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Docetaxel chemotherapy temporarily improved pulmonary tumor thrombotic microangiopathy induced by prostate cancer secreting carcinoembryonic antigen and carbohydrate antigen 19-9: A case report

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ABSTRACT

Pulmonary tumor thrombotic microangiopathy (PTTM) is a rare, rapidly progressive, and often fatal complication of cancer, particularly prostate cancer. A 67-year-old man with advanced prostate cancer developed dyspnea. Chest computed tomography revealed ground-glass opacities across bilateral lung fields, and echocardiography showed right heart failure. As PTTM was suspected, docetaxel chemotherapy was administered immediately. His respiratory condition and right heart failure improved; however, 2-months later his respiratory symptoms were exacerbated, causing death. Autopsy showed fibrocellular intimal proliferation of the small pulmonary arteries, which confirmed PTTM induced by prostate cancer. Although PTTM is fatal, early diagnosis and treatment would improve the prognosis.

Introduction

Pulmonary tumor thrombotic microangiopathy (PTTM) is a rare complication of malignancy. Gastric cancer is the most common cause of PTTM, with a few cases induced by prostate cancers also reported; however, effective treatment is not clear. PTTM is reported to have a high mortality rate; therefore, early antemortem diagnosis and treatment are extremely difficult but important. We report a case of PTTM caused by advanced prostate cancer, where immediate docetaxel chemotherapy temporarily improved the patient's respiratory condition and prognosis.

Case presentation

A 67-year-old man with no medical history consulted a local doctor for constipation. High-resolution computed tomography (HRCT) revealed metastatic bone tumors. His serum prostate-specific antigen (PSA) level was elevated to 96.9 ng/ml. Carcinoembryonic antigen (CEA: 458.0 ng/ml) and carbohydrate antigen 19-9 (CA19-9: 227 U/ml) were also elevated. MRI/HRCT and FDG PET-CT findings indicated prostate cancer (cT3N1M1, stageD2). Colon fiberscopy (CF) and gastrointestinal fiberscopy (GIF) were performed; however, neither detected digestive cancers. Prostate biopsy was performed immediately, and the pathological diagnosis was adenocarcinoma (Gleason score 4 + 5). In the prostate biopsy sample, PSA and CEA immunostaining were positive, but CA19-9 was negative. Prostate cancer was suspected as there was no evidence of any other digestive cancer secreting not only PSA but also CEA and CA19-9. He was treated with androgen-deprivation therapy, and PSA decreased immediately, while CEA and CA19-9 remained elevated. He presented with 2 weeks of progressive dyspnea without any associated symptoms. Oxygen saturation was 80% (room air), and D-dimer levels were elevated. Contrast-enhanced CT was performed to rule out a pulmonary embolism. Chest radiography demonstrated ground-glass opacities (GGOs) on bilateral lungs fields, but there was no evidence of pulmonary emboli (Fig. 1). *Trans*-thoracic echocardiography (TTE) showed that tricuspid regurgitation pressure gradient (TRPG) was 57 mmHg (normal, <30 mmHg), suggesting pulmonary hypertension. PTTM was strongly suspected; therefore, chemotherapy with docetaxel (75 mg/m^2) was administered immediately. His respiratory condition improved, and TRPG decreased. Chemotherapy was administered three times, during which time, his respiratory condition was stable. However, it worsened during the 4th chemotherapy. TTE revealed that TRPG was 50 mmHg; although pulmonary hypertension worsened, there was no evidence of pulmonary embolism on contrast enhanced CT. Because he was suspected to have a re-exacerbation of PTTM, chemotherapy was continuously

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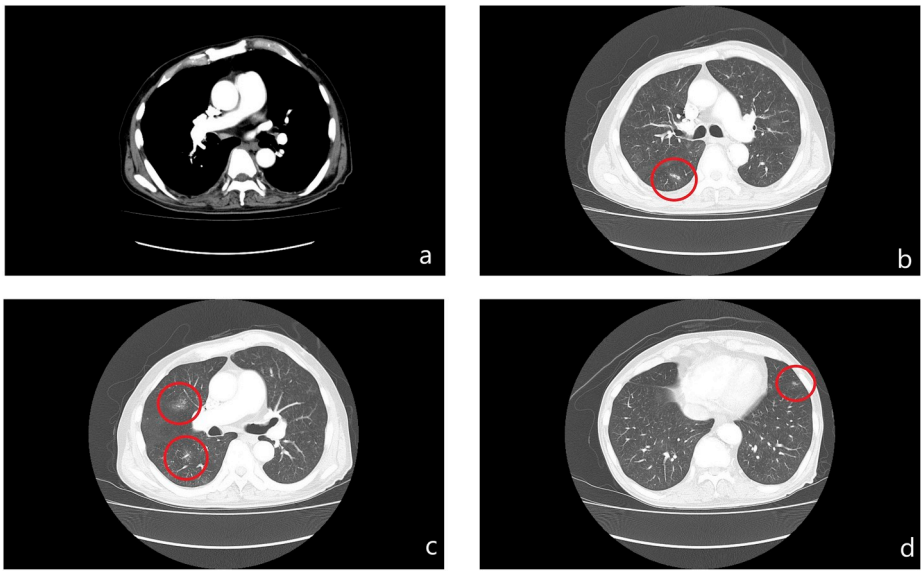

Fig. 1. (a) Contrast-enhanced computed tomography (CT) shows no arterial defects. (b–d) CT in the lung window setting shows diffuse ground-glass opacities (GGOs).

administered, but his general condition gradually worsened. His respiratory status rapidly deteriorated on Day 85, and he died of the primary disease on the 86th day.

Autopsy revealed a Gleason score of 4 + 5 of prostate cancer with intraductal carcinoma of the prostate invading the seminal vesicle and bladder. Prostate cancer immunostaining showed that PSA was diffusely positive, and CEA and CA19-9 were partially positive. Metastases were detected in the bones, liver, and lymph node, and these immunostaining profiles were of primary prostate cancer (Fig. 2). Lungs showed bilateral congestive edema and hemorrhage; however, there were no tumor lesions on the macroscopic cut surface of the lungs. Histological examination of the lungs revealed tumor emboli, fibrocellular intimal proliferation, stenosis, and recanalization of the lung arterioles (Fig. 3). Immunostaining of the lung arterial tumor emboli showed that CEA was diffusely positive, and PSA was partially positive, but CA19-9 was negative. These differences seen in immunostaining profiles between primary prostate cancer and lung arterial tumor emboli suggest that components of prostate cancer strongly secreted CEA, which induced PTTM. A definitive diagnosis of PTTM derived from prostate cancer was made based on the autopsy findings.

Discussion

Our case suggested that docetaxel chemotherapy is effective for treatment of PTTM induced by prostate cancer, especially that which secretes not only PSA but also CEA and CA119-9.

PTTM is observed in 1.4%–3.3% of consecutive autopsy cases of carcinoma.[1,2] The most common cause of PTTM is poorly differentiated gastric cancer. A few cases of PTTM caused by prostate cancer have been reported. PTTM, which is characterized by microscopic tumor embolization and fibrocellular intimal proliferation of the small pulmonary arterioles, has a poor prognosis. The mean time from the onset of dyspnea to death is reported to be only 3–4 weeks.[1]

Antemortem diagnosis of PTTM is difficult and, to date, the condition has been detected at autopsy. However, recent studies have reported the possibility of antemortem diagnosis with the help of pulmonary microvascular cytology on samples drawn through a wedged pulmonary artery catheter, with a reported sensitivity of 80%–88% and specificity of 82%–94%.[3] Godbole et al. reported that common findings on chest CT included GGOs and nodules.[4]

In our case, GGOs in bilateral lung fields on the chest HRCT and right heart failure shown by TTE strongly suggested PTTM; therefore, our clinical diagnosis was PTTM. Following chemotherapy with docetaxel, we performed pulmonary microvascular cytology on samples drawn through a wedged pulmonary artery catheter, but it did not show evidence of PTTM. However, results suggested that chemotherapy helped in the removal of malignant cells from the pulmonary circulation.

Although some reports have shown improvement in survival by the use of Imatinib (PDGF receptor inhibitor),[5] it has not been successful as a treatment modality for PTTM, and further studies are needed to assess the optimal therapeutic strategy. Our case was successfully treated with docetaxel chemotherapy. Docetaxel chemotherapy may remove malignant cells from the pulmonary circulation and thus, reduce the stimulus for thrombus formation and fibrointimal proliferation.

Conclusion

Prognosis of PTTM is extremely poor, but our case suggests that early chemotherapy for the primary cancer may improve survival. Large scale studies are needed to assess the optimal therapeutic strategy.

Consent

Written informed consent was obtained from the subject for publication of this case report and accompanying images.

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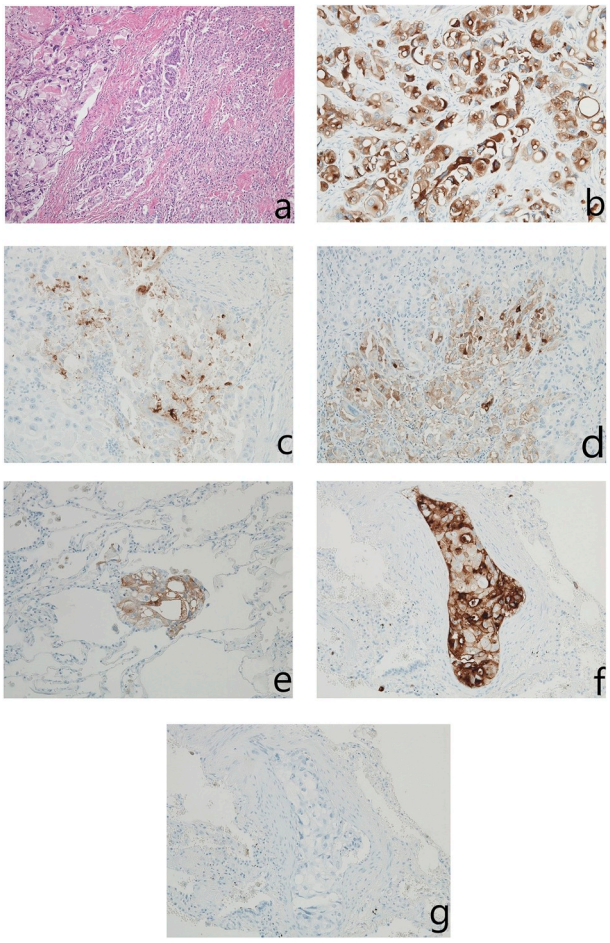

Fig. 2. (a) Hematoxylin and eosin (H&E × 100) staining of the prostate shows adenocarcinoma (Gleason score 4 + 5). (b) Prostate-specific antigen (PSA × 400) immunostaining of prostate is diffusely positive. (c) Carcinoembryonic antigen (CEA × 400) immunostaining of prostate is partially positive. (d) Carbohydrate antigen 19-9 (CA19-9 × 400) immunostaining of prostate is partially positive. (e) PSA immunostaining of lung is partially positive (× 400). (f) CEA immunostaining of lung is diffusely positive (× 400). (g) CA 19-9 immunostaining of prostate is negative (× 400).

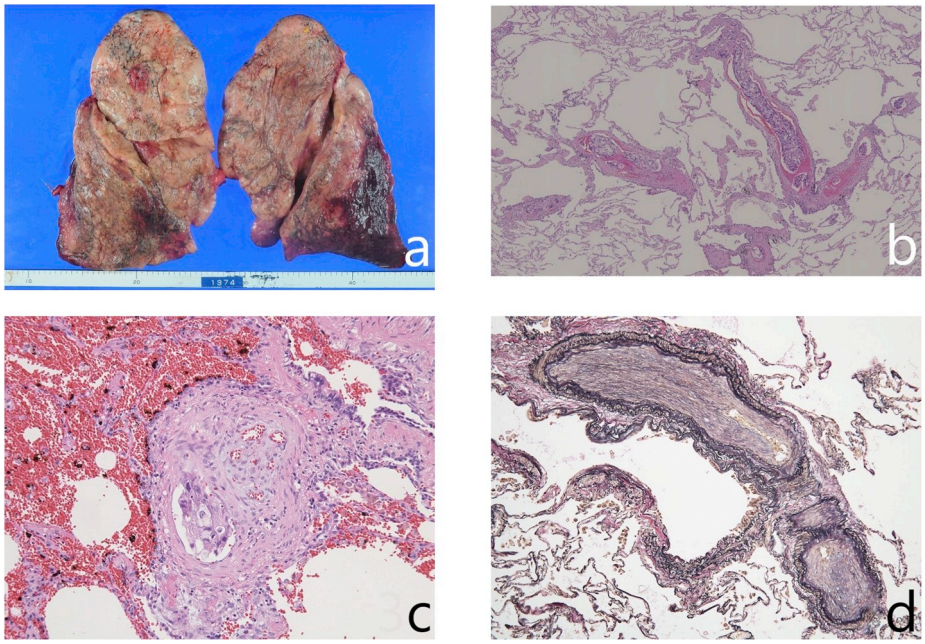

Fig. 3. (a) Hemorrhage in the lung seen in macroscopic view. (b–c) Hematoxylin and eosin (H&E × 100) staining of the lung shows embolization of small pulmonary arteries by adenocarcinoma cells with fibrocellular intimal proliferation and recanalization. (d) Elastic van Gieson staining (EVG × 400) shows fibrous thickening and fibrocellular intimal proliferation of endothelial cells on the internal elastic membrane.

agencies in the public, commercial, or not-for-profit sectors.

Declaration of competing interest

None.

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