Case Report

Case of acute respiratory distress syndrome in a patient with an extragonadal germ cell tumor without lung metastasis in which choriocarcinoma syndrome was suspected

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Abbreviations & Acronyms
ARDS = acute respiratory distress syndrome
BEP = bleomycin etoposide cisplatin
CT = computed tomography
HCG = human chorionic gonadotropin
TIP = paclitaxel ifosfamide cisplatin

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Introduction: Choriocarcinoma syndrome is caused by bleeding from metastatic germ cell tumors with choriocarcinoma components. Here, we report a case of acute respiratory distress syndrome, which arose after first-line chemotherapy for an extragonadal germ cell tumor without lung metastasis.

Case presentation: A 41-year-old male visited our institution with chief complaints of back pain and weight loss. Computed tomography showed multiple lymph node metastases in the retroperitoneal cavity. There were no lung metastases. A lymph node biopsy resulted in a diagnosis of choriocarcinoma. Bleomycin etoposide cisplatin therapy was started as induction chemotherapy. On the first day, he was diagnosed with acute respiratory distress syndrome due to choriocarcinoma syndrome. We administered high-dose hydrocortisone therapy for 3 days. The patient's respiratory status improved.

Conclusion: In patients who are at high risk of developing choriocarcinoma syndrome, induction chemotherapy might lead to the development of acute respiratory distress syndrome due to the release of cytokines despite the absence of lung metastasis.

Key words: acute respiratory distress syndrome, choriocarcinoma, choriocarcinoma syndrome, extragonadal germ cell tumor, induction chemotherapy.

Keynote message

In patients who are at high risk of developing choriocarcinoma syndrome, the vital signs should be strictly monitored during first-line chemotherapy. If ARDS does occur, it should be treated as an emergency.

Introduction

Choriocarcinoma syndrome is a type of tumor lysis syndrome caused by bleeding from metastatic germ cell tumors with choriocarcinoma components. Typically, bleeding from lung metastases causes ARDS, which is often life-threatening. Here, we report a case of ARDS, which arose after first-line chemotherapy for an extragonadal germ cell tumor without lung metastasis. In this case, it was suspected that choriocarcinoma syndrome had been caused by cytokine release.

Case presentation

A 41-year-old male, with no relevant medical or family history, visited our institution with chief complaints of back pain and weight loss. At his first visit, no abnormal vital signs were noted. However, CT showed multiple lymph node metastases in the cervical region and retroperitoneal cavity (around the abdominal aorta to the common iliac artery bifurcation) (Fig. 1). There were no lung metastases, and no abnormal findings were seen in the testes. The patient's tumor marker levels were as follows: lactate dehydrogenase: 1096 IU/dL, HCG: 822 290 mIU/mL, and alpha-fetoprotein: 61.5 ng/mL. A percutaneous cervical lymph node

biopsy resulted in a diagnosis of choriocarcinoma. Therefore, the patient was diagnosed with a retroperitoneal primary extragonadal germ cell tumor (poor risk according to the International Germ Cell Consensus Classification).

BEP therapy (30 mg bleomycin on days 1, 8, and 15, 100 mg/m^2 etoposide on days 1–5, and 20 mg/m^2 cisplatin on days 1–5) was started as induction chemotherapy. On the first day, the administration of cisplatin and etoposide was completed without any problems. During the administration of bleomycin, it is about 10 h after cisplatin administration and about 7 h after etoposide administration, the patient's oxygen saturation level decreased to 88%, and so we started administering oxygen. There were no accompanying symptoms, such as dyspnea or fever, or significant changes in the patient's laboratory data. Contrast-enhanced CT showed ground glass opacity and an enhanced pulmonary vascular shadow, and small amounts of pleural effusion in both lungs (Fig. 2). The patient was diagnosed with ARDS due to bleomycin toxicity or choriocarcinoma syndrome caused by elevated inflammatory cytokine levels. We administered high-dose hydrocortisone therapy for 3 days. The patient's respiratory status gradually improved, and on day 5 the administration of oxygen was stopped. On day 7, the BEP therapy was restarted, and four courses were administered. The patient's HCG level did not normalize, so we administered four courses of TIP therapy (210 mg/m^2 paclitaxel on day 1, 1.2 g/m^2 ifosfamide on days 2–6, and 20 mg/m^2 cisplatin on days 2–6) as additional chemotherapy. After confirming that the patient was negative for tumor markers, we performed retroperitoneal lymph node dissection. No viable cancer cells were detected, and the patient is currently under surveillance and free from recurrence.

Discussion

It has been reported that choriocarcinoma syndrome should be suspected in patients who exhibit high HCG levels, large tumors, and multiple metastases in the early stages of chemotherapy.[1] ARDS due to bleeding from lung metastases has been well characterized,[2,3] and there have also been reports about bleeding from liver[4] and brain metastases.[5]

In the current case, ARDS occurred immediately after the initiation of induction chemotherapy in a case of choriocarcinoma involving a large retroperitoneal lymph node, but not lung metastasis. As for the possible differential diagnoses, we considered a pulmonary embolism, a drug-induced lung injury, and choriocarcinoma syndrome due to cytokine release. A pulmonary embolism was ruled out by contrast-enhanced CT. Bleomycin is well known to cause pulmonary toxicities, but they are reported to arise as subacute dose-dependent conditions.[6] In the present case, the onset of the patient's condition occurred just after the start of bleomycin treatment, and no lung injuries occurred after bleomycin treatment was restarted, and so a drug-induced lung injury was ruled out.

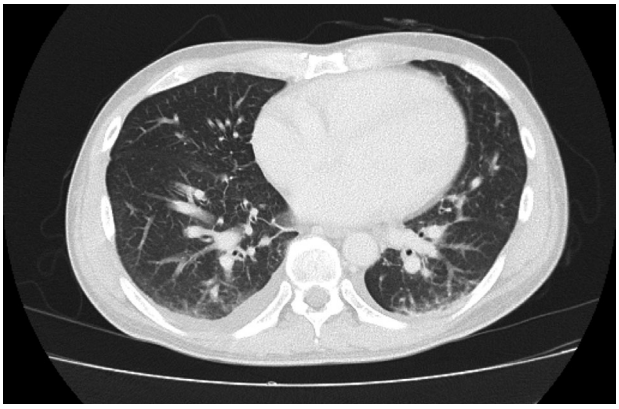

Fig. 2 Contrast-enhanced CT showed ground glass opacity and an enhanced pulmonary vascular shadow, and small amounts of pleural effusion in both lungs.

As mentioned above, choriocarcinoma syndrome is caused by bleeding from a metastatic lesion, but there have not been any reports about ARDS occurring in patients without lung metastasis, as was seen in our case. Oshima *et al*. reported a case of ARDS that occurred due to the release of cytokines, which in turn was caused by the lysis of a lung metastasis without obvious bleeding.[7] In addition, Takahashi *et al*. reported that they resected lung lesions with choriocarcinoma components, and ARDS occurred 1 month after the resection procedure despite the removal of the primary lesion.[8] These cases suggest that choriocarcinoma syndrome is not simply caused by bleeding from metastatic lesions, but rather might be caused by cytokine release associated with tumor lysis. We propose that there may be a different mechanism than previously thought. But we did not measure serum level of cytokines, it is the limitation of this report. Kirch *et al*. investigated 16 cases of non-seminoma with diffuse lung metastasis, in which the patients were admitted to intensive care units. They reported that the patients' tumor marker levels peaked within 2 days after the initiation of induction chemotherapy. Furthermore, a large amount of cytokines was released due to the massive cell death caused by the chemotherapy, and on average choriocarcinoma syndrome developed within 2.5 days.[9]

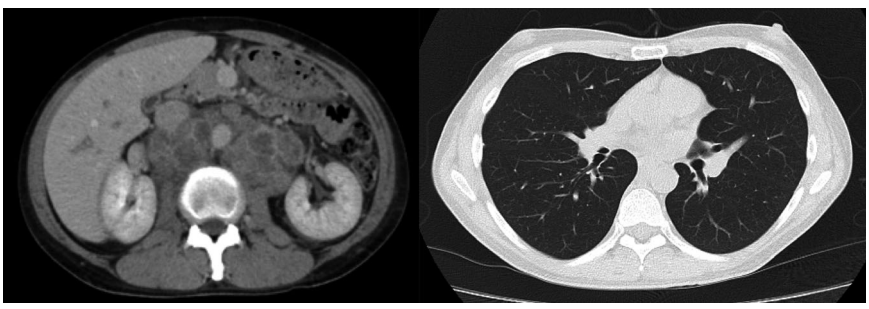

Fig. 1 Contrast-enhanced CT showed multiple lymph node metastases in the cervical region and retroperitoneal cavity (around the abdominal aorta to the common iliac artery bifurcation). There were no lung metastases.

Although this case did not involve lung metastasis, cytokine release derived from the retroperitoneal lymph node will have had an influence on remote organs. Such cytokine release can enhance the permeability of pulmonary blood vessels, which is considered to be one of the pathologies of choriocarcinoma syndrome. Although there are no established treatments for choriocarcinoma syndrome, the modified BEP regimen is one of the treatment options for patients who are thought to be at high risk of choriocarcinoma syndrome. The modified BEP regimen for non-seminomas with multiple lung metastases involves treatment with cisplatin and etoposide for 3 days followed by the administration of bleomycin on day 10. Massard *et al*. reported that compared with the normal BEP regimen, the modified BEP regimen exhibited similar efficacy, but resulted in a significantly lower incidence of ARDS.[10] Although there was a risk of ARDS, we continued BEP after ARDS. It was because the large amount of tumor and the height of the tumor marker suggested that this case is likely to require second line chemotherapy, so we should complete the first line as much as possible. We suggest that steroid pulse therapy might be effective in such cases when combined with supportive therapy, such as the administration of oxygen and/or blood transfusions. In this case, we chose to restart BEP therapy after the patient's respiratory status improved.

In patients who are at high risk of developing choriocarcinoma syndrome, induction chemotherapy might lead to the development of ARDS due to the release of cytokines despite the absence of lung metastasis. Therefore, the vital signs of such patients should be strictly monitored during first-line chemotherapy. If ARDS does occur, it should be treated as an emergency.

Conflict of interest

The authors declare no conflict of interest.

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