

1 **Case reports**

2 **Pulmonary artery pseudoaneurysm caused by *Streptococcus constellatus***

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13 *Running title: S. constellatus*-induced Pulmonary artery pseudoaneurysm

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19

20 **Abstract**

21           We report a rare case of mycotic pulmonary artery pseudoaneurysm (PAP) secondary  
22 to lung abscess due to *Streptococcus constellatus*. PAP was confirmed by the pathological  
23 findings of the pseudoaneurysm, the presence of bacteria, and the microbiological analysis.  
24 PAP is uncommon, but it is important to recognize this condition because PAP can lead to fatal  
25 hemoptysis.

26

27 **Key words:** Pulmonary artery pseudoaneurysm, *Streptococcus constellatus*, hemoptysis

28

29 **Introduction**

30 Life-threatening massive hemoptysis accompanied by infection sometimes occurs in  
31 patients with bronchiectasis and pulmonary tuberculosis, but infection-associated hemorrhage  
32 from pulmonary artery pseudoaneurysms (PAPs) is rare. Here, we report a case of infectious  
33 PAP confirmed by pathological and microbiological examinations in a patient who presented  
34 with hemoptysis.

35

36 **Case report**

37 A 63-year-old Japanese man with hypertension had a 10-day history of cough and  
38 fever. He was an ex-smoker and had had pneumonia when he was 58 years old. Chest  
39 computed tomography (CT) revealed an infiltration in the right upper and middle lobes. He  
40 was diagnosed with pneumonia and recovered well after taking oral levofloxacin for 2 weeks.  
41 However, a follow-up CT scan performed a month later revealed a persistent mass lesion, and  
42 he was scheduled for admission to our hospital for an extensive examination that would  
43 include investigations for malignancy. However, before admission, he visited our emergency  
44 department because of sudden massive hemoptysis.

45 His body temperature was 37.3°C, blood pressure was 128/81 mmHg, pulse rate was  
46 126 beats/min, and oxygen saturation was 96% in room air. Rhonchi were heard in the right  
47 middle chest during auscultation. Laboratory analysis determined a white blood cell count of

48 10,100/ $\mu$ L, a hemoglobin level of 10.1 g/dL, and a C-reactive protein level of 11.83 mg/dL. To  
49 prevent further hemoptysis, intravenous hemostatic agents were immediately administered and  
50 complete bed rest was prescribed.

51 An enhanced CT scan showed an enlarged mass lesion enclosing an aneurysm (Fig. 1),  
52 but embolization was not performed because the aneurysm was considered inaccessible.  
53 Although no bacterial infection was detected by microbiological examinations, including  
54 sputum and blood cultures, intravenous tazobactam/piperacillin (13.5 g/day) was administered  
55 for the possibility of lung abscess. Improvement of laboratory inflammatory parameters was  
56 seen, but surgical management was required because of recurrent hemoptysis. The patient  
57 underwent right middle lobectomy and right upper lobe segmentectomy.

58 The major pathological findings were pneumonia with organization and multiple small  
59 abscess formations (Fig. 2). Detailed examination uncovered destruction of vessel walls at the  
60 site of the severe inflammation and around the abscess, and fibrin deposition from fresh blood  
61 around a hematoma. These findings indicated pseudoaneurysm associated with inflammation.  
62 There was no evidence of malignancy.

63 The surgical tissue in anaerobic transport medium was inoculated onto HK semisolid  
64 medium (Kyokuto Pharmaceutical Industrial Co., Tokyo, Japan) and cultured under anaerobic  
65 condition. On postoperative day 8, the culture became positive. The pathogen was identified as  
66 *Streptococcus constellatus* by a biochemical identification method using the Phoenix100

67 system (Becton Dickinson, Franklin Lakes, NJ) and exhibited good susceptibility to penicillins.  
68 After 20 days' treatment with tazobactam/piperacillin, the patient was discharged and made an  
69 uneventful recovery.

70

## 71 **Discussion**

72 Pulmonary artery aneurysms (PAAs) and PAPs are uncommon but important, as  
73 diagnostic and therapeutic procedures can affect the associated morbidity. An aneurysm is  
74 defined as a permanent dilatation of blood vessels that involves all layers of the vessel wall. In  
75 contrast, a pseudoaneurysm is a hematoma involving destruction of the entire vessel wall and  
76 surrounding tissues, and is therefore associated with a higher risk of rupture.

77 PAAs are commonly associated with congenital anomalies, and are usually observed  
78 in a major pulmonary artery such as the pulmonary artery trunk and major branches. Acquired  
79 PAAs are associated with pulmonary hypertension and infections, including tuberculosis,  
80 syphilis, and endocarditis. However, the incidence of infection-associated PAAs has decreased  
81 due to progress in the treatment of infectious diseases. In contrast to PAAs, PAPs are typically  
82 caused by traumatic events, including catheterization procedures, and in some cases are  
83 associated with chronic lung diseases, such as cavitary pulmonary disease and bronchiectasis  
84 (1). PAPs associated with tuberculosis are known as Rasmussen aneurysms (1), but PAPs  
85 caused by non-tuberculous infections are very rare.

86 Lung abscess is a less common cause of massive hemoptysis than active pulmonary  
87 tuberculosis and bronchiectasis. In cases of hemoptysis associated with lung abscess,  
88 radiologically visualized PAPs can be observed within the abscess (2-3). Non-tuberculosis  
89 microorganisms that have been implicated in PAAs include *Staphylococcus aureus* (4), viridans  
90 Streptococci (4-5), *Enterococcus* species (4), and *Candida albicans* (6). However, these  
91 previous reports included microorganisms that were not detected directly at the site of the  
92 infection. Therefore, our case differs in that it is a confirmed case of infectious PAP based on  
93 the pathological findings of the pseudoaneurysm, the presence of bacteria, and the  
94 microbiological analysis.

95 *S. constellatus* is a component of the normal flora of the human oral cavity, and has  
96 been recognized as a cause of pulmonary infections (7). Identification of *S. constellatus* is  
97 sometimes difficult for the clinical laboratory because of requirement of anaerobic condition  
98 and long culture. The anginosus group, formerly the *S. milleri* group, includes *S. anginosus*, *S.*  
99 *intermedius*, and *S. constellatus*, and these organisms are often isolated from abscesses.  
100 However, the frequency with which each species of the anginosus group is associated with  
101 abscess varies. Claridge reported that approximately 80% of *S. intermedius* and *S. constellatus*  
102 isolates, but only 19% of *S. anginosus* isolates, were associated with abscess (8). Thus,  
103 continuous invasion of *S. constellatus* could lead to the destruction of the pulmonary arterial  
104 wall.

105           The case we report was initially suspected to be lung cancer because of the persistent  
106 mass opacity after antibiotic therapy. Therefore, hospital admission was scheduled so that  
107 pathological diagnosis could be performed by endoscopic biopsy. As we detected an aneurysm  
108 on contrast CT after his arrival at the emergency department with massive hemoptysis, we did  
109 not need to perform that invasive procedure. This is indeed fortunate, as a fatal case of  
110 pulmonary artery aneurysm hemorrhage after endobronchial lung biopsy has been reported (9).

111           PAPs are uncommon but important, as PAP can lead to fatal hemoptysis. In cases of  
112 suspected lung cancer accompanied by prolonged inflammatory findings, non-invasive  
113 examinations, such as contrast CT scanning, which can provide information on the coexistence  
114 of pseudoaneurysms, should be performed before biopsy.

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116   **Conflict of Interest**

117   None.

118

119 **References**

- 120 1. Sbano H, Mitchell AW, Ind PW, Jackson JE. Peripheral pulmonary artery  
121 pseudoaneurysms and massive hemoptysis. *AJR Am J Roentgenol.* 2005;184:1253-9.
- 122 2. Shin TB, Yoon SK, Lee KN, Choi JS, Kim YH, Sung CG, et al. The role of pulmonary CT  
123 angiography and selective pulmonary angiography in endovascular management of pulmonary  
124 artery pseudoaneurysms associated with infectious lung diseases. *J Vasc Interv Radiol.*  
125 2007;18:882-7.
- 126 3. Khalil A, Parrot A, Nedelcu C, Fartoukh M, Marsault C, Carette MF. Severe hemoptysis of  
127 pulmonary arterial origin: signs and role of multidetector row CT angiography. *Chest.*  
128 2008;133:212-9. doi:10.1378/chest.07-1159.
- 129 4. Tan LK, Powrie DJ, Rowland R, Cropley I, Lipman M. Fever and haemoptysis in an  
130 injecting drug user. *Eur Respir J.* 2007;29:1061-3. doi: 10.1183/09031936.00139206.
- 131 5. Haranaga S, Teruya H, Nakamura H, Higa F, Tateyama M, Fujita J. Pulmonary artery  
132 pseudoaneurysm secondary to lung abscess. *Intern Med.* 2009;48:2159-60.  
133 doi.org/10.2169/internalmedicine.48.2610.
- 134 6. Mody GN, Lau CL, Bhalla S, Picus D, Ritter J, McCardle T, et al. Mycotic pulmonary  
135 artery pseudoaneurysm. *J Thorac Imaging.* 2005;20:310-2.
- 136 7. Shinzato T, Saito A. The *Streptococcus milleri* group as a cause of pulmonary infections.  
137 *Clin Infect Dis.* 1995;21:S238-43. doi: 10.1093/clind/21.Supplement\_3.S238.
- 138 8. Claridge JE, 3rd, Attorri S, Musher DM, Hebert J, Dunbar S. *Streptococcus intermedius*,  
139 *Streptococcus constellatus*, and *Streptococcus anginosus* ("Streptococcus milleri group") are of  
140 different clinical importance and are not equally associated with abscess. *Clin Infect Dis.*  
141 2001;32:1511-5. doi: 10.1086/320163
- 142 9. Dransfield MT, Johnson JE. A mycotic pulmonary artery aneurysm presenting as an  
143 endobronchial mass. *Chest.* 2003;124:1610-2. doi: 10.1378/chest.124.4.1610.

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146 Figure 1. Contrast chest CT scan on admission

147 The mass lesion in the right middle lobe contains a low-density area with a pulmonary artery  
148 aneurysm (white arrow).

149

150 Figure 2. Pathological findings of the excised lung

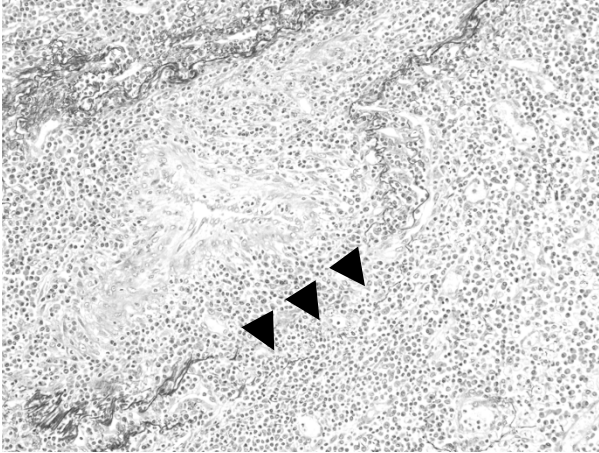
151 In the Elastica van Gieson–stained sections (A, original magnification  $\times 100$ ), multiple small  
152 abscess formations with complete destruction of the vessel wall layers (arrowheads) were  
153 observed. In the Gram-stained sections (B, original magnification  $\times 1000$ ), Gram-positive cocci  
154 (white arrows) were observed in the abscess lesions around the pseudoaneurysmal changes.

Figure 1



Figure 2

A



B

