

CT evaluation of systemic artery to pulmonary artery fistula: an underdiagnosed disease in patients with hemoptysis

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Background: Systemic artery to pulmonary artery fistula (SA-PAF) is an uncommon disease which is often incidentally diagnosed during evaluation of hemoptysis patients. The aim of our study was to describe the cases of SA-PAF in our institution and to report the correlating clinical and radiological findings.

Methods: We reviewed 231 chest computed tomography (CT) scans performed in our institution due to hemoptysis from January 2020 to February 2023. In patients diagnosed with SA-PAF had their electronic medical records and CT images analyzed.

Results: In 231 patients, 19 (8.2%) of them had SA-PAF findings which was characterized by a peripheral nodular soft tissue opacity in the subpleural lung and traceable vascular structure in continuity with one or more peripheral pulmonary artery branches in CT. Etiology of each patient was categorized as either congenital (7, 36.8%), and acquired (12, 63.2%). The origins of SA-PAFs were 16 intercostal, two anterior mediastinal, and one costocervical artery. Eight of 19 patients did not show any associated intralobar imaging abnormalities, while bronchiectasis, cellular bronchiolitis, centrilobular emphysema, and pleura effusion were observed in 11 patients.

Conclusions: SA-PAF is a benign vascular anomaly which is frequently overlooked when evaluating hemoptysis by either clinician or radiologists but is an important factor in the differential diagnosis of patients with hemoptysis.

Keywords: Systemic artery to pulmonary artery fistula (SA-PAF); hemoptysis; computed tomography (CT); pulmonary arteriography; bronchial artery embolization (BAE)

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Introduction

Systemic artery-to-pulmonary artery fistula (SA-PAF) is an uncommon clinical entity. Patients with SA-PAF are usually asymptomatic; nevertheless, significant complications such as hemoptysis, pulmonary hypertension, congestive heart failure, and recurrent pneumonia have been reported (1). Among various symptoms, hemoptysis is common yet can be life-threatening (2). Bronchial artery embolization (BAE) is usually the first-line treatment in patients with pathologic bronchial arteries as bleeding focus, with symptoms ranging from blood-tinged sputum to life-threatening hemorrhage (3,4). Despite of high clinical success rate (70–99%) (5,6), BAE has a significant recurrence rate (10–57%) in patients with recurrent hemoptysis with various etiology (7-9), such as non-bronchial systemic arteries (10), SA-PAF (11), aspergillomas (12), and tuberculosis (Tb) (13,14).

SA-PAF has been traditionally diagnosed with conventional angiography. However, recent innovation of computed tomography (CT) enables non-invasive diagnosis of SA-PAF prior to invasive procedure. Furthermore, SA-PAF is often misdiagnosed as either arteriovenous malformation or pulmonary embolism in CT, which are often seen as an aberrant pulmonary artery filling defect (1,15). The reported CT findings of SA-PAF are either nodular or diffuse soft tissue opacity in the lung periphery abutting the pleura, or hypertrophy of intercostal or other systemic arteries connected to peripheral pulmonary arteries (16).

Chronic inflammatory process involving pleura is known

Highlight box

Key findings

 Systemic artery to pulmonary artery fistula (SA-PAF) might be one of the possible underdiagnosed etiologies of hemoptysis, especially in tuberculosis (Tb) or non-tuberculous mycobacteria (NTM) endemic areas.

What is known and what is new?

- SA-PAF is an uncommon disease which is incidentally diagnosed during evaluation of patient with hemoptysis.
- However, it is far more common than expected, and might be one of the possible underdiagnosed etiologies of hemoptysis, especially in Tb or NTM endemic areas.

What is the implication, and what should change now?

• Diagnosis of SA-PAF prior to conventional angiography might avoid unnecessary examinations or invasive diagnostic procedures and might serve as a starting point for treatment such as bronchial artery embolization. to cause non-bronchial systemic arterial supply from various arteries, including intercostal arteries, thoracic branches of the subclavian and axillary arteries, and diaphragmatic branches of inferior phrenic arteries. SA-PAF may be classified as either congenital or acquired. Congenital SA-PAF may result from functional activation by genetic or external influences of relatively dormant pre-capillary and post-capillary bronchopulmonary arterial anastomosis found in the normal lung (17). Acquired causes include chest trauma, thoracic surgery, chronic thromboembolic disease, malignancy, and infections (18-21). SA-PAFs may also occur in within or outside the lung parenchyma, in the chest wall, or in the diaphragm (22). The most frequently involved vessels include internal mammary and intercostal arteries. SA-PAF is known to be exceedingly rare and underlying pathophysiology has not been completely understood. Diagnosis is often incidental as many patients are initially asymptomatic (23).

Only limited number of SA-PAF cases have been published in the English literature, and SA-PAF is currently described as an extremely rare disease. However, after reviewing several incidental SA-PAF cases diagnosed in our institution during hemoptysis evaluation, we hypothesized that this condition could be overlooked or underdiagnosed by both clinician and radiologist. Therefore, the aim of our study was to report the cases of SA-PAF in our institution and to describe the associated clinical and radiological findings. We present this article in accordance with the STROBE reporting checklist (available at https://jtd. amegroups.com/article/view/10.21037/jtd-23-861/rc).

Methods

Patient selection

The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by the institutional review board of Samsung Medical Center (IRB, file No. 2023-02-107) and individual consent for this retrospective analysis was waived. We searched electronic medical records from January 2020 to February 2023, who visited Samsung Medical Center (a tertiary referral hospital located in Seoul, South Korea) due to hemoptysis, and found 307 patients who performed chest CT scans. Of 307 patients, 75 (24%) patients with only non-contrast CT, and one pediatric patient were excluded. CT images of total 231 patients were reviewed and found 19 (8.2%) cases of SA-PAF based on CT

imaging.

Clinical and pathologic data

The clinicopathologic data of patients were retrospectively reviewed for the following variables: age, sex, amount of hemoptysis (mild, <100 mL/day; moderate, 100–300 mL/day; massive, >300 mL/day), follow-up period (months), etiology (congenital or acquired), and treatment history if exists.

Image acquisition

CT studies from various helical CT scanners (from 16- to 64-MDCT scanners) from several vendors were performed. The scanning parameters were 120 kVp and 100 to 150 mAs under automatic exposure control; beam width, 10 to 20 mm; and rotation time, 0.3 to 0.4 seconds. CT image data were reconstructed using standard soft-tissue algorithms, with a section thickness of 2.5 to 3.0 mm for axial images. Both contrast and noncontrast CT scans were obtained. IV contrast medium injection was given in all patients: 1.5 mL/kg of body weight of iobitridol (300 mgI/mL; Xenetics, Guerbet) was injected at an infusion rate of 3 mL/s using a power injector (MCT Plus, Medrad). Both mediastinal (width, 400 HU; level, 20 HU) and lung (width, 1,500 HU; level, -700 HU) window settings were adapted during image review.

Image interpretation

CT findings were reviewed by three radiologists with thoracic CT interpretation experience of 6, 15, and 16 years, respectively, and decisions about CT findings were reached by consensus. The review included the presence of SA-PAF, location, number, diameter (maximum, in mm), and origin of culprit artery. Lesion diameter was determined as the largest diameter on the transverse image where the center of the lesion was scanned. The origin of culprit artery was recorded after tracing the vessel at mediastinal window in serial transverse images. We defined SA-PAF as the presence of hypertrophied intercostal or other systemic arteries which was continuous with subsegmental branches of pulmonary arteries at the lung periphery abutting pleura.

Statistical analysis

The presentation of continuous variables included the mean and range, while categorical variables were expressed as counts and percentages (%). All statistical analyses were performed using SPSS (version 25.0).

Results

Patient characteristics

We included a total of 231 adult patients with hemoptysis who underwent chest CT exams. SA-PAF was found in 19 patients (8.2%; summarized in Table 1) and absent in 212 patients (91.8%). The average age of SA-PAF patients was 67±14.8 years, including 12 (63.2%) men and 7 (36.8%) women (Table 2). The average CT follow-up period was 45±59.3 months. Underlying comorbidities of each patient were categorized as Tb (2, 16.7%), non-tuberculous mycobacteria (NTM) (4, 33.3%), Tb/NTM co-infection (3, 25%), thoracic malignancy (4, 33.3%), chronic cavitary pulmonary aspergillosis (CCPA) (2, 16.7%), and extrathoracic disease [chronic heart disease (1, 5.2%), extrathoracic malignancy (7, 36.8%)] (Table 2). The proportions of mild (<100 mL/day), moderate (100-300 mL/day) and massive (>300 mL/day) hemoptysis were as follows: 15 (78.9%) mild, 3 (15.8%) moderate, and 1 (5.2%) massive.

Etiology

Etiology of each patient of SA-PAF was classified as congenital (7, 36.8%), and acquired (12, 63.2%). In acquired patients, potential causes were observed as follows: NTM (4, 33.3%), CCPA (1, 8.3%), cancer (2, 16.7%), Tb (2, 16.7%), and Tb-NTM co-infection (3, 25%). SA-PAF patients without any clinical history or abnormal CT imaging features except SA-PAF were considered as congenital type (n=7).

CT characteristics of SA-PAF

The origins of SA-PAF were 16 (84.2%) intercostal, 2 (10.5%) anterior mediastinal, and 1 (5.2%) costocervical artery. The location of each SA-PAF lesion was as follows: RUL (3, 15.8%), RML (4, 21.1%), RLL (4, 21.1%), LUL (6, 28.6%), and LLL (2, 10.5%). Of 19 cases, nine (47%) cases were located at upper lobes, 4 (21%) cases were located at mid-lung zone (right middle lobe, left upper lobe lingular division), and 6 (32%) cases were in lower lobes. The average diameter of SA-PAF was 2±1.55 mm, and in all cases, the number of SA-PAF was single. SA-PAF in CT

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Sex	Age (years)	Follow-up (months)	Hemoptysis [†]	Etiology	Culprit artery origin	Location	Segment	Size (mm)	Treatment
М	60	10	Mild	Congenital	Intercostal	LLL	Posterobasal	1	N
Μ	62	76	Mild	Acquired (NTM)	Intercostal	LUL	Anterior	2	Ν
Μ	87	28	Mild	Acquired (CCPA)	Intercostal	LUL	Apicoposterior	2	Ν
F	70	27	Mild	Acquired (cancer)	Anterior mediastinal	LUL	Lingular	1	Ν
F	66	0	Mild	Acquired (NTM)	Intercostal	LUL	Posterior	2	Ν
Μ	68	218	Moderate	Congenital	Intercostal	LUL	Lingular	5	Ν
М	58	0	Massive	Acquired (Tb/NTM)	Intercostal	LUL	Apicoposterior	1	Y (BAE)
F	91	32	Mild	Congenital	Intercostal	RLL	Posterobasal	4	Ν
М	19	12	Moderate	Acquired (cancer)	Intercostal	RLL	Anterobasal	2	Ν
F	80	15	Mild	Acquired (Tb/NTM)	Intercostal	RLL	Posterobasal	1	Ν
F	80	154	Mild	Congenital	Intercostal	RML	Posterior	3	Ν
F	53	0	Mild	Acquired (NTM)	Intercostal	RML	Posterior	1.5	Ν
F	66	126	Moderate	Acquired (Tb/NTM)	Intercostal	RML	Medial	2	Ν
М	64	16	Mild	Acquired (Tb)	Anterior mediastinal	RML	Medial	2	Ν
М	72	0	Mild	Congenital	Intercostal	RUL	Apical	4	Ν
М	65	6	Mild	Congenital	Costocervical	RUL	Apical	1	Y (BAE)
М	78	0	Mild	Acquired (Tb)	Intercostal	RUL	Apical	2	Ν
Μ	68	56	Mild	Congenital	Intercostal	RLL	Superior	7	Y (BAE)
Μ	66	75	Mild	Acquired (NTM)	Intercostal	LLL	Posterobasal	3	Ν

Table 1 Clinical and demographic features of systemic artery to pulmonary artery fistulas patients

[†], massive hemoptysis: a single event of maximal bleeding volume ≥300 mL/day or ≥100 mL once; moderate hemoptysis: 100–300 mL/day; mild hemoptysis: <100 mL/day. LLL, left lower lobe; N, no; NTM, non-tuberculous mycobacteria; LUL, left upper lobe; CCPA, chronic cavitary pulmonary aspergillosis; Tb, tuberculosis; BAE, bronchial arterial embolization; Y, yes; RLL, right lower lobe; RML, right middle lobe; RUL, right upper lobe.

were mostly seen as subpleural nodular vascular enhancing structure with fistulous formation between hypertrophied intercostal or other systemic arteries to peripheral pulmonary arteries (*Figures 1-3*).

Associated intralobar CT imaging findings

Of 19 cases, 8 (42%) cases did not show any abnormal imaging features within same lobe of SA-PAF. In 11 (58%) cases, there were abnormal imaging findings as follows: aspirated blood in form of centrilobular ground-glass opacity (1, 5%), bronchiectasis only (5, 26%), bronchiectasis with cellular bronchiolitis (2, 11%), centrilobular emphysema (2, 11%), and bronchiectasis with pleural effusion (1, 5%). In 6 (31.6%) patients, bronchial artery hypertrophy (>2 mm in

axial diameter) was observed (Table 2).

Treatment and follow-up

Of 19 patients with SA-PAF, 16 patients were managed conservatively, and 3 patients attempted BAE (1 mild, 1 moderate, 1 massive hemoptysis). Only one patient underwent embolization, while in two patients only pulmonary arteriography were performed. Due to high systemic arterial pressure, existing SA-PAF was not visualized during conventional angiography (*Figure 2E*). During the follow-up period, no additional hemoptysis occurred in patients with previous BAE attempts. In all patients, median CT follow-up period was 16 months (range, 0–218 months).

 Table 2 Patient characteristics of systemic artery to pulmonary artery fistulas

Clinicodemographic variables	All patients (n=19)				
Age, years	67 [19–91]				
Gender, male	12 (63.2)				
Comorbidities					
Underlying lung disease					
Tuberculosis	2 (10.5)				
Nontuberculous mycobacterial disease	4 (21.1)				
Tuberculosis/nontuberculous mycobacterial disease co-infection	3 (15.8)				
Nontuberculous mycobacterial disease	4 (21.1)				
Thoracic malignancy	4 (21.1)				
Chronic cavitary pulmonary aspergillosis	2 (10.5)				
Other comorbidities					
Chronic heart disease	1 (5.2)				
Extrathoracic malignancy	7 (36.8)				
Computed tomography findings					
Bronchiectasis	8 (42.1)				
Pleural effusion	1 (5.2)				
Emphysema	2 (10.5)				
Bronchiolitis	2 (10.5)				
Bronchial artery hypertrophy (>2 mm)	6 (31.6)				

Data are presented as median [interquartile range] or number (%).

Discussion

In this study, we retrospectively collected data on clinical features and CT imaging findings in patients who complained of hemoptysis and 19 cases of SA-PAFs (8.2%) were incidentally diagnosed. Among 19 cases, only 4 (21%) CT reports accurately mentioned the presence of SA-PAFs. We predicted possible underdiagnosis of SA-PAFs, and after thorough review of previous CT exams, 15 additional cases were observed. Underdiagnosis bias of this disease might end up far less frequent treatment (i.e., BAE) compared to true indication.

In our study, the most common cause of hemoptysis in patients were Tb (16.7%), NTM (33.3%), and Tb-NTM co-infection (25.0%). This result was predictable considering high prevalence of mycobacterial infection in South Korea (14). Also, 13 of 19 cases (68%) were present in upper and mid lung zones, which was predictable based on the high prevalence of Tb and NTM endemic infections. In our study, 7 out of 19 patients were classified as congenital SA-PAF due to lack of concurrent parenchymal lung disease seen in CT. However, considering high prevalence of Tb and NTM in Korean population, we carefully hypothesized that previous indolent or latent Tb infection causing microvascular injury of bronchial or pulmonary arterioles in subpleural lung, which is not visible in CT, leading to the development of SA-PAF.

The exact underlying pathophysiology of SA-PAF has not been known. It is known that within normal lung, there is bronchial artery to pulmonary artery communications measuring up to 500 µm (24,25). Chronic pleural inflammation causes decreased pulmonary arterial perfusion and overproduction of angiogenic growth factors, leading to systemic artery development (17). These friable pulmonary arteries might be exposed to systemic arterial pressure resulting in hemoptysis. Until now, no published studies covered the possible relationship between the presence of SA-PAF and hemoptysis. Based on our experience, we assumed that no direct correlation would exist. However, when hemoptysis occurs and incidental SA-PAF is observed in CT prior to conventional angiography, it would be reasonable to assume SA-PAF as a possible source of bleeding and serve as a great starting point for embolization if needed.

This study was one of the first to evaluate chest CT scans for hemoptysis evaluation and studied SA-PAF imaging findings, and the largest reported case series of SA-PAF from a single institution. Although symptoms and CT findings of SA-PAF have been described in the previous literature, there is no description of its true incidence in the general population or in hemoptysis patients. Although we cannot directly extrapolate our findings to the true incidence in general patients with hemoptysis, we found a proportion of 8.2% SA-PAFs in patients with hemoptysis who underwent chest CT for evaluations.

Recent study by Zhang *et al.* have reported clinical characteristics and outcomes of BAE performed in 184 SA-PAF cases (26). They defined SA-PAF based on radiographic appearance on digital subtraction angiography (DSA) with characteristics of an axifugal blood flow, smaller sized caliber with denser contrast filling, sharper vessel wall borders, and dichotomous branching patterns. In contrast, our study was the first to report multiple SA-PAF cases diagnosed solely based on contrast chest CT by identification of continuous traceable fistulous connection



Figure 1 A 55-year-old male with incidental finding of right upper SA-PAF during hemoptysis evaluation. Axial (A,B) and coronal (C,D) CT images obtained demonstrates hypertrophy of costocervical branch of right subclavian artery with pulmonary artery shunt (white arrows). (E) Right subclavian arteriogram demonstrated tortuous shunt vessel between right costocervical trunk (white arrow) and pulmonary artery (black arrow), which was embolized with diluted glue material and Gelfoam. SA-PAF, systemic artery-to-pulmonary artery fistula; CT, computed tomography.

between systemic and pulmonary arteries.

During treatment planning of hemoptysis, identification of SA-PAF based on contrast chest CT prior to procedure would be helpful, providing a reasonable starting point. However, if pulmonary arteriography was only performed (*Figure 2E*), due to high pressure from systemic arteries, existing SA-PAFs would not be visualized on DSA, preventing further necessary treatment. Therefore, systemic arteriography should be performed first to exactly localize SA-PAFs and to treat hemoptysis.

Our study has several limitations. First, our analysis was performed in retrospective setting. Second, only three of 19 cases underwent conventional angiography and only one patient received embolization. However, we were able to confidently diagnose SA-PAFs prior to invasive procedures solely based on CT imaging studies. Third, no exact explanation was provided for possible correlation between actual hemoptysis and the presence of SA-PAFs, leading



Figure 2 A 68-year-old male with previous tuberculosis history showed incidental right middle SA-PAF during hemoptysis work-up. Axial (A-C) and coronal (D) CT images demonstrated SA-PAF with hypertrophic intercostal arteries at subpleural lung of right lower lobe superior segment (white arrows), which was thought to be pulmonary arteriovenous malformation at first. (E) Right pulmonary arteriography was performed but failed to demonstrate known SA-PAF due to high systemic pressure from hypertrophied intercostal arteries. SA-PAF, systemic artery-to-pulmonary artery fistula; CT, computed tomography.



Figure 3 A 65-year-old male with no previous medical history showed incidental right upper SA-PAF in contrast enhanced MR image. (A,B) Coronal noncontrast CT images (lung window) demonstrated engorged SA-PAF (arrow) in right upper lobe. (C) In MIP coronal MR image, fistulous connection of pulmonary artery (arrow) and costocervical trunk (arrowhead) was well-demonstrated. SA-PAF, systemic artery-to-pulmonary artery fistula; CT, computed tomography; MIP, maximum intensity projection.

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to reasonable assumptions based on clinical history and imaging findings.

Conclusions

In conclusion, we herein described 19 cases of SA-PAFs observed during evaluation of spontaneous hemoptysis. Diagnosis of SA-PAF prior to conventional angiography might avoid unnecessary examinations or invasive diagnostic procedures and might serve as a starting point if treatment requires. Furthermore, SA-PAF might be one of the possible underdiagnosed etiologies of hemoptysis, especially in Tb or NTM endemic areas.

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Footnote

Reporting Checklist: The authors have completed the STROBE reporting checklist. Available at https://jtd. amegroups.com/article/view/10.21037/jtd-23-861/rc

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Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://jtd.amegroups. com/article/view/10.21037/jtd-23-861/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by the institutional review board of Samsung Medical Center (IRB, file No. 2023-02-107) and individual consent for this retrospective analysis was waived.

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