in vivo *36*: 1519-1522 (2022)
doi:10.21873/invivo.12861

Difficulty in Distinguishing Pulmonary Arterial Intimal Sarcoma from Pulmonary Thromboembolism Using FDG PET/CT

HIROTAKA SUTO[1,2], MAKIKO SUTO[3], YUMIKO INUI[2] and ATSUO OKAMURA[2]

[1]*Department of Medical Oncology, The Cancer Institute Hospital of Japanese Foundation for Cancer Research, Tokyo, Japan;*
[2]*Department of Medical Oncology/Hematology, Kakogawa Central City Hospital, Hyogo, Japan;*
[3]*Department of Cardiovascular Medicine, Takarazuka City Hospital, Hyogo, Japan*

Abstract. *Background/Aim: Pulmonary arterial intimal sarcoma (PAIS) is a rare malignant soft tissue tumor that is difficult to differentiate from pulmonary thromboembolism (PTE). Therefore, pre-operative diagnosis is often difficult. However, recent advances in fluorodeoxyglucose positron emission tomography (FDG-PET) have enabled the use of standardized uptake values (SUVs) for the differential diagnosis of PAIS from PTE, and the frequency of diagnosis of PAIS has increased. Here, we report a case of PAIS that was difficult to differentiate from PTE despite using FDG-PET. Case Report: A 40-year-old woman presented with gradually worsening exertional dyspnea. Contrast-enhanced computed tomography (CT) revealed lesions with poor enhancement in the right lateral basal pulmonary artery. FDG-PET/CT did not reveal any tumor or thrombosis in other areas. Cytological evaluation using a right ventricular catheter did not lead to a definitive diagnosis. Because the patient did not respond to anticoagulation, we performed pulmonary artery endarterectomy. Pathological examination of the pulmonary artery tumor revealed a mucinous tumor with an edematous stroma and spindle-shaped tumor-cell proliferation, which confirmed the diagnosis of PAIS. However, FDG/PET demonstrated a low SUV of 3.4. Conclusion: Some PAISs with low cellular densities and high mucous tissue proportions have SUVs similar to those in PTE. In patients with low FDG uptake, if PAIS is suspected based on other objective findings, additional exploration using highly invasive tests or surgical procedures specific to PAIS is warranted.*

Correspondence to: Hirotaka Suto, MD, Ph.D., Department of Medical Oncology, The Cancer Institute Hospital of Japanese Foundation for Cancer Research, 3-8-31, Ariake, Koto, Tokyo 135-8550, Japan. Tel: +81 335200111, Fax: +81 335200141, e-mail: hirotaka.suto@jfcr.or.jp

Key Words: Pulmonary arterial intimal sarcoma, pulmonary thromboembolism, FDG–PET/CT, standard uptake value.

Pulmonary arterial intimal sarcoma (PAIS) is a rare, highly malignant, soft tissue tumour with a poor prognosis that is difficult to differentiate from pulmonary thromboembolism (PTE) (1-5). Because biopsy of pulmonary artery lesions is difficult, preoperative diagnosis is often challenging as well. However, recent advances in F-18-fluorodeoxyglucose positron emission tomography (FDG-PET) have enabled the use of standardized uptake values (SUVs) for the differential diagnosis of PAIS from PTE and similar diseases (6, 7); thus, the frequency of diagnosis of PAIS has increased. Here, we report a case in which it was difficult to differentiate PAIS from PTE despite using F-18 FDG-PET.

Case Report

A 40-year-old woman presented with exertional dyspnoea and was referred to a nearby clinic, but the clinician was unable to make a definitive diagnosis. Thirteen months after the initial symptoms, she visited our hospital. She did not smoke or drink alcohol and had no previous medical history. The findings of the physical examination at the first visit were as follows: body temperature, 36.1˚C; heart rate, 100 beats per min; blood pressure, 152/92 mmHg; respiratory rate, 16 breaths per min; blood oxygen saturation, 94%; no murmur; and no peripheral oedema. Laboratory tests showed C-reactive protein, D-dimer, and brain natriuretic peptide levels of 0.6 mg/dl, 2.5 μg/ml, and 207.0 pg/ml, respectively. The electrocardiogram was normal, and a chest radiograph showed no cardiac enlargement or pleural effusion. Transthoracic echocardiography revealed normal left

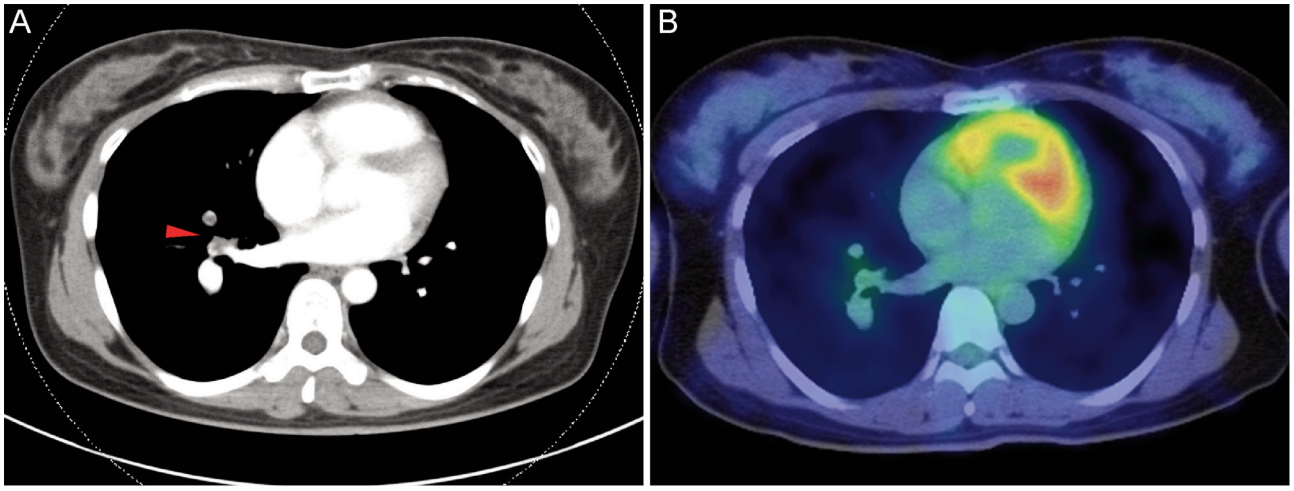

Figure 1. *Imaging findings at the first visit to our hospital. (A) Enhanced computed tomography (CT) shows a poorly enhanced lesion in the right lateral basal pulmonary artery (arrow). (B) F-18-fluorodeoxyglucose positron emission tomography/CT. The SUV of the lesions is as low as 3.4. SUV: Standard uptake value.*

ventricular wall motion and a tricuspid regurgitation pressure gradient of 39.2 mmHg, whereas contrast-enhanced computed tomography (CT) showed lesions with poor enhancement in the right lateral basal pulmonary artery (Figure 1A). The differential diagnosis included pulmonary embolism with PAIS, PTE, tumour embolism, and deep vein thrombosis. Ultrasonography of the lower extremities and F-18 FDG-PET/CT imaging did not reveal any tumour or thrombosis in other areas. The SUV of the lesion was as low as 3.4 (Figure 1B). Ventilation blood flow scintigraphy of the lungs showed a mismatch defect in ventilation blood flow in the middle and lower lobes of the right lung. We initially suspected PTE and initiated anticoagulation therapy. However, there was no improvement in clinical symptoms after one week. Therefore, the patient was transferred to another hospital for a differential diagnosis of the lesions and specialized treatment. Cytological evaluation using a right ventricular catheter did not lead to a definitive diagnosis. Subsequently, cardiovascular surgeons performed pulmonary artery endarterectomy. Histological examination of the pulmonary artery tumour showed proliferation of spindle-shaped tumour cells on a myxomatous, oedematous stromal background (Figure 2). Immunohistochemical (IHC) expression of mouse double minute 2 (MDM2) was confirmed (Figure 3), although the density of spindle-shaped tumour cells within the tumour mass was low. In addition, IHC staining was positive for Cyclin-dependent kinase 4, muscle actin, alpha-smooth muscle actin, and Ets-related gene (focal), and negative for desmin, cytokeratin AE1/AE3, CD31, and CD34. Based on the morphological and IHC findings, we finally diagnosed the lesions as PAIS. Written informed consent was obtained from the patient for the publication of this paper.

Discussion

We present a case of PAIS in which the possibility of intimal sarcoma was suspected and diagnosed based on the fact that anticoagulation therapy was ineffective, even though we did not actively suspect PAIS on PET-CT.

The prognosis of untreated patients with intimal sarcoma is poor, with a survival period of 1.5 to 5.5 months from diagnosis (1). In contrast, patients with localized disease treated with a curative intent have a recurrence-free survival period of 14.6 months, and patients with advanced disease treated with a palliative intent have an overall survival period of 21.8 months (8). Therefore, early diagnosis is critical. Previously, the pre-operative diagnosis of PAIS was difficult, and >70% of cases were misdiagnosed as PTE (3). With the widespread use of F-18 FDG-PET/CT, PAIS can be differentiated from other diseases such as PTE, and the frequency of diagnosis of PAIS has increased. In pulmonary artery sarcoma (PAS), FDG-PET often shows a high uptake of F-18, and the reported mean maximum SUV (SUVmax) is 7.63±2.21 (6). von Falck *et al.* reported similar findings (7). Another study used a cutoff value of 3.5 for SUVmax for cardiac malignancies and benign tumors (9). In addition, Gan *et al.* reported that patients with PAS had normal D-dimer levels, elevated CRP levels, fewer complications such as deep venous thrombosis, lower Wells scores, and shorter symptom duration (10). In contrast, Wittram *et al.* reported that SUVmax values of pulmonary emboli ranged from 0.45 to 3.03 (11). However, some PAISs have SUVs similar to those in PTE. Studies have shown that FDG uptake is lower in cancers with a high mucous component (12-14). The low FDG uptake in solid tumors with a high mucous component may be partly explained by the low malignant

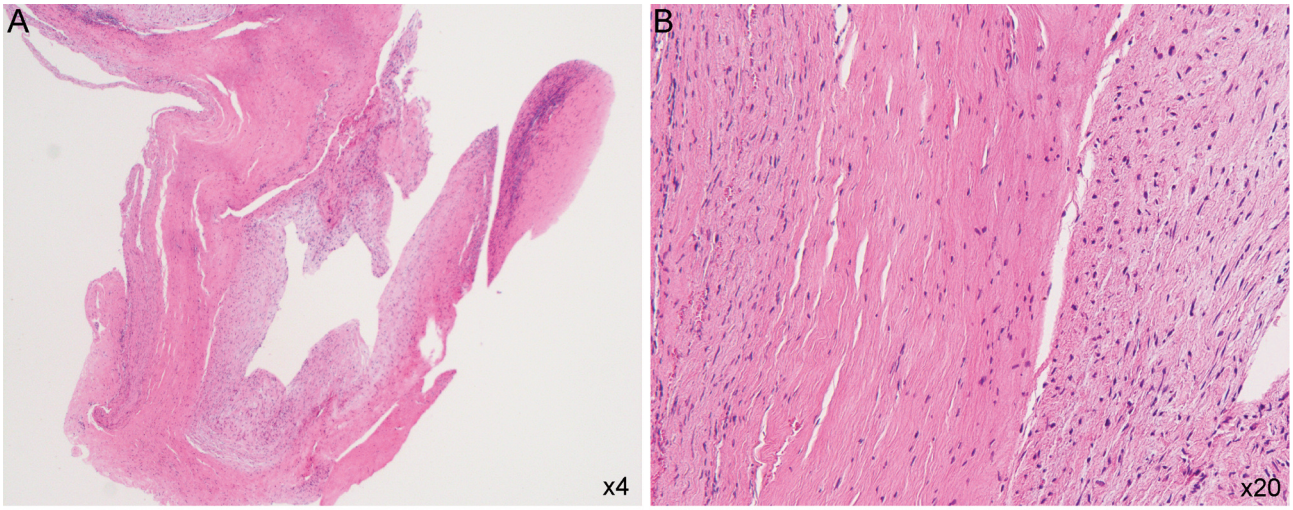

Figure 2. *Histopathological examination shows proliferation of spindle-shaped tumor cells on a myxomatous, edematous stromal background. Hematoxylin and eosin staining: (A) ×4, (B) ×20.*

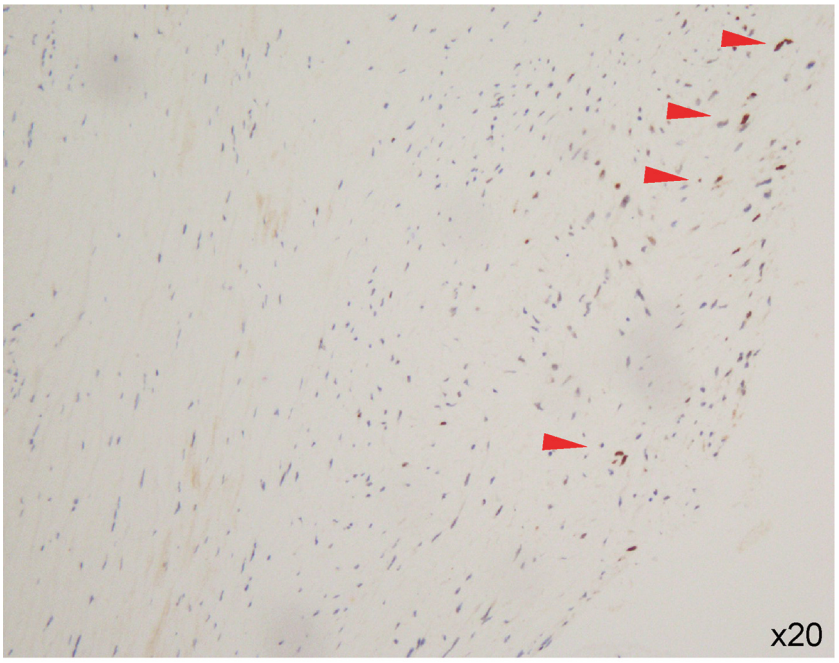

Figure 3. *Immunohistochemical staining shows focal expression of mouse double minute 2 (MDM2) (arrows).*

tumor-cell density within the tumor mass (14). In our case, the mucous component and edematous stroma were more than those seen in the usual PAIS, which may be one of the reasons for the low SUV. A previous study reported that patients with intimal sarcoma have normal D-dimer levels (10), whereas other studies reported elevated D-dimer levels (15, 16). Therefore, it is impossible to exclude intimal sarcoma based on D-dimer levels outside the normal range. In addition, despite the recent use of liquid biopsy in oncology, invasive testing and surgery still play an active role in defining PAIS because of the absence of PAIS-specific genetic mutations. Although the prognosis of intimal sarcoma is generally poor, our patient was diagnosed approximately one year after the initial symptoms. Perhaps, as with low-grade lung adenocarcinoma and low-grade

lymphoma, the relatively low grade of intimal sarcoma in this case might have contributed to the low FDG uptake and long-term survival (17).

In conclusion, we reported a case of PAIS that was difficult to differentiate from PTE on F-18 FDG-PET/CT. In patients presenting with thrombi with atypical clinical findings, such as unresponsiveness to anticoagulation, intimal sarcoma should be considered, even if F-18 FDG uptake is low. Invasive tests such as right ventricular catheterization or surgical procedures specific to PAIS are warranted in such patients.

Conflicts of Interest

The Authors have no conflicts of interest to declare regarding this study.

Authors' Contributions

Conceptualization, H.S., M.S., and A.O.; methodology, H.S., and A.O.; investigation, H.S, M.S., Y.I., and A.O.; data curation, H.S, M.S., Y.I., and A.O.; writing – original draft preparation, H.S.; writing – review and editing, H.S., M.S., Y.I., and A.O.; supervision, A.O. All Authors have read and agreed to the published version of the manuscript.

Acknowledgements

The Authors would like to thank Editage (www.editage.com) for English language editing.

References

1 Krüger I, Borowski A, Horst M, de Vivie ER, Theissen P and Gross-Fengels W: Symptoms, diagnosis, and therapy of primary sarcomas of the pulmonary artery. Thorac Cardiovasc Surg *38(2)*: 91-95, 1990. PMID: 2190350. DOI: 10.1055/s-2007-1014001

2 Neuville A, Collin F, Bruneval P, Parrens M, Thivolet F, Gomez-Brouchet A, Terrier P, de Montpreville VT, Le Gall F, Hostein I, Lagarde P, Chibon F and Coindre JM: Intimal sarcoma is the most frequent primary cardiac sarcoma: clinicopathologic and molecular retrospective analysis of 100 primary cardiac sarcomas. Am J Surg Pathol *38(4)*: 461-469, 2014. PMID: 24625414. DOI: 10.1097/PAS.0000000000000184

3 Parish JM, Rosenow EC 3rd, Swensen SJ and Crotty TB: Pulmonary artery sarcoma. Clinical features. Chest *110(6)*: 1480-1488, 1996. PMID: 8989065. DOI: 10.1378/chest.110.6.1480

4 Evison M, Crosbie P, Chaturvedi A, Shah R and Booton R: Pulmonary artery sarcoma: a rare thoracic tumor frequently misdiagnosed at presentation. Thorac Cancer *6(6)*: 797-799, 2015. PMID: 26557921. DOI: 10.1111/1759-7714.12213

5 Wong HH, Gounaris I, McCormack A, Berman M, Davidson D, Horan G, Pepke-Zaba J, Jenkins D, Earl HM and Hatcher HM: Presentation and management of pulmonary artery sarcoma. Clin Sarcoma Res *5(1)*: 3, 2015. PMID: 25628857. DOI: 10.1186/s13569-014-0019-2

6 Ito K, Kubota K, Morooka M, Shida Y, Hasuo K, Endo H and Matsuda H: Diagnostic usefulness of 18F-FDG PET/CT in the differentiation of pulmonary artery sarcoma and pulmonary embolism. Ann Nucl Med *23(7)*: 671-676, 2009. PMID: 19680740. DOI: 10.1007/s12149-009-0292-y

7 von Falck C, Meyer B, Fegbeutel C, Länger F, Bengel F, Wacker F and Rodt T: Imaging features of primary sarcomas of the great vessels in CT, MRI and PET/CT: a single-center experience. BMC Med Imaging *13*: 25, 2013. PMID: 23924063. DOI: 10.1186/1471-2342-13-25

8 Frezza AM, Assi T, Lo Vullo S, Ben-Ami E, Dufresne A, Yonemori K, Noguchi E, Siontis B, Ferraro R, Teterycz P, Duffaud F, Ravi V, Vincenzi B, Gelderblom H, Pantaleo MA, Baldi GG, Desar I, Fedenko A, Maki RG, Jones RL, Benjamin RS, Blay JY, Kawai A, Gounder M, Gronchi A, Le Cesne A, Mir O, Czarnecka AM, Schuetze S, Wagner AJ, Adam J, Barisella M, Sbaraglia M, Hornick JL, Meurgey A, Mariani L, Casali PG, Thornton K and Stacchiotti S: Systemic treatments in MDM2 positive intimal sarcoma: A multicentre experience with anthracycline, gemcitabine, and pazopanib within the World Sarcoma Network. Cancer *126(1)*: 98-104, 2020. PMID: 31536651. DOI: 10.1002/cncr.32508

9 Rahbar K, Seifarth H, Schäfers M, Stegger L, Hoffmeier A, Spieker T, Tiemann K, Maintz D, Scheld HH, Schober O and Weckesser M: Differentiation of malignant and benign cardiac tumors using 18F-FDG PET/CT. J Nucl Med *53(6)*: 856-863, 2012. PMID: 22577239. DOI: 10.2967/jnumed.111.095364

10 Gan HL, Zhang JQ, Huang XY and Yu W: The wall eclipsing sign on pulmonary artery computed tomography angiography is pathognomonic for pulmonary artery sarcoma. PLoS One *8(12)*: e83200, 2013. PMID: 24391746. DOI: 10.1371/journal.pone.0083200

11 Wittram C and Scott JA: 18F-FDG PET of pulmonary embolism. AJR Am J Roentgenol *189(1)*: 171-176, 2007. PMID: 17579168. DOI: 10.2214/AJR.06.0640

12 Queiroz MA, Naves A, Dreyer PR, Cerri GG and Buchpiguel CA: PET/MRI characterization of mucinous versus nonmucinous components of rectal adenocarcinoma: a comparison of tumor metabolism and cellularity. AJR Am J Roentgenol *216(2)*: 376-383, 2021. PMID: 33295813. DOI: 10.2214/AJR.19.22627

13 Stahl A, Ott K, Weber WA, Becker K, Link T, Siewert JR, Schwaiger M and Fink U: FDG PET imaging of locally advanced gastric carcinomas: correlation with endoscopic and histopathological findings. Eur J Nucl Med Mol Imaging *30(2)*: 288-295, 2003. PMID: 12552348. DOI: 10.1007/s00259-002-1029-5

14 Kwee TC, Basu S, Saboury B, Ambrosini V, Torigian DA and Alavi A: A new dimension of FDG-PET interpretation: assessment of tumor biology. Eur J Nucl Med Mol Imaging *38(6)*: 1158-1170, 2011. PMID: 21225422. DOI: 10.1007/s00259-010-1713-9

15 Lee DH, Jung TE, Lee JH, Shin DG, Park WJ and Choi JH: Pulmonary artery intimal sarcoma: poor 18F-fluorodeoxyglucose uptake in positron emission computed tomography. J Cardiothorac Surg *8*: 40, 2013. PMID: 23497592. DOI: 10.1186/1749-8090-8-40

16 Sakai K, Minoura Y, Matsui T, Kaneko K and Kobayashi Y: Primary pulmonary artery intimal sarcoma case with elevated coagulation markers. J Clin Diagn Res *11(4)*: OD10-OD11, 2017. PMID: 28571195. DOI: 10.7860/JCDR/2017/23423.9609

17 Flavell RR, Naeger DM, Aparici CM, Hawkins RA, Pampaloni MH and Behr SC: Malignancies with low fluorodeoxyglucose uptake at PET/CT: Pitfalls and prognostic importance: Resident and fellow education feature. Radiographics *36(1)*: 293-294, 2016. PMID: 26761542. DOI: 10.1148/rg.2016150073

Received March 10, 2022
Revised March 31, 2022
Accepted April 1, 2022