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CASE REPORT

Peripheral Pulmonary Artery Stenosis (PPAS) Mimicking Chronic Thromboembolic Pulmonary Hypertension (CTEPH) in SAPHO Syndrome: A Case Report and Review of the Literature

Katsuyuki Tomita[1], Mitsuhiro Yamamoto[1], Ryohei Katou[1], Tomoyuki Ikeuchi[1], Hirokazu Touge[1], Masaharu Fukuki[2], Shuji Sugihara[3], Akira Yamasaki[4]

[1]Department of Respiratory Medicine, NHO Yonago Medical Center, Yonago, Tottori, Japan.

[2]Department of Cardiology Medicine, NHO Yonago Medical Center, Yonago, Tottori, Japan.

[3]Department of Radiology, NHO Yonago Medical Center, Yonago, Tottori, Japan.

[4]Division of Respiratory Medicine and Rheumatology, Department of Multidisciplinary Internal Medicine, Faculty of Medicine, Tottori University, Yonago, Tottori, Japan.

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Corresponding Author: Katsuyuki Tomita, Department of Respiratory Medicine, NHO Yonago Medical Center, Yonago, Tottori, Japan.

Abstract

Background: Synovitis, acne, pustulosis, hyperostosis, and osteitis (SAPHO) syndrome is a rare systemic auto-inflammatory disease characterized by chronic nonbacterial osteomyelitis and neutrophilic cutaneous involvement.

Case Presentation: We report a case of an 83-year-old man with SAPHO syndrome complicated by pulmonary hypertension attributed to multiple perfusion defects on a ventilation-perfusion scan, suggestive of chronic thromboembolic pulmonary hypertension (CTEPH). Computed tomography angiography revealed peripheral pulmonary artery stenosis (PPAS). He also demonstrated pyoderma gangrenosum (PG) as skin manifestation. Our lethal case of a patient with SAPHO syndrome presented with pulmonary hypertension due to PPAS and PG.

Conclusions: SAPHO syndrome can result in heterogeneous phenotypes as systematic auto-inflammatory diseases.

Keywords: Chronic Thromboembolic Pulmonary Hypertension (CTEPH), Peripheral Pulmonary Artery Stenosis (PPAS), SAPHO syndrome.

1. Introduction

Synovitis, acne, pustulosis, hyperostosis, and osteitis (SAPHO) syndrome is a rare systemic auto-inflammatory disease characterized by osteoarticular inflammatory lesions and dermatological disorders. A few risks of pulmonary hypertension (PH) due to peripheral pulmonary artery stenosis (PPAS) were previously demonstrated in SAPHO syndrome [1,2], which could lead to the misdiagnosis of chronic thromboembolic pulmonary hypertension (CTEPH). PPAS is uncommon and underdiagnosed in adult patients [3], and is characterized as a narrowing in one or more of the branches of the pulmonary arteries. When multiple segmental ventilatory-blood mismatches on lung V/Q scintigraphy occur, CTEPH as well as PPAS can be cited as differential diagnosis.

Here, we report a case of an 83-year-old man,who demonstrated multiple segmental ventilatory-blood mismatches and PH, with SAPHO syndrome.

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Finally, he was diagnosed SAPHO syndrome complicated by PPAS in an adult. In this report, we also summarize the previously published data of these cases [1, 2].

2. Case Presentation

An 83-year-old Japanese man presented to our hospital with severe pain and swelling of the right sternoclavicular joint. Two months prior, he experienced spontaneous remission of sternocostoclavicular hyperplasia within 1 week. There were no other skin symptoms (severe acne and psoriasis), or other osteoarticular symptoms (spinal and sacroiliac involvement, peripheral synovitis, vertebral column involvement, or enthesitis).

Laboratory examinations performed at our hospital showed a white cell count (WBC) of 12.6×10^9 per L and a C reactive protein (CRP) level of 28.16 $mg\cdot L^{-1}$ (normal <5). Antinuclear antibodies, anti-neutrophil cytoplasmic antibodies, anticardiolipin antibodies, lupus anticoagulants, and rheumatoid factors were negative. Prothrombin and activated partial thromboplastin times were normal. Human leukocyte antigen (HLA) typing of locus B was positive for both B55 and B71. The test result for the HLA-B27 antigen was negative.

Computed tomography (CT) revealed typical hyperostosis of the sternoclavicular and sternocostal joints (Fig. 1). Bone scintigraphy was performed to rule out any other infra-clinical osteoarticular localizations. Increased tracer uptake was observed in the clavicle and manubrium sternoclavicular joint (Fig. 2). Our patient was diagnosed with spondyloarthritis (SpA)-preceding SAPHO syndrome. He was initially treated with nonsteroidal anti-inflammatory drug (NSAID).

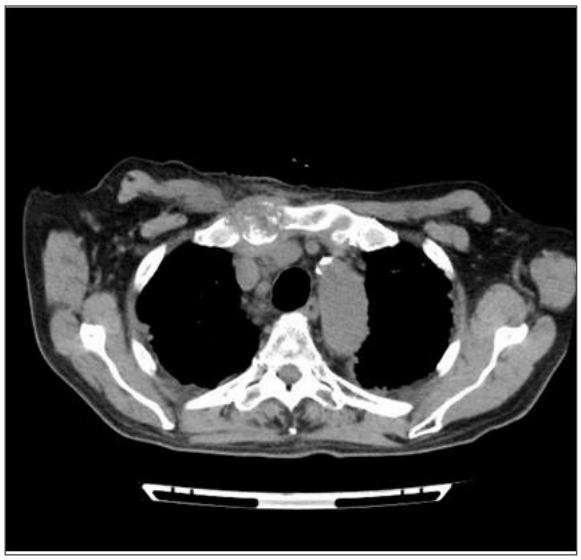

Figure 1. *Chest CT reveals clavicular hyperostosis and ankylosis of the sternoclavicular joint.*

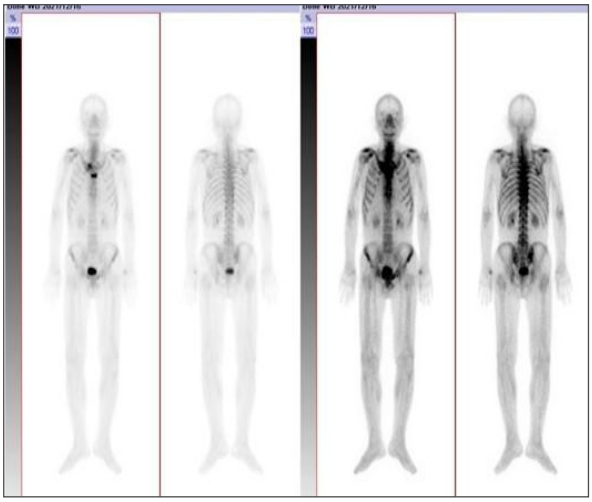

Figure 2. *Whole-body bonescan anterior and posterior images show increased tracer uptake in the right sternoclavicular joint and sternum. Increased uptake was also observed in the shoulders, which was considered to be indicative of osteoarthritis.*

One month after starting NSAID, the patient presented with warm swelling, painful tension, and purpura of the fingers and lower extremities. Four days later, he visited our hospital complaining of exertional dyspnea. Laboratory testing showed a WBC of 9.0×10^9 per L and CRP level of 0.38 mg·L^{-1}. Biochemical data demonstrated a D-dimer level of 8.1 μg·mL^{-1}. Arterial blood gas analysis at room air revealed hypoxemia (artery oxygen partial pressure of 43.9 torr). Despite the suspicion of pulmonary thromboembolism, enhanced CT was avoided due to renal insufficiency complications (creatinine 2.28 mg·dL^{-1}).

Transthoracic echocardiography showed a normal-sized left ventricle with mild systolic dysfunction, moderate-to-severe right ventricular (RV) enlargement with moderate dysfunction, and severe RV hypertrophy. It revealed a sign of RV load as a high tricuspid regurgitation peak gradient (estimated at 80 mmHg) with out systolic flattening of the interventricular septum. Lung ventilation/perfusion (V/Q) scintigraphy (99mTc – macroaggregated albumin) revealed multiple segmental ventilatory-blood mismatches in the lungs (Fig. 3). Right heart catheterization confirmed PH (mean pulmonary artery pressure, 45 mmHg; pulmonary capillary wedge pressure, 8 mmHg). As systemic arterial stiffness was measured using thecardio-ankle vascular index (CAVI) as an early marker of CTEPH [4], the CAVI was 11.4, which is high for the patient's age. Skin biopsy of the left lower extremity suggested neutrophilic dermatitis, consistent with pyoderma gangrenosum (PG). Based on the diagnosis of SAPHO complicated by CTEPH and PG, the patient was started on anticoagulants, including warfarin and domiciliary oxygen therapy.

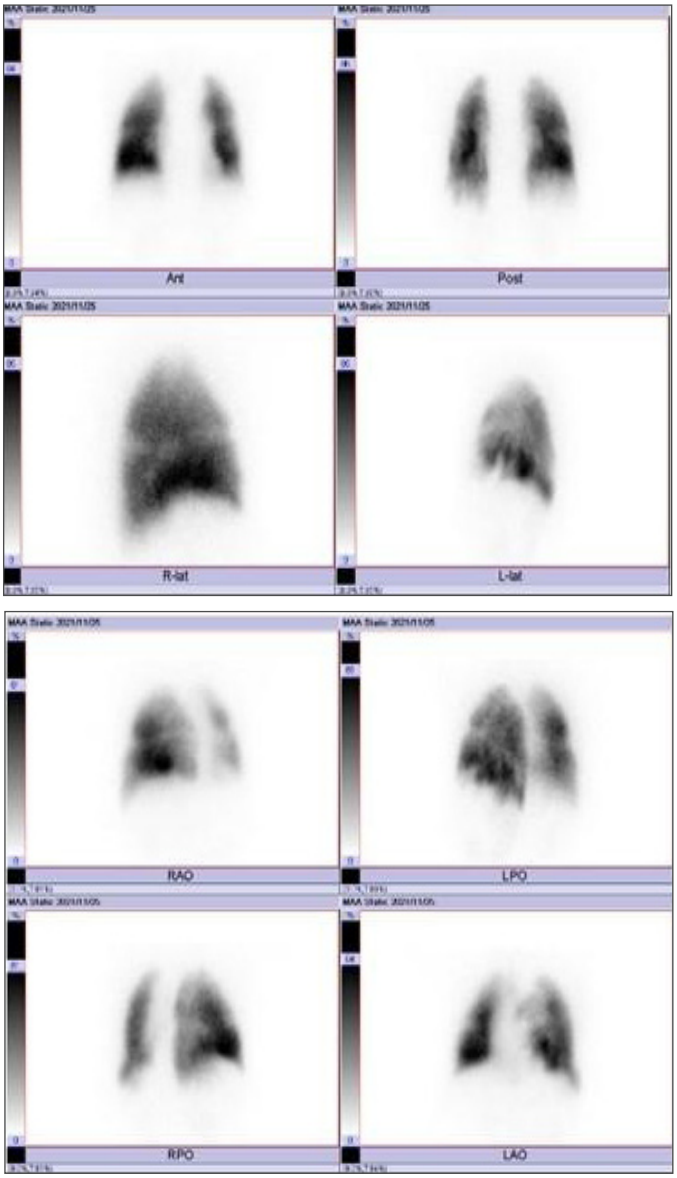

Figure 3. *Ventilation-perfusion scintigraphy (99m-technetium macroaggregate albumin) shows multiple segmental and subsegmental defects in normally ventilated lungs. ANT : anterior, POS: posterior, RAD: right anterior oblique, RPO: right posterior oblique, LAO: left anterior oblique, LPO: left posterior oblique.*

One week later, renal function was recovered, and contrast-enhanced CT revealed compression of the left subclavian vein by the clavicular hyperostosis and tapering of the peripheral pulmonary artery but no signs of pouch defects, webs and bands, intimal irregularities, abrupt narrowing, or complete obstruction (Fig. 4). The patient was finally diagnosed with adult-onset PPAS. Anticoagulant use seemed to lead to the development of exertional dyspnea with reduced D-dimer levels. The patient was scheduled to undergo balloon pulmonary angioplasty. However, 2 months later, he died at home of sudden dyspnea. The patient's family refused postmortem procedures for emotional reasons.

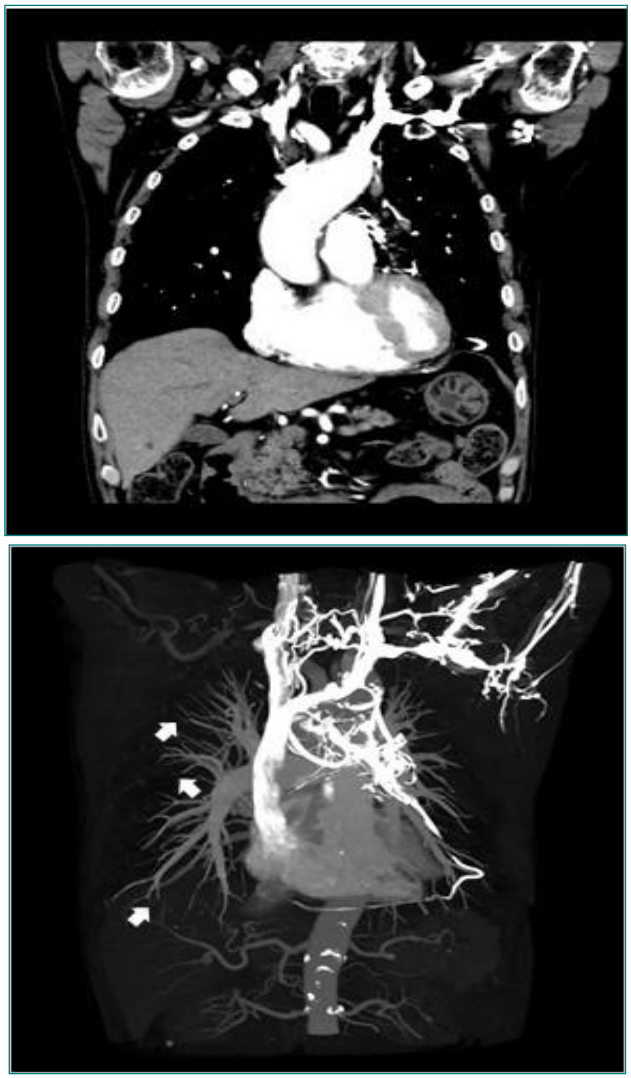

Figure 4. *Contrast-enhanced computed tomography (CT) (upper panel) and digital subtraction CT angiography of the chest (lower panel) .*
Contrast-enhanced CT revealed compression of the left subclavian vein by the clavicular hyperostosis. Digital subtraction CT angiography shows tapering in the segmental pulmonary arteries of the right upper and lower lobes (arrow), but no signs of pouch defects, webs, and bands, intimal irregularities, abrupt narrowing, or complete obstruction.

3. Discussion

SAPHO syndrome complicated by PPAS is a rare acquired disease of unknown etiology. We report a case of a patient who died suddenly due to a speculated cause of PH. Initially, we suspected as CTEPH, because of multiple segmental ventilation-perfusion mismatches.

CTEPH is a rare complication of pulmonary embolism, characterized by the presence of multiple perfusion defects on V/Q scans, evidence of organized emboli on CT pulmonary angiogram and pulmonary angiography.

Three cases of SAPHO syndrome complicated by PPAS mimicking CTEPH, including the one described in this study, have been recorded (Table 1). From the literature view, there are no characteristic findings as for the acquired PPAS in SAPHO syndrome. The underlying mechanism leading to the acquired PPAS was supposed to be systemic vasculitis. The cases with acquired PPAS were reported to be complicated

with tumors, constrictive pericarditis, tuberculosis, Takayasu's arteritis [5,6], Behçet disease [7], and ANCA-associated vasculitis [8,9]. Although the pathophysiology of SAPHO syndrome is still unclear, auto-inflammatory illness is the common consensus. Numerous pro-inflammatory factors, including tumor necrosis factor-α interleukins (IL-1, IL-17, and IL-23) may have a role in the pathophysiology of SAPHO syndrome. As chronic inflammation-related PH phenotype was induced by IL-17A-dependent mechanisms [10], this systemic inflammation may contribute to the acquired PPAS in SAPHO syndrome.

In our case, PG, the cutaneous manifestation of SAPHO disease, was also complicated with SAPHO syndrome. PG is extremely rare, and a potentially fatal chronic neutrophilic inflammatory dermatosis that is frequently linked to systemic disease [11]. With a favorable long-term prognosis, SAPHO syndrome is a pertinent and stable entity [12]. However, we experienced a lethal case of SAPHO syndrome with PPAS and PG. When a case of SAPHO syndrome complicated with some auto-inflammatory manifestations including PPAS and PG, we should need to pay an attention to the risk of worse prognosis.

Table 1. *SAPHO syndrome complicated with peripheral pulmonary artery stenosis*

Series	Sex	Age	mPAP	Skin lesions	Treatment
Kamado et al. 2020 [1]	F	68	25 mmHg	N.A.	BPA
Norikane et al. 2022 [2]	M	37	N.A.	N.A.	BPA
Present	M	83	45 mmHg	PG	Anti-coagulant, NSAID

F, female; M, male; BPA, balloon pulmonary angioplasty; mPAP, mean pulmonary artery pressure; N.A., not available; NSAID, nonsteroidal anti-inflammatory drug; PG, pyoderma gangrenosum.

4. Conclusion

According to our case, SAPHO syndrome can result in heterogeneous phenotypes, such as PPAS and PG as the complication. Thus, patients with SAPHO complicated with systemic inflammation should be closely monitored for signs and symptoms of PH.

Conflict of Interest

The authors have no conflict of interest to declare.

Ethical Approval

Approval has been obtained from Yonago Medical Center Ethical Committee (No. 0508-01).

Consent

A written informed consent has been taken from the patient's family for publication of this report.

Author Contribution

K.T: Writing the manuscript, reviewing the literature, and following up with final approval of the manuscript. M.Y., R.K., T.I., H.T., M.F., and S.S.: Literature review and final approval of the manuscript.

A.Y.: Final approval of the manuscript.

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