Case Report

Pembrolizumab for treatment of a male with primary mediastinal choriocarcinoma: a case report

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Background: Primary mediastinal choriocarcinoma is an extremely rare malignant tumor, that is prone to early metastasis and often misdiagnosed. Currently, there is no standardized treatment for primary mediastinal choriocarcinoma. Herein, we report a case to share our experience in the diagnosis and treatment of primary mediastinal choriocarcinoma.

Case Description: A 19-year-old male patient who presented with chest pain and occasional cough for 1 month. He was diagnosed as mediastinal tumor with multiple lung metastases by imaging modalities in a local hospital, and therapeutic surgical excision was performed for the metastasis lesions in lower lobe of right lung. The pathological examination of the surgical specimens supported lung metastasis of choriocarcinoma. Then he was transferred to our hospital for further treatment. Elevated β-human chorionic gonadotropin (β-hCG) serum levels (>200,000 mIU/mL, normal <5 mIU/mL) combined with imaging modalities and pathological consultation of the surgical specimens at admission in our hospital supported the diagnosis of primary mediastinal choriocarcinoma with multiple metastases. During the treatment, we used a variety of treatments, including chemotherapy, radiotherapy and Pembrolizumab. After one cycle of EP chemotherapy (etoposide and cisplatin), computed tomography (CT) scan showed that new nodules appeared in the liver, mass in the anterior mediastinum and part of the nodules in the lungs were enlarged. Pembrolizumab was initiated because of the tumor cells were positive for programmed cell death 1 ligand 1 (PD-L1). The mediastinal mass shrank after two cycles of Pembrolizumab. However, due to the rapid progress of the disease, the patient died of the disease 4 months after the initial symptoms.

Conclusions: Advanced primary mediastinal choriocarcinoma is highly aggressive and insensitive to chemotherapy. Pembrolizumab may be used as a salvage treatment for primary mediastinal choriocarcinoma.

Keywords: Primary mediastinal choriocarcinoma; Pembrolizumab; programmed cell death 1 ligand 1 (PD-L1); case report

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Introduction

Primary choriocarcinoma (PCC) is a rare malignant tumor, mainly occurs in the gonads. The extragonads are distributed along the midline of the body, such as the pineal gland, mediastinum, lung, liver, etc. (1). Primary mediastinal choriocarcinoma is extremely rare (2), and is often misdiagnosed or delayed in treatment. Currently, there is no standardized treatment for primary mediastinal choriocarcinoma. EMA/CO regimen (etoposide, methotrexate, actinomycin D, cyclophosphamide and vincristine), which is widely used in gestational trophoblastic neoplasia (GTN), is usually given to primary mediastinal choriocarcinoma patients. However, due to drug resistance and heavy tumor burden, the prognosis is poor (3).

Programmed cell death 1 ligand 1 (PD-L1) is ubiquitously expressed in choriocarcinoma tumors (4), indicating programmed cell death 1 (PD-1) inhibitor,

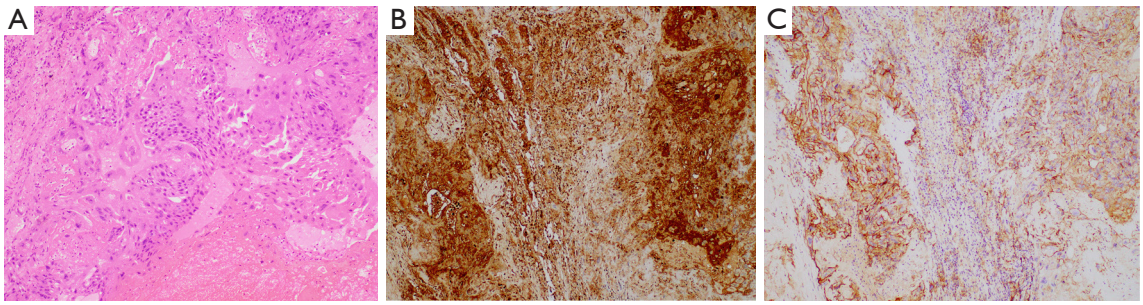

Figure 1 The surgical specimen of lung. (A) Histologic examination reveals that the tumor consists of two types of trophoblastic cells, the cytotrophoblastic cells grow in clusters, separated by syncytiotrophoblastic cells (hematoxylin and eosin stain, magnification, ×100). (B,C) Tumor cells are positive for β-hCG (B) and PD-L1 (C) (immunohistochemical staining, magnification, ×100). β-hCG, β-human chorionic gonadotropin; PD-L1, programmed cell death 1 ligand 1.

such as Pembrolizumab, might be a salvage treatment for chemotherapy-resistant male PCC patients (5). We present the following case in accordance with the CARE reporting checklist (available at https://tcr.amegroups.com/article/view/10.21037/tcr-22-766/rc).

Case presentation

A 19-year-old man referred to our hospital with mediastinal malignant tumor for 1-month duration. In his past medical history, 1 month ago, he presented to a local hospital with chest pain and occasional cough for 1-month, computed tomography (CT) scan of the thorax showed an 8.8 cm × 6.3 cm mass in the anterior mediastinum and diffuse rounded nodules in bilateral lung. There was no trauma or disease history. The preliminary diagnosis was a mediastinal tumor with multiple lung metastases. Diagnostic and therapeutic surgical excision was performed for the metastasis lesions in lower lobe of right lung by thoracoscopic surgery. Following surgery, pathological examination showed a malignant tumor with massive necrosis. There were diffusely distributed atypical cells around the necrosis, with abundant cytoplasm and large nuclei (*Figure 1A*). The immunohistochemical (IHC) staining showed that the tumor cells were positive for β-human chorionic gonadotropin (β-hCG), pan-cytokeratin, but negative for octamer-binding transcription factor 4, vimentin, cluster of differentiation (CD) 30, α-fetoprotein, CD 117, epithelial membrane antigen, human placental lactogen, placental alkaline phosphatase (*Figure 1B*). Histological examination and IHC staining of the surgical specimens supported lung metastasis of choriocarcinoma.

Based on these findings and the absence of clinical or sonographic findings of testicular involvement, a diagnosis of primary mediastinal choriocarcinoma with diffuse lung metastases was made. The patient was immediately referred to our hospital. Test findings at admission in our hospital showed the patient had elevated serum β-hCG level (>200,000 mIU/mL, normal <5 mIU/mL). Brain magnetic resonance imaging (MRI) demonstrated multiple nodules and masses in the left cerebellar hemisphere and bilateral brain parenchyma. The pathological consultation of the surgical specimen confirmed the diagnosis of metastatic choriocarcinoma. Further IHC staining showed that the tumor cells were positive for PD-L1 (*Figure 1C*).

The patient began to receive an induction regimen of EP (etoposide and cisplatin). Head radiotherapy was performed on the patient's intracranial tumor lesions. After one cycle, CT scan showed that new nodules appeared in the liver, mass in the anterior mediastinum and part of the nodules in the lungs were enlarged (*Figure 2A-2C*). Pembrolizumab was initiated because of the tumor cells were positive for PD-L1, and two cycles were performed (100 mg fixed dose, every 3 weeks). During this period, ^{18}F-fluorodeoxyglucose (FDG) positron emission tomography (PET)/CT scan and PET/MRI scan revealed disease progression with new multiple lesions in lung, liver, spleen, kidney, brain, and skeletal (*Figure 2D-2F*). Two cycles of Pembrolizumab later, the patient's serum β-hCG level was dramatically dropped from >200,000 to 12,611 mIU/mL, and then it rose again. CT scan showed that the mediastinal mass shrank, and the lung lesions partly shrank and partly enlarged (*Figure 2G-2I*). Because the patient's condition deteriorated rapidly, the treatment was adjusted, and he was given Pembrolizumab (200 mg fixed dose) and paclitaxel for one cycle and EMA/CO regimen for another cycle. After chemotherapy, the

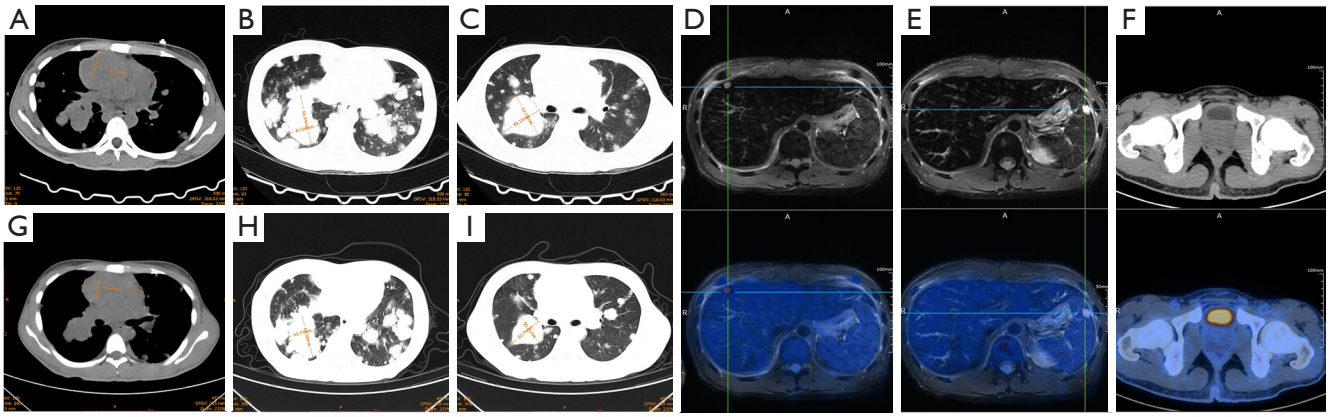

Figure 2 CT, PET/MRI and PET/CT scans evaluate the progression of disease. (A-C) CT scan of the thorax reveals an enlarged anterior mediastinal mass and multiple metastatic lung nodules after the one cycle of chemotherapy. (D,E) PET/MRI imaging demonstrates metastatic lesions in the liver and spleen. (F) PET/CT imaging showed no abnormal FDG accumulation in bladder and gonads. (G-I) Both mediastinal and pulmonary lesions are partially reduced after two cycles of pembrolizumab. CT, computed tomography; PET, positron emission tomography; FDG, ^{18}F-fluorodeoxyglucose; MRI, magnetic resonance imaging; A, anterior; R, right; L, left; DFOV, display field of view.

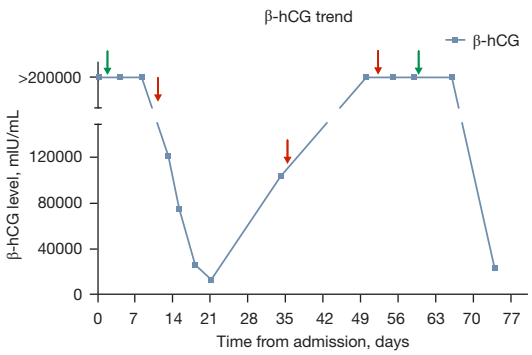

Figure 3 β-hCG trend from the admission to hospital through final testing, with red arrows indicating treatment with Pembrolizumab and green arrows indicating chemotherapy. During the last two cycles of treatment, the patient did not detect β-hCG level. β-hCG, β-human chorionic gonadotropin.

patient experienced neutropenia and was given leukocyte-raising treatment, and serum β-hCG level of the last detection decreased dramatically to 22,653 mIU/mL. All β-hCG test results were shown in *Figure 3*. The patient continued to receive the previous treatment with one cycle of Pembrolizumab (200 mg fixed dose) and one cycle of EMA/CO regimen. On the second day after chemotherapy, he developed symptoms of a headache, speech disorder, and urinary incontinence. Emergency head CT scan showed intracranial hemorrhage and brain herniation, his guardian gave up surgery and invasive rescue, he deceased with an overall survival of 4 months.

All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee(s) and with the Helsinki Declaration (as revised in 2013). Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the editorial office of this journal.

Discussion

PCC is a rare trophoblastic tumor that can occur in both sexes. PCC of the mediastinum is even rarer, with less than 50 cases reported since it was first reported in 1931 until 2022 (3,6-10). The clinical symptoms are atypical, including chest pain, cough, hemoptysis, short of breath, and weakness. Laboratory testing often shows a high level of β-hCG, which could be a vital diagnosis and prognosis marker. For primary mediastinal choriocarcinoma, although some patients can get partial remission by multiple chemotherapy regimens and radiotherapy, rapid drug resistance and rapid progression of disease usually lead to extremely poor prognosis. A majority of patients succumb within a short period of time, with overall survival ranging from 20 days to 115 months (9).

PD-1 inhibitor might be an attractive alternative treatment. According to recent National Comprehensive

Cancer Network guidelines, PD-1/PD-L1 inhibitors have been recommended to play a role in the treatment of drug-resistant GTN, and Pembrolizumab has been found effective against drug-resistant GTN (11). Female patients with chemotherapy-resistant choriocarcinoma achieved effective remission following Pembrolizumab treatment (12). Han et al. reported that one male with primary neck choriocarcinoma achieved remission after Pembrolizumab combined with chemotherapy (10). In our case, chemotherapy and radiotherapy were not effective on the patient. He got partial remission after two cycles of Pembrolizumab, but also developed resistance immediately. After attempting treatment with Pembrolizumab in combination with chemotherapy, the patient's serum β-hCG decreased, but treatment failed due to rapid disease progression.

Therapeutic options for patients with PCC remain limited, with the role of immunotherapy not fully clarified. This case suggested that PCC patients can get partial remission by treated with Pembrolizumab, Pembrolizumab in combination with chemotherapy may be a promising treatment option, but clinical studies are still needed to determine the optimal population and treatment for Pembrolizumab treatment.

In conclusion, primary mediastinal choriocarcinoma is an extremely rare and aggressive malignancy. When patients with masses in the mediastinum have elevated β-hCG levels, choriocarcinoma should be considered as a differential diagnosis. Pembrolizumab could serve as an important novel approach for the management of primary mediastinal choriocarcinoma with high expression of PD-L1.

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Footnote

Reporting Checklist: The authors have completed the CARE reporting checklist. Available at https://tcr.amegroups.com/article/view/10.21037/tcr-22-766/rc

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://tcr.amegroups.com/article/view/10.21037/tcr-22-766/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee(s) and with the Helsinki Declaration (as revised in 2013). Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the editorial office of this journal.

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