MICROSCOPIC PULMONARY TUMOR EMBOLISM SECONDARY TO ADENOCARCINOMA OF THE PROSTATE

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We report a case of pulmonary tumor embolism involving multiple emboli from an unusual site, an adenocarcinoma of the prostate. A 78-year-old Japanese man was diagnosed with stage IV (1997 version of the TNM classification) moderately differentiated adenocarcinoma of the prostate in December 1997. He underwent bilateral orchiectomy and hormonal therapy with flutamide was started. The patient suffered from relapse in April 1998, and estramustine phosphate was administered as treatment for hormone-refractory prostate cancer. He noticed a dry cough in May 1998, and on June 13, he developed acute progressive dyspnea and was admitted to our hospital. Radiological findings, blood gas analysis, and clinical symptoms suggested pulmonary thrombosis. Despite anticoagulation and oxygen therapy, he remained severely dyspnoeic. He died of respiratory failure 4 days after admission. Autopsy confirmed dissemination of poorly differentiated adenocarcinoma of the prostate to the majority of the pulmonary muscular arteries.

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Key words : Pulmonary tumor embolism, Dyspnea, Prostate cancer

INTRODUCTION

Pulmonary tumor emboli in patients with cancer are occasionally found at autopsy without antemortem detection[1–3]. Emboli from an adenocarcinoma of the prostate are extremely rare. We report a case of respiratory insufficiency caused by such an etiology. Four similar cases are reviewed.

CASE REPORT

A 78-year-old Japanese man was diagnosed stage IV prostate cancer (T3aN0M1b, 1997 version of the TNM classification) in December 1997. He underwent bilateral orchiectomy and was administered flutamide. The disease was well controlled and serum prostate-specific antigen (PSA) level remained low. Relapse was suggested in April 1998 by re-elevated serum PSA level, increased uptake on bone scintigraphy and his complaint of lumbar pain. A daily dose of 560 mg of estramustine phosphate was administered as a treatment for relapsed hormone-refractory prostate cancer. One month later, he began noticing a dry cough, and on June 10, 1998, he developed acute progressive dyspnea and was admitted to the hospital on June 13, 1998. A physical examination revealed central cyanosis, although lung sounds and heart sounds were clear. An electrocardiogram showed inverted T waves in leads V1 trough V4. Chest radiography showed slight cardiomegaly (cardiothoracic ratio : 54%), but his lung fields were clear. Blood gas analysis revealed an arterial oxygen pressure of 43.4 torr, carbon dioxide of 24.2 torr, and pH 7.525 on room air. A pulmonary perfusion scan revealed multiple subsegmental defects (Fig. 1). Computed tomography of the thorax revealed slightly enlarged pulmonary vessels with no parenchymal lesions. The patient was diagnosed with pulmonary thrombosis. Treatment with oxygen inhalation, intravenous instillation of heparin, and urokinase was ineffective. The patient died of respiratory failure 4 days after admission. An autopsy confirmed the dissemination and formation of micro-metastases of poorly differentiated adenocarcinoma of the prostate in many pulmonary muscular arteries, intrahepatic portal veins, bones, and the liver, but no solid tumor

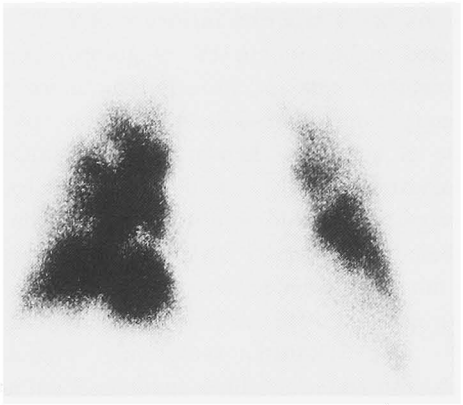

Fig. 1. Pulmonary perfusion scan (anterior). Multiple subsegmental defects are visible in both lungs.

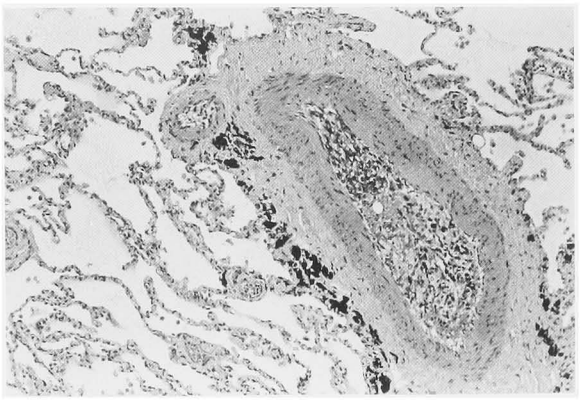

Fig. 2. Microscopic appearance (Hematoxylin and eosin stain). Micrometastatic nests of adenocarcinoma of the prostate are seen in most pulmonary muscular arteries (original magnification ×100).

masses were found in the lungs (Fig. 2). The cause of death, confirmed by autopsy, was massive pulmonary tumor embolism. Poorly differentiated adenocarcinoma of pathological local stage was pT3a in the prostate and there was no metastasis in the obturator and para-aortic lymph nodes.

DISCUSSION

Pulmonary tumor embolism associated with carcinoma has a reported incidence of 2.4% and is considered to be fatal in 1% of autopsy studies[4] The reported rate of antemortem detection of pulmonary tumor embolism is very low, probably because of a lack of known specific clinical and radiological features[1-3] Patients with widespread microscopic tumor emboli of the lung develop acute or subacute progressive dyspnea. Other clinical symptoms have been reported: cough (8 to 47%), pleuritic chest pain (18 to 28%), and hemoptysis (5 to 18%)[2] The clinical symptoms, radiological findings, and laboratory investigations of pulmonary tumor embolism resemble those of pulmonary thromboembolism[1-3] In patients with cancer and progressive dyspnea, the main differential diagnoses are thromboemboli, lymphangitis carcinomatosis, pulmonary metastasis, and cardiac failure. Chan et al. reviewed 164 cases of pulmonary tumor embolism associated with malignancies[6], including 7 (4%) prostate cancer patients. Although prostate cancer occasionally metastasizes to the lung, pulmonary tumor embolism in patients with disseminated prostate cancer is rarely recognized to be fatal, possibly because some cases are misdiagnosed as pulmonary thromboembolism[8]

We reviewed 5 well documented cases in patients who died of pulmonary tumor embolism secondary to prostate cancer (Table 1)[4,7,8] The average age was 71 years, clinical stage was IV (M1a–M1c), and common clinical symptoms were progressive dyspnea and chest pain. The other main metastatic sites were liver and bone. The duration of dyspnea prior to death ranged from 2 days to 4 weeks. In these 5 patients, the antemortem diagnosis was incorrect (pulmonary thrombosis, heart failure, and respiratory distress)[4,7,8] None of these patients were suspected of having pulmonary tumor emboli before death. Although these types of patients are in a very critical condition, it is still important to distinguish pulmonary thrombosis from tumor embolism because subsequent treatment differs for these two conditions. Anticoagulant therapy is helpful for improving the prognosis of pulmonary thrombosis. The treatment for pulmonary tumor embolism is more difficult because of lack of sufficient information available for treatment and diagnosis. The effectiveness of treatment for pulmonary tumor emboli has been reported to be similar to that of treatment for primary lesions, i.e., chemotherapy for choriocarcinoma and breast cancer[2]

Estramustinephosphate acts as an antimitotic agent and causes disruption of microtubule organization. Adverse effects has been reported to be nausea, breast tenderness, gynecomastia, diarrhea and thrombosis[5] However, as there have been no reports on pulmonary tumor emboli related to estramustinephosphate, the relationship between pulmonary tumor embolism and estramustinephosphate is unknown in this case and further research is needed.

When patients with advanced prostate cancer complain of acute or subacute onset of progressive

Table 1. Clinical features of five patients with pulmonary tumor embolism secondary to adenocarcinoma of the prostate

Reference	Age (years)	Metastatic involvement		Duration of dyspnea prior to death	Chest radiograph	ECG	Clinical diagnosis of cause of dyspnea	Treatment for respiratory symptoms
		Liver	Bone					
Kane, 1975[4]	59	+	+	3–4 weeks	Normal	LAD	Unknown	Unknown
Kane, 1975[4]	81	+	+	4 days	Normal	LAD	Unknown	Unknown
Miedema, 1981[7]	71	−	+	2 days	Normal	RBBB	Unknown	Optimal therapy
Keeping, 1982[8]	66	−	+	2–3 weeks	Normal	Normal	Thrombosis	Anticoagulant
Current case	78	+	+	8 days	Cardiomegaly Normal lung field	Inverted T	Thrombosis	Anticoagulant

ECG, electrocardiogram ; LAD left axial deviation ; RBBB, right bundle branch block ; RVH, right ventricular hypertrophy.

dyspnea, physicians must consider pulmonary tumor embolism as a possible diagnosis and differentiate between it and pulmonary thromboembolism[3]. The correct diagnosis of pulmonary tumor embolism will improve the prognosis of these patients and avoid unnecessary anticoagulant therapy[1,2] Although hormone therapy may not be effective for pulmonary tumor emboli from hormone-refractory prostate cancer as in our patient, early diagnosis and treatment of pulmonary tumor emboli from prostate adenocarcinoma with chemotherapy or hormone (estrogen) therapy may improve the chance of a better prognosis.

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和文抄録

前立腺癌患者に発生した肺腫瘍塞栓の1例

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症例は78歳の男性．1997年12月に骨転移を有する中分化型前立腺癌 stage IV（T3bN0M1b，1997年版TNM分類）と診断し，両側精巣摘除術と flutamide による治療を行っていた．1998年4月より一時測定感度以下に下がっていた PSA が再上昇しはじめ，骨シンチグラフィーにて骨転移巣の増大も認めたため，ホルモン抵抗性再燃前立腺癌と診断し，estramustine phosphate の投与を開始した．1998年5月に乾性咳嗽を自覚．同年6月10日より急速に進行する呼吸困難が出現し，6月13日に入院した．理学的所見では全身倦怠感とチアノーゼを認めた．胸部 CT 検査，肺血流シンチ，血液ガス検査，胸部レントゲン検査，心臓超音波検査，心電図，臨床経過などより肺動脈血栓症が疑われた．酸素投与と抗凝固療法を行ったが呼吸困難は改善せず，入院後4日目に死亡した．病理解剖所見では，低分化型前立腺癌が多数の肺筋性動脈，肝静脈，肝内門脈内に播種しており，前立腺癌由来の肺腫瘍塞栓による呼吸不全が死亡原因と診断した．詳細な臨床経過が記載されていた5例（本症例を含む）の肺腫瘍塞栓合併前立腺癌の報告例について検討した．

肺動脈血栓症と肺腫瘍塞栓症はともに致死率が高く，鑑別困難な疾患であるが，肺腫瘍塞栓例の中には化学療法によって症状が改善したとの報告もあり，正しい診断が出来れば予後を改善させる可能性もあると思われた．

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