A case of pulmonary artery intimal sarcoma successfully treated using concurrent chemoradiotherapy and subsequent chemotherapy

Terumi Aso¹ · Masako Terao¹ · Hisashi Endo¹ · Masahiro Tabata²

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Abstract

Pulmonary artery intimal sarcoma (PAIS) is a rare malignancy with an extremely poor prognosis. A 43-year-old man visited our hospital with shortness of breath and suddenly experienced cardiopulmonary arrest before he could be examined. After prompt resuscitation, we diagnosed PAIS, but the patient refused to undergo surgery because of the high perioperative mortality risk. Thus, the patient was treated using concurrent chemoradiotherapy with weekly paclitaxel therapy, as well as subsequent chemotherapy. The patient continued chemotherapy for 36 months until he elected to discontinue treatment. To the best of our knowledge, this is the first case of PAIS, which is difficult to resect, that was successfully treated using concurrent chemoradiotherapy and subsequent chemotherapy.

Keywords Pulmonary artery · Intimal sarcoma · Chemoradiotherapy

Introduction

Pulmonary artery intimal sarcoma (PAIS) is a rare malignancy that was initially identified during an autopsy in 1923 [1]; there are only a few hundred reported cases globally [2–4]. As this tumor mainly arises in the main trunk of the pulmonary artery and causes vascular occlusion symptoms, many patients die as a result of decompensated heart failure before they receive effective treatment [2, 3, 5, 6]. We report about a 43-year-old man who experienced cardiopulmonary arrest was diagnosed with PAIS after resuscitation, and was successfully treated using concurrent chemoradiotherapy with subsequent weekly paclitaxel therapy.

Case report

A 43-year-old man presented to our internal medicine department with headache, anorexia, and shortness of breath. He was admitted with clear consciousness, a blood pressure of 123/91 mmHg, a temperature of 36.8 °C, a respiratory rate of 20/min, a heart rate of 112/min, and 98% percutaneous arterial blood oxygen saturation in room air. While waiting for an examination, the patient experienced a brief period of cardiopulmonary arrest and collapsed; thereafter, he was promptly resuscitated and transferred to our critical care center. Laboratory test results revealed nearly normal values for his complete blood count and blood chemistry, although his serum brain natriuretic peptide (BNP) level was elevated to 684.7 pg/mL. Coagulation test results revealed only minor changes, with a prothrombin time percentage of 80%, an activated partial thromboplastin time of 22.6 s, a fibrinogen level of 397 mg/dL, and a D-dimer level of 3.9 µg/dL. No tumor markers, including carcinoembryonic antigen, carbohydrate antigen 19-9, neuron-specific enolase, or keratoprotein 21-1, were detected.

A transthoracic echocardiogram revealed remarkable right heart enlargement, and the pressure gradient at the tricuspid valve was estimated to be 75 mmHg. We initially suspected pulmonary thromboembolism, despite contrast-enhanced computed tomography (CT) revealing a slightly enhanced mass in the pulmonary artery (Fig. 1). In addition,

✉ Terumi Aso
shimin-byounin@city.fukuyama.hiroshima.jp;
terumi-aso@umin.ac.jp

¹ Department of Clinical Oncology, Fukuyama City Hospital, Hiroshima, Japan

² Center for Clinical Oncology, Okayama University Hospital, Okayama, Japan

Fig. 1 Contrast-enhanced computed tomography (CT) results from before the treatment. **a** CT image shows an obstructive pulmonary tumor extending from the main pulmonary trunk into the bilateral branches in the aortic phase. **b** Tumor has a weak contrast effect in the venous phase

fludeoxyglucose uptake was detected during positron emission tomography (PET) (Fig. 2). Thus, we suspected a tumor, although no other suspicious primary or metastatic lesions were detected. Three days later, the patient was transferred to a university hospital, where right heart biopsy was performed. Histological examination revealed atypical and pleomorphic cells with spindle- or oval-shaped nuclei and cytoplasm. The immunohistological test results were negative for keratin AE1/AE3, and S-100 and partially positive

for CD31 and CD34; many cells were positive for Ki-67 (Fig. 3). Thus, the tumor was diagnosed as PAIS.

Left pneumonectomy and right pulmonary artery replacement were planned as surgical therapy, although the patient refused to undergo surgery because of the high perioperative mortality risk. Therefore, weekly treatment was initiated using paclitaxel (80 mg/m^2), although the patient subsequently experienced cardiopulmonary arrest 4 days after initiating chemotherapy. Although prompt resuscitation was

Fig. 2 Positron emission tomography results from before the treatment reveal fluorodeoxyglucose accumulation in the center of the tumor (maximum standardized uptake value [SUV_{max}] = 6.9)

Fig. 3 **a** Histopathological examination of the tumor revealed a hypercellular pattern of pleomorphic spindle and epithelioid cells with prominent nuclei (hematoxylin and eosin staining, $\times 400$). **b, c** Immunohistochemical examination revealed partially positive results

for CD31 and CD34 ($\times 100$). **d, e** Immunohistochemical examination revealed negative results CKAE1/AE3 and S-100 ($\times 100$). **f** Many Ki-67-positive cells were observed ($\times 100$)

again performed, it appeared that chemotherapy alone was ineffective in controlling his condition. Thus, concurrent radiotherapy was initiated (66 Gy in 2-Gy fractions). Grade 3 elevations in aspartate transaminase (AST) and alanine transaminase (ALT) levels were detected after the third dose (based on version 4.0 of the Common Terminology Criteria for Adverse Events), and drug-induced liver damage was suspected. Thus, we reduced the paclitaxel dose to 55 mg/m², and AST and ALT levels decreased to Grade 1. Chest CT revealed that the radiotherapy had slightly reduced the

tumor's size (Fig. 4). In addition, cardiac ultrasonography revealed remarkable improvement in the right heart load, with a pressure gradient at the tricuspid valve of 41 mmHg and a normalized serum BNP level. The schema of the patient's progress in the university hospital is shown in Fig. 5.

The patient was discharged from the hospital 3 months after transfer and continued outpatient treatment at our hospital using weekly paclitaxel therapy (55 mg/m²). The patient continued to experience adverse events (Grade 1

Fig. 4 Computed tomography results after completing chemoradiotherapy revealed that the tumor had slightly decreased in size (**a, b**)

Fig. 5 Schema showing the patient's progress at the university hospital. The patient was hospitalized for 84 days at a university hospital. He received chemotherapy with weekly paclitaxel from day 5; however, he experienced CPA again on day 9. Combined administration of radiotherapy was initiated from day 15

AST and ALT elevation, Grade 2 peripheral neuropathy and fatigue), but could continue treatment using 1-week breaks between 3-week treatment cycles.

The patient did not experience exacerbation of the right heart failure symptoms, any increase in BNP levels, or right heart overloading during the treatment course. A PET scan after 33 months of treatment revealed that the tumor's size

had not increased, although the fludeoxyglucose uptake persisted, indicating that there was an active tumor remnant (Fig. 6). The patient elected to discontinue therapy after 36 months, although continued follow-up showed that he maintained his activities of daily living and was seeking employment.

Discussion

PAIS is a rare sarcoma that arises from the intimal cells of the pulmonary artery [5, 7], and it can be difficult to diagnose and distinguish it from pulmonary embolisms [2, 4, 5, 8, 9]. For example, pulmonary embolism was suspected in the present case, although there was no evidence of major coagulation dysfunction, and the enhanced mass that was detected during CT suggested the presence of a neoplastic lesion. Interestingly, PAIS often exhibits fludeoxyglucose uptake during PET, which can help differentiate it from a pulmonary embolism [10–12]; this supported our suspicion of PAIS. Moreover, a pathologically definitive diagnosis is not frequently achieved before PAIS treatment [2, 5]; however, the right heart biopsy results facilitated a definitive diagnosis of PAIS in our case.

PAIS prognosis is extremely poor, with the average survival after a diagnosis of pulmonary arterial sarcoma being 1.5 months [6]. In addition, chemotherapy or radiotherapy

Fig. 6 Positron emission tomography results after 33 months during the subsequent chemotherapy revealed that the tumor had not increased in size, but the fluorodeoxyglucose uptake had persisted. (SUVmax = 7.31)

alone is thought to have limited effects on this lesion, with surgical resection being considered a more useful treatment for improving prognosis [2, 4, 13]. Furthermore, chemotherapy and radiotherapy, which may be associated with a survival benefit when compared to surgery alone, are mainly used as adjunctive therapy for patients who have undergone surgical treatment [2, 3, 9, 13, 14]. However, to the best of our knowledge, this is the first report to describe successful concurrent chemoradiotherapy without surgical resection for non-metastatic PAIS.

Bandyopadhyay et al. performed a 20-year observational analysis of PAIS and reported that chemotherapy mainly involved an anthracycline agent (i.e., doxorubicin or epirubicin with or without cisplatin), which could be combined with an alkylating agent (i.e., dacarbazine, ifosfamide, or cyclophosphamide) [2]. Weekly paclitaxel therapy is effective for unresectable cases of angiosarcoma, which is similar to PAIS in that the sarcoma is derived from the endometrium [15]. The National Comprehensive Cancer Network guidelines list paclitaxel as a potentially effective systemic therapy agent for angiosarcoma, along with several other agents and treatment options that are used for other sarcomas [16]. Fujiwara et al. also retrospectively revealed that concurrent chemoradiotherapy with taxanes (i.e., docetaxel and weekly paclitaxel) and subsequent chemotherapy provided better survival than resection and radiotherapy alone in cases of cutaneous angiosarcoma [17].

Resection was considered in the present case; however, the perioperative mortality risk was considered to be high because of the patient's poor circulation, and thus, he refused to undergo surgery. Thus, we selected paclitaxel treatment as the preferred chemotherapy regimen to avoid cardiotoxic agents and the need for large fluid infusions. Radiotherapy was also initiated after the first chemotherapy cycle to enhance the anti-tumor effects, and weekly paclitaxel chemotherapy was continued after radiotherapy was completed. This provided a slight reduction in the tumor size, and the patient experienced a remarkable improvement with stable hemodynamics and maintained a good quality of life. An early reduction in the paclitaxel dose was necessitated by Grade 3 AST and ALT elevations; however, the subsequent adverse events were manageable (Grade 2 peripheral neuropathy, Grade 2 fatigue, and persistent Grade 1 edema of the fingers and lower limbs), and his symptoms were not exacerbated. Thus, the patient continued outpatient treatment, although PET after 32 months revealed residual tumor activity based on the continued fludeoxyglucose uptake in the tumor area. It would have been preferable to continue the paclitaxel treatment; however, the patient elected to discontinue treatment after 36 months based on the significant mental and physical burden. We will continue follow-up of this patient using CT and cardiac ultrasonography and will

consider resuming chemotherapy if we detect further tumor growth.

In conclusion, we encountered a patient with PAIS who experienced a good outcome after concurrent chemoradiotherapy and subsequent weekly paclitaxel therapy.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Research involving Human Participants For this type of study, formal consent is not required.

Informed consent Informed consent was obtained from all individual participants included in the study.

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