.[14] In the updated report of the World Health Organization (WHO),[15] the criteria for discharging patients from isolation without requirement of retesting PCR is

**TABLE 1** Comparison of our case with cases in previous reports

| | Age | Sex | PS | Tumor type | Cancer stage | COVID-19 main symptoms | Severity of COVID-19 | The duration of COVID-19 onset from the last chemotherapy (days) | The duration of chemotherapy restart from COVID-19 onset (days) | Therapies for COVID-19 | Regimen | RT-PCR before restarting chemotherapy | Recurrence of COVID-19 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Horiguchi, et al.[10] | 38 | F | Not available | Breast cancer | Stage IIB | Fever | Moderate | 21 | 45 | — | FEC | Negative | — |
| Nagai et al.[11] | 67 | M | Not available | Pancreatic cancer | Stage III | Fever | Moderate | 8 | 49 | Favipiravir, lopinavir and ritonavir | GEM + nabPAC | Negative | — |
| Liontos et al.[12] | 60 | F | Not available | Ovarian cancer | Stage IIIc | Fever, respiratory failure | Severe | 2 | 27 | Hydroxy chloroquine | Weekly PAC | Negative | — |
| Our case | 18 | M | 0 | PMNSGCTs | — | Fever, coughs | Mild | 26 | 16 | Casirivimab and imdevimab | BEP | — | — |

10 days after symptom onset, plus at least three additional days without symptoms. The patient met these criteria without any risk factors that could worsen his COVID-19, and his CT showed no findings, and therefore the severity of his COVID-19 was judged as mild illness.[16] We judged the risk of restarting chemotherapy was low and restarted it after adequate informed consent. Although it is difficult to establish definitive criteria as to when chemotherapy should be restarted in post-COVID-19 patients with malignant tumors, it may be safe to restart chemotherapy under the conditions that the patient has recovered from the COVID-19 and its severity was mild illness,[15] and patients have no additional risk factors, as in our case. We believe that this report is important for the establishment of criteria for restarting cancer chemotherapy during the COVID-19 pandemic. Further investigations are required to draw a more definite conclusion as to when chemotherapy can be restarted after COVID-19, according to patient characteristics such as type of malignant disease, age, complication, and type of chemotherapy.

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## CONFLICT OF INTEREST

The authors have no conflicts of interest to declare.

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