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Case Report

An autopsy case of pulmonary artery intimal sarcoma: detailed observation of tumor and its related lesions in pulmonary arteries☆,☆☆

Ayako Ro [a, b, *], Shinjirou Mori [b], Hiroaki Sugiura [c], Toshiyuki Furukawa [d], Kumiko Asakura [b], Satoko Kimura [b], Norimasa Kageyama [a, b], Shoetsu Chiba [a], Toshiji Mukai [a]

[a] Department of Legal Medicine, St. Marianna University School of Medicine, Kanagawa, 216-8511, Japan
[b] Tokyo Medical Examiner's Office, Tokyo,112-0012, Japan
[c] Department of Radiology, National Defense Medical College, Saitama, 359-8513, Japan
[d] Syncope Unit, Toyoko Hospital, St. Marianna University, Kanagawa, 211-0063, Japan

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ABSTRACT

We report an autopsy-proven case of a 33-year-old man who died of intimal sarcoma of the pulmonary artery. A large mass (5×4 cm) occluded the main and bilateral pulmonary arteries. Tumor cell morphology was consistent with that of undifferentiated pleomorphic sarcoma. Comprehensive histological observation of 18 pulmonary arteries from proximal to distal revealed continuous extension of the tumor from the main to the subsegmental arteries along the intima, forming an arteriosclerosis-like intimal thickening. Distal small arteries were also affected by eccentric intimal thickening or recanalization. Lung parenchyma was not involved, although there were two wedge-shaped small pulmonary infarctions caused by tumorous obstruction of the associated arteries. Histological results indicated that the intimal sarcoma in the pulmonary artery, which appeared occlusive with growth limited to the proximal artery, had in fact already spread more peripherally than expected. Both the proximal lesions and the distal small arteries were affected by peripheral tumor emboli or by pulmonary hypertension induced by the proximal tumor. However, as seen in this case, most of the occlusive tumor was located locally and intraluminally, in the proximal artery, and removing the proximal tumor by pulmonary endarterectomy was considered effective for symptomatic improvement.

1. Introduction

Pulmonary artery intimal sarcoma (PAIS) is an extremely rare malignant tumor, with only approximately 500 cases reported to date [1]. Because PAIS has the characteristic growth pattern of arising at the proximal pulmonary artery and developing intraluminally [2], it is usually misdiagnosed as chronic thromboembolic pulmonary hypertension (CTEPH) [3,4]. The small number of published case reports includes autopsy cases [5,6] because of the high mortality rate of this tumor [1]. However, previous autopsy reports focused on the proximal large tumor, with little information regarding the distal lesions in the pulmonary arteries. We experienced a case of sudden death in a young man with undiagnosed PAIS. We performed a detailed histopathological examination of the entire pulmonary artery focusing not only on the proximal tumor but also on the distal arterial lesions to investigate the distribution of the tumor and the related lesions.

2. Case report

A 33-year-old man visited a hospital because of two episodes of syncope; no specific findings were found on echocardiography and chest X-rays (Supplementary Fig. 1). Electrocardiography showed slight right axis deviation and R-wave progression at V1 and V2 (Supplementary Fig. 2). A Holter electrocardiogram revealed early repolarization, and blood brain natriuretic peptide level was within normal limits. He returned home without medication and did not undergo additional examinations. Seventeen days after his first visit, he was admitted to the emergency department because of abdominal pain and was diagnosed as having acute cholecystitis. He was treated with fasting and antibiotics; however, he collapsed suddenly and died the next morning. Medicolegal autopsy was performed 24 h postmortem.

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* Corresponding author at: Department of Legal Medicine, St. Marianna University School of Medicine, 2-16-1 Sugao, Miyamae-ward, Kanagawa, 216-8511, Japan. Tel.: +81 44 977 8111x3556; fax: +81 44 977 3902.
E-mail address: chaeja@marianna-u.ac.jp (A. Ro).

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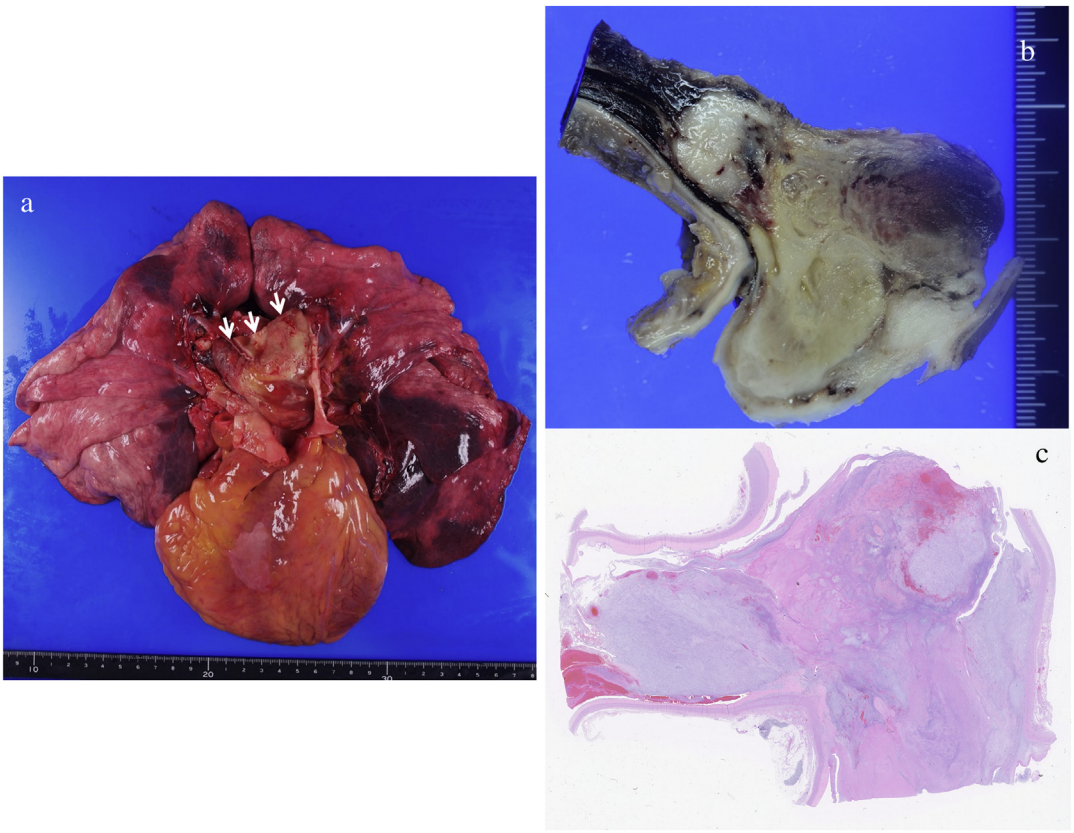

Fig. 1. (a) An occlusive tumor in the main pulmonary artery (arrows). (b) The cut surface of the tumor and pulmonary artery after formalin fixation. (c) Histological section of panel b with hematoxylin & eosin staining (original magnification: ×1).

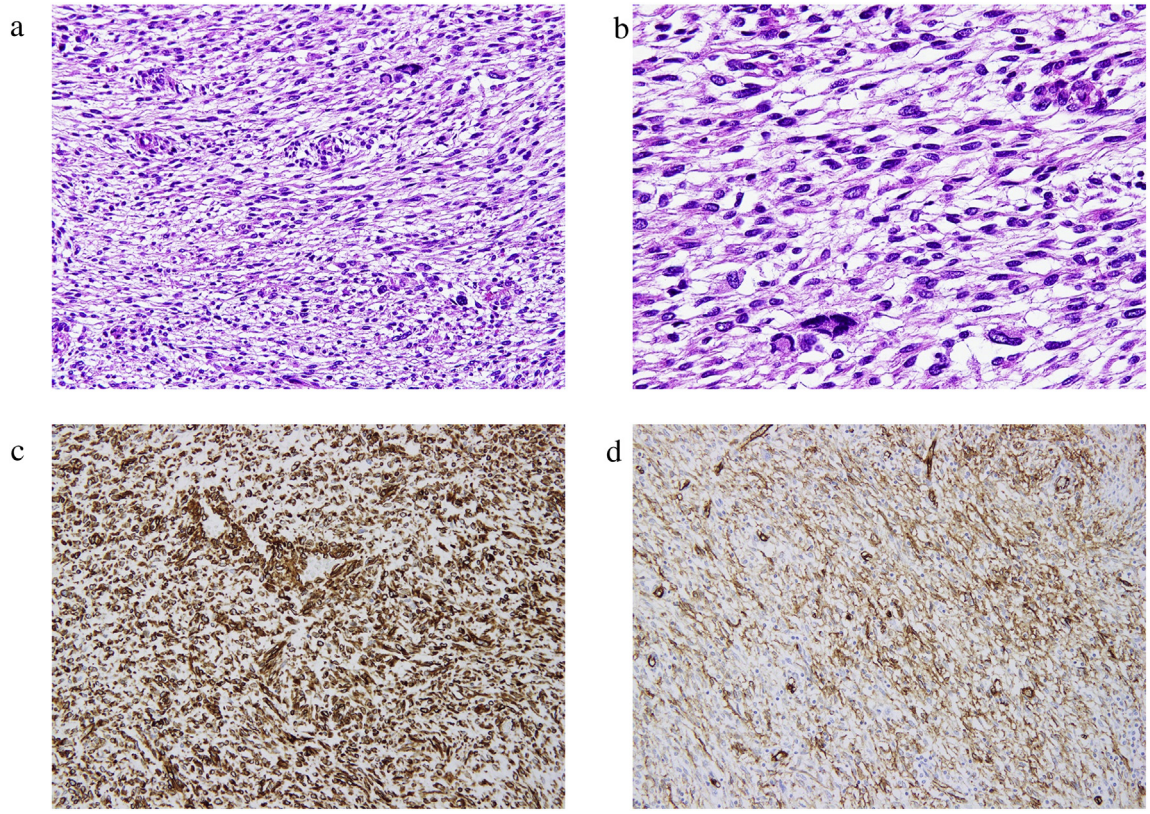

Fig. 2. (a) Histological section of the tumor with hematoxylin & eosin staining (original magnification: ×2). Atypical spindle cells arranged in a storiform pattern. (b) Higher-magnification photo of panel a. Multinucleated cells are seen (original magnification: ×20). (c) Immunohistochemistry of the tumor for vimentin (original magnification: ×20). (d) Immunohistochemistry of the tumor for CD34 (original magnification: ×20).

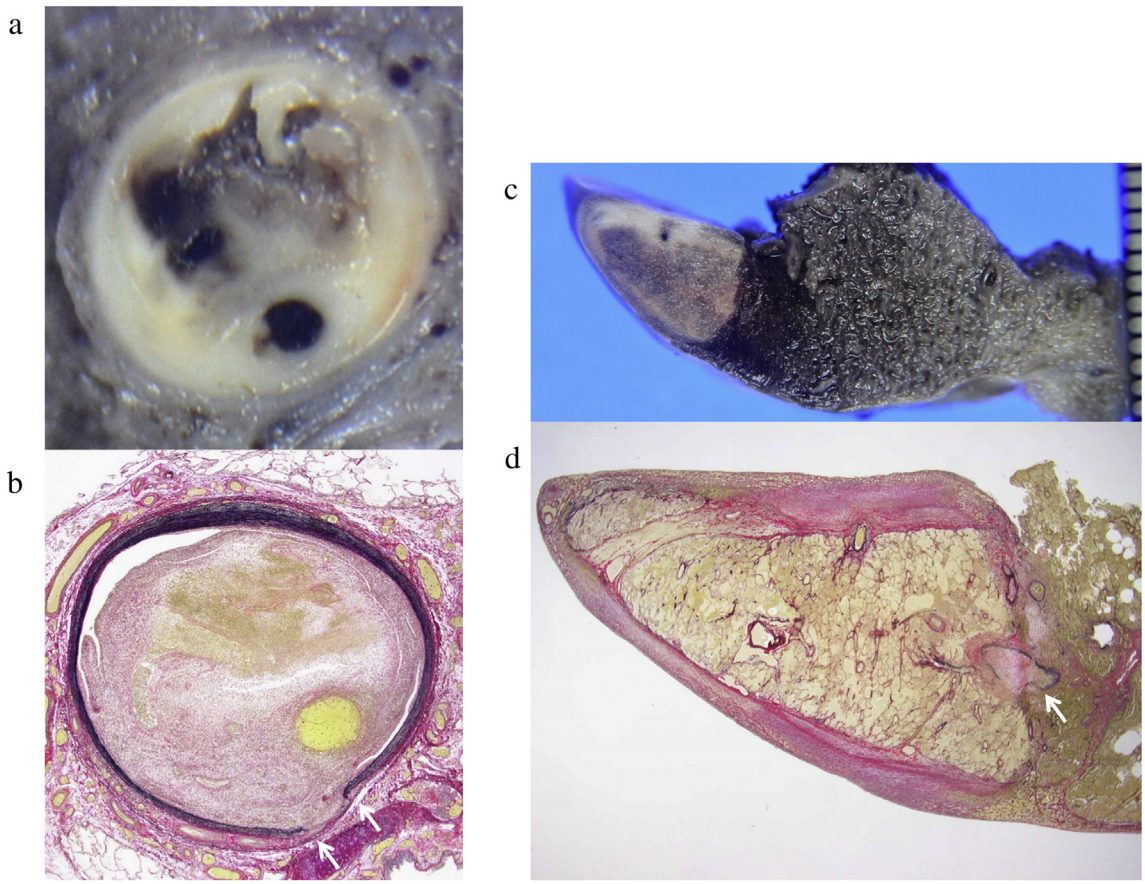

Fig. 3. (a) Cut surface of the tumor in the left pulmonary artery (A3). (b) Histological section of panel a with elastica Van Gieson staining (original magnification: ×2). The arrows indicate arterial wall destroyed by the tumor. (c) Small pulmonary infarction caused by tumor emboli at the periphery of the left pulmonary artery (A8). (d) Histological section of panel c with elastica Van Gieson staining (original magnification: ×1). The arrow indicates the dominant artery destroyed by tumor invasion.

The autopsy revealed that a widely dilated main pulmonary artery with white or yellowish solid mass, 5×4 cm in size, was occluding the pulmonary trunk and bilateral main pulmonary arteries (Fig. 1a). The tumor was partly coated with black thrombi (Fig. 1b and c). Invasion of the pulmonary valves and right ventricle was not observed.

Microscopically, the tumor was composed of spindle cells exhibiting partial mitosis or multinucleated cells (Fig. 2a and b). Multinucleated cells were positive for vimentin and CD31 immunostaining and negative for CD68 immunostaining. These results indicated that the multinucleated cells were not reactive histiocytic giant cells but tumor giant cells. The majority of the tumor showed a storiform pattern, although a small part (less than 5%) had an angiomatous or chondromatous appearance. The results of immunostaining were as follows: diffusely positive for vimentin (Fig. 2c); partially positive for CD34 (Fig. 2d) and CD31; slightly positive for caldesmon; and negative for desmin, cytokeratin, ETS-related gene, and factor VIII. This cell morphology was consistent with that of undifferentiated pleomorphic sarcoma. Our department could not afford to perform MDM2 amplification.

We performed detailed histological analyses to incorporate all pulmonary arterial lesions in accordance with our previous study on pulmonary thromboembolism [7]. We detected 18 segmental arteries and made 5 histological sections representing different arterial sizes from proximal to distal (segmental, subsegmental, tertiary, small elastic arteries, small muscular arteries, and alveoli) for each of the arteries. The results revealed continuous intravascular extension of the proximal tumor to segmental arteries. To some extent, the occlusive tumor destroyed the arterial wall (Fig. 3a and b). Although pulmonary parenchyma was not involved, there were two wedge-shaped small pulmonary infarctions at A5 and A8 of the left pulmonary artery with tumorous obstruction of its associated arteries (Fig. 3c and d). The tumor continuously spread to the subsegmental arteries along the intima, forming an arteriosclerosis-like intimal thickening (Fig. 4a).In addition to the proximal lesion, we identified intimal thickening caused by tumor emboli in the distal elastic arteries (Fig. 4b). Eccentric intimal thickening or recanalization of peripheral muscular arteries as a result of organized tumor emboli was detected in peripheral small arteries (Fig. 4c). Neither medial thickening of the muscular artery nor plexiform lesions were observed. Platelet thrombi were perceptible in some parts of small elastic pulmonary arteries (Fig. 4d). The schematic appearance of the distribution of the tumor and related lesions is shown in Fig. 5. Regarding other organs, the heart showed dilation and mild hypertrophy of the right ventricle as a result of prolonged pulmonary hypertension (Supplementary Fig. 3). There was no tumor metastasis to other organs or lymph nodes. The gallbladder contained some small gallstones, but there was no cholecystitis. No deep vein thrombosis was present in either leg. Based on these findings, the cause of death was certified as acute right heart failure caused by a giant PAIS.

3. Discussion

PAIS is a rare malignant mesenchymal tumor for which only 381 cases have been reported in the past 20 years [1]. The true incidence of PAIS is unclear because a certain proportion of PAIS patients are believed to die without a clinical diagnosis [5]. In fact, the

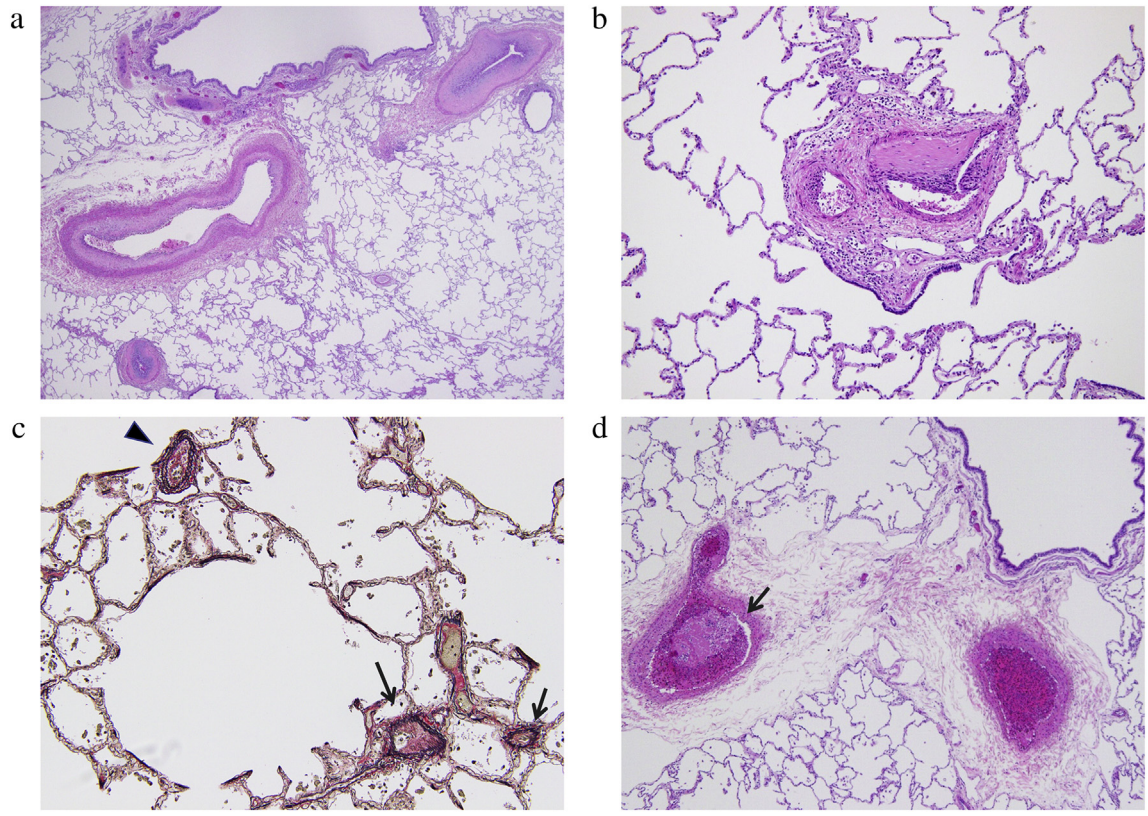

Fig. 4. (a) Tumor invasion resembling intimal thickening in the segmental arteries and accompanying small arteries. Hematoxylin & eosin staining (original magnification: ×2). (b) Eccentric intimal thickening caused by tumor emboli in a distal elastic artery (hematoxylin & eosin staining; original magnification: ×10). (c) Eccentric intimal thickening (arrows) and recanalization (arrowhead) of the peripheral muscular arteries (elastica van Gieson stain; original magnification: ×10). (d) Platelet thrombi in a small elastic artery (arrow) (hematoxylin & eosin staining; original magnification: ×4).

reported proportion of patients whose PAIS was initially diagnosed by autopsy among all case series was as high as 60% in 1989 [5]. However, because of advances in diagnostic imaging technology, this proportion decreased to 14% in 2008 [8] and 5% in 2016 [1]. Our case is also an autopsy-proven PAIS. We believe that the patient's antemortem symptom of syncope was caused by the PAIS because it is a frequently reported symptom of this disease [4,5,8].

PAIS is also known as a disease with exceptionally poor prognosis, with a median survival time of 1.5 months without surgical treatment reported in 1989 [5]. Even in 2018, the median survival was as short as 18 months even with surgical treatment [4]. The main reason for the poor prognosis is the characteristic growth of the tumor. PAIS usually arises in the pulmonary trunk and/or main pulmonary artery and grows intravascularly to a size of 4–5 cm [8]. The large occlusive mass in the proximal pulmonary artery causes severe pulmonary hypertension. The clinical manifestation caused by PAIS resembles that of CTEPH, and pulmonary endarterectomy (PEA) is often performed to remove the proximal tumor and relieve the associated pulmonary hypertension, similar to patients with CTEPH [3,4]. Because of the peculiar tendency of PAIS tumor growth being restricted to the vascular lumen, PEA often results in significant improvement of symptoms [4,9]. However, because the resection margins are rarely clear, the procedure is deemed noncurative [9].

In our case, the majority of the proximal tumors were located within the vessel lumen (Fig. 1b and c). However, in some parts, the tumor showed invasive growth that broke through the arterial wall (Fig. 3b). Furthermore, histological sections revealed that the proximal tumors spread broadly along the intima to the subsegmental arteries where the lesion could not be reached by PEA (Fig. 4a). Broad extension of residual tumor through the intima has been confirmed previously by autopsy after PEA [6].

Little is known about lesions in more distal areas in the case of proximal PAIS. In our case, multiple tumor lesions thought to be fragmented from the proximal large tumor were found in the small elastic arteries (Fig. 4b). Eccentric intimal thickening and recanalization of peripheral muscular arteries were also seen (Fig. 4c). “Small vessel disease,” such as intimal thickening, eccentric intimal fibrosis, and intimal fibromuscular proliferation at distal arteries, is known to be a result of mechanical obstruction of proximal arteries in CTEPH patients [10]. These findings indicate that PAIS patients undergo the same pathological changes as do CTEPH patients not only in the proximal artery but also in the distal lesions. In CTEPH patients, small vessel disease contributes to persistent pulmonary hypertension after PEA and a higher risk of postoperative mortality [10]. Therefore, distal arterial lesions also represent an important prognostic factor for PAIS patients.

Our case showed small vessel lesions; however, medial hypertrophy or plexiform lesions reflecting sustained pulmonary hypertension were not observed. Furthermore, X-ray images and echocardiographic findings 17 days before death showed no specific change (Supplementary Fig.1 and 2). Retrospectively, right axis deviation and R-wave progression at V1 and V2 in his electrocardiogram indicated right ventricular hypertrophy; however, according to the other examination results, the physician concluded that the electrocardiographic results were nonsignificant changes at the time of examination. Because of the rapid growth of our patient's tumor, the duration of his pulmonary hypertension was shorter compared with CTEPH patients. Increased cardiac reserve because of his young age might also explain the lack of X-ray and echocardiographic changes in our patient. The difficulty diagnosing this disease might have resulted from the lack of specific clinical changes on cardiac examination despite the presence of the large tumor.

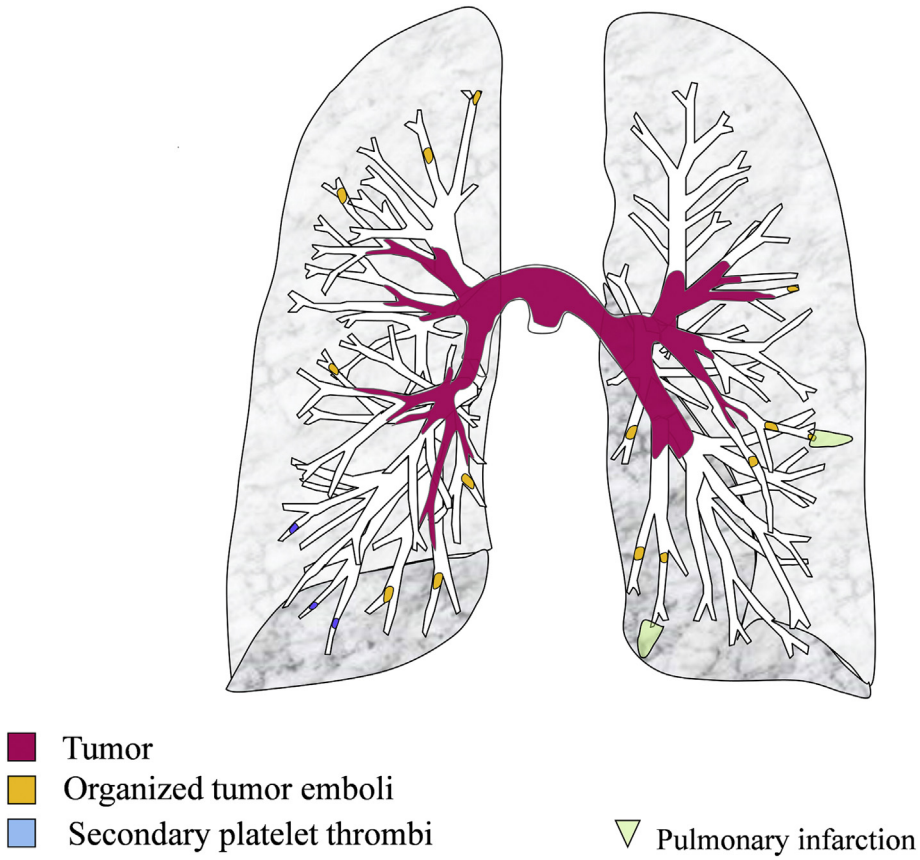

Fig. 5. Schematic appearance of the tumor and related lesions. The tumor is present continuously from the proximal trunk to the segmental or subsegmental arteries. In contrast, the distal arteries are affected by organized tumor emboli or secondary platelet thrombi. Two small pulmonary infarctions are also seen.

Small pulmonary infarctions were observed as a result of distal tumor embolism (Fig. 3c and d). Yin et al. reported that three-fourths of late deaths in patients with pulmonary arterial sarcoma were associated with recurrence in the distal pulmonary artery or pulmonary trunk [4]. Distal tumor embolism might induce both distal tumor recurrence and peripheral pulmonary infarction.

A surgical review concluded that because of the very poor prognosis, complete surgical resection of the tumor could never be achieved in PAIS [3] and that surgery is performed mainly for palliation to prolong survival rather than to cure the disease [4]. Indeed, Wong et al. reported no difference in median overall survival between patients who underwent PEA and those who did not, although surgery did provide significant symptomatic and hemodynamic improvement [9]. Our histological findings indicated that the PAIS, which appeared to be occlusive with growth limited to the proximal artery, had already spread more peripherally than expected and that as well as the proximal lesions, distal small arteries were affected by peripheral tumor emboli or by pulmonary hypertension induced by the proximal tumor. However, even in our case, most of the occlusive tumor was located locally and intraluminally in the proximal artery; therefore, removing the proximal tumor by PEA is considered effective for symptomatic improvement.

Supplementary data to this article can be found online at https://doi.org/10.1016/j.carpath.2019.07.002.

References

[1] Bandyopadhyay D, Panchabhai TS, Bajaj NS, Patil PD, Bunte MC. Primary pulmonary artery sarcoma: a close associate of pulmonary embolism — 20-year observational analysis. J Thorac Dis 2016;8:2592–601. https://doi.org/10.21037/jtd.2016.08.89.

[2] Burke AP, Yi ES. Pulmonary artery intimal sarcoma. In: Travis WD, Brambilla E, Burke AP, Marx A, Nicholson AG. WHO classification of tumours of the lung, pleura, thymus and heart. 4th ed. Lyon: International Agency for Research on Cancer (IARC); 2015. p. 128–9.

[3] Mussot S, Ghigna MR, Mercier O, Fabre D, Fadel E, Le Cesne A, et al. Retrospective institutional study of 31 patients treated for pulmonary artery sarcoma. Eur J Cardiothorac Surg 2013;43:787–93. https://doi.org/10.1093/ejcts/ezs387.

[4] Yin K, Zhang Z, Luo R, Ji Y, Zheng D, Lin Y, et al. Clinical features and surgical outcomes of pulmonary artery sarcoma. J Thorac Cardiovasc Surg 2018;155:1109–1115.e1. https://doi.org/10.1016/j.jtcvs.2017.10.101.

[5] Krüger I, Borowski A, Horst M, de Vivie ER, Theissen P, Gross-Fengels W. Symptoms, diagnosis, and therapy of primary sarcomas of the pulmonary artery. Thorac Cardiovasc Surg 1990;38:91–5. https://doi.org/10.1055/s-2007-1014001.

[6] Miyai K, Takeo H, Matsukuma S. Intimal sarcoma of the pulmonary trunk showing broad intimal extension and focal chondrosarcomatous differentiation: an autopsy case. Cardiovasc Pathol 2017;31:5–8. https://doi.org/10.1016/j.carpath.2017.07.002.

[7] Ro A, Kageyama N, Tanifuji T, Sakuma M. Autopsy-proven untreated previous pulmonary thromboembolism: frequency and distribution in the pulmonary artery and correlation with patients' clinical characteristics. J Thrombo Haemost 2011;9:922–7. https://doi.org/10.1111/j.1538-7836.2011.04225.x.

[8] Tavora F, Miettinen M, Fanburg-Smith J, Franks TJ, BurkeA. Pulmonary artery sarcoma: a histologic and follow-up study with emphasis on a subset of low-grade myofibroblastic sarcomas with a good long-term follow-up. Am J Surg Pathol 2008;32:1751–61. doi: https://doi.org/10.1097/PAS.0b013e31817d7fd0.

[9] Wong HH, Gounaris I, McCormack A, Berman M, Davidson D, Horan G, et al. Presentation and management of pulmonary artery sarcoma. Clin Sarcoma Res 2015;5:3. https://doi.org/10.1186/s13569-014-0019-2.

[10] Simonneau G, Torbicki A, Dorfmüller P, Kim N. The pathophysiology of chronic thromboembolic pulmonary hypertension. Eur Respir Rev 2017;26:160112. https://doi.org/10.1183/16000617.0112-2016.