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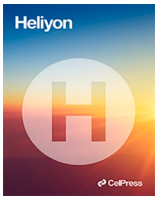

Case report

Giant pulmonary artery aneurysm associated with SARS-CoV-2 infection and Actinomyces odontolyticus sepsis: A case report

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ABSTRACT

Giant septic pulmonary artery aneurysms (PAAs) are rare but important entities, with few cases having been reported worldwide. Early diagnosis and prompt treatment are crucial in the management of such cases. We report a 56-year-old female patient presenting with fatigue, nausea and vomiting who was first diagnosed with diabetic ketoacidosis (DKA) and developed life-threatening giant infectious PAA secondary to SARS-CoV-2 infection and *Actinomyces odontolyticus* sepsis. The patient did not develop any specific symptoms, and enhanced computed tomography (CT) revealed a massive PAA of 5.6 × 4.9 cm in size at the left pulmonary hilar with normal pulmonary artery (PA) pressures. After multidisciplinary discussion and after considering the critical condition accompanied by sepsis increased the risk of surgery, endovascular treatment was the first therapy of choice for the patient; nevertheless, the patient ultimately opted for hospice care. This case report aims to raise awareness of PAAs, which are rare but potentially fatal complications of infectious diseases such as COVID-19 pneumonia and *Actinomyces odontolyticus* sepsis.

1. Introduction

Pulmonary artery aneurysms (PAAs) are rare conditions with a high mortality rate, and few cases have been reported in patients with severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) infection [1,2]. Acquired PAAs are thought to result from infections, malignancy, vascular injury and vasculitis that cause a local inflammatory response in the arterial wall [3]. The common symptoms of coronavirus disease 2019 (COVID-19) pneumonia are respiratory tract symptoms such as fever, cough, fatigue and dyspnea, but in severe cases, patients can develop vascular endothelial injury, severe pneumonia and systemic inflammatory response syndrome (SIRS) [4,5]. A. odontolyticus is a gram-positive facultative anaerobic bacterium that colonizes the oral cavity, respiratory tract and gastrointestinal tract [6]. *Actinomyces odontolyticus* infection is generally an opportunistic infection that frequently occurs in immunosuppressed patients [6]. *Actinomyces odontolyticus* sepsis is very rare in routine clinical practice, especially in combination with SARS-CoV-2 infection, and contributes to giant PAA [7].

Here, we describe the case of a 56-year-old female presenting with fatigue, nausea and vomiting and was diagnosed with diabetic

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ketoacidosis (DKA). She developed a life-threatening giant infectious PAA secondary to SARS-CoV-2 infection and *Actinomyces odontolyticus* sepsis. To our knowledge, this is the first reported case of PAA associated with SARS-CoV-2 infection and *Actinomyces odontolyticus* sepsis worldwide.

2. Case report

A 56-year-old female was admitted to the Department of Endocrinology with a chief complaint of fatigue, nausea and vomiting for 3 days and was diagnosed with diabetes mellitus (DM) for 9 years. Upon admission, laboratory tests showed a blood glucose level greater than 27.8 mmol/L, a white cell count of 17.9 × 10^9/L and a pH value of 6.95, and she was subsequently diagnosed with infection-associated metabolic DKA. She had no specific previous family history of autoimmune diseases or aneurysms, and she was completely vaccinated against SARS-CoV-2. The blood parameters at admission are shown in Table 1. Chest computed tomography (CT) at admission demonstrated bilateral pulmonary infection and regional multiple bullae, especially around the left pulmonary hilum (Fig. 1 ab). Meanwhile, on the day of admission, the SARS-CoV-2 RNA transcription-mediated amplification test was positive, consistent with the diagnosis of COVID-19 pneumonia. The initial management included fluid resuscitation, insulin therapy, control of water and electrolyte balance, and empiric antibiotic treatment with intravenous ceftazidime after blood and sputum culture sampling (Fig. 2). The patient also received oxygen inhalation through a nasal tube, azvudine, intravenous methylprednisolone and heparin. By day 5 of hospitalization, the comprehensive treatment improved blood glucose control, and the clinical symptoms and infection indicators improved.

On day 7 of hospitalization, the patient had intermittent fever and worsening respiratory symptoms (cough, sputum and dyspnea) in parallel with an elevated C-reactive protein (CRP) level of 223.55 mg/L (normal <5 mg/L). These findings were suspicious for superimposed bacterial infection on COVID-19, and aerobic and anaerobic blood and sputum cultures were obtained (these were ultimately negative). We engaged in consultations (e.g., pharmacists and pulmonary physicians), and the anti-infective regimen was subsequently escalated to piperacillin/tazobactam (Fig. 2).

Despite the patient being treated with mask oxygen inhalation, the immunomodulator thymalfasin, and antiviral and antibiotic treatment, she experienced cough with purulent sputum, recurrence of high fever and developed shortness of breath on hospital day 10. A second chest CT was performed that demonstrated worsening of the left pulmonary infection, regional multiple bullae, pleural effusion on the left side and a left hilar mass (Fig. 1 cd). Blood culture tested positive for meropenem sensible *Actinomyces odontolyticus* (Table 1). Oral clinical examination of the patient showed various oral conditions, such as halitosis, dental caries and swollen gums. A diagnosis of *Actinomyces odontolyticus* sepsis was made by combining the clinical manifestations and laboratory test results. Repeat sputum cultures were negative. The anti-infective regimen was subsequently escalated to meropenem in accordance with the tested

Table 1
Blood parameters at admission and tested antibiogram.

Laboratory findings	
pH $_{(ABG)}$	6.95
pCO_2 $_{(ABG)}$	10 mmHg
pO_2 $_{(ABG)}$	112 mmHg
$HCO3^-$ $_{(ABG)}$	<3 mmHg
Base Excess $_{(ABG)}$	−24.7 mmol/L
Serum Glucose	39.63 mmol/L
Serum β-Hb	9.20 mmol/L
Anti IAA-IgG	Negative
Anti ICA-IgG	Negative
Anti GAD	1.81 U/mL
Serum CRP	2.07 mg/L
Serum PCT	0.256 ng/mL
WBC	17.9 × 10^9/L
Neutrophils	89.9%
Eosinophils	0.0%
Basophils	0.0%
Monocytes	4.5%
Lymphocytes	5.6%
Actinomyces odontolyticus	
Time to positivity = 46 h, 33 min	
Antibiogram	Ampicillin [I] (MIC = 0.25)
[R = resistant, I = intermediate, S = sensible]	Meropenem [S] (MIC = 0.25)
Minimal inhibitory concentration (MIC)	Erythromycin [S] (MIC <0.016)
	Ciprofloxacin [R] (MIC = 16)
	Tetracycline [S] (MIC = 0.094)
	Gentamicin [S] (MIC = 3)
	Linezolid [S] (MIC = 0.19)

ABG: Aerial blood gas, *Anti*-IAA: Asulin autoantibody, *Anti*-ICA: islet cell antibody, Anti-GAD: glutamic acid decarboxylase antibodies, CRP: c-reactive protein, PCT: procalcitonin, WBC: white blood cell count, β-Hb: β-hydroxybutyrate.

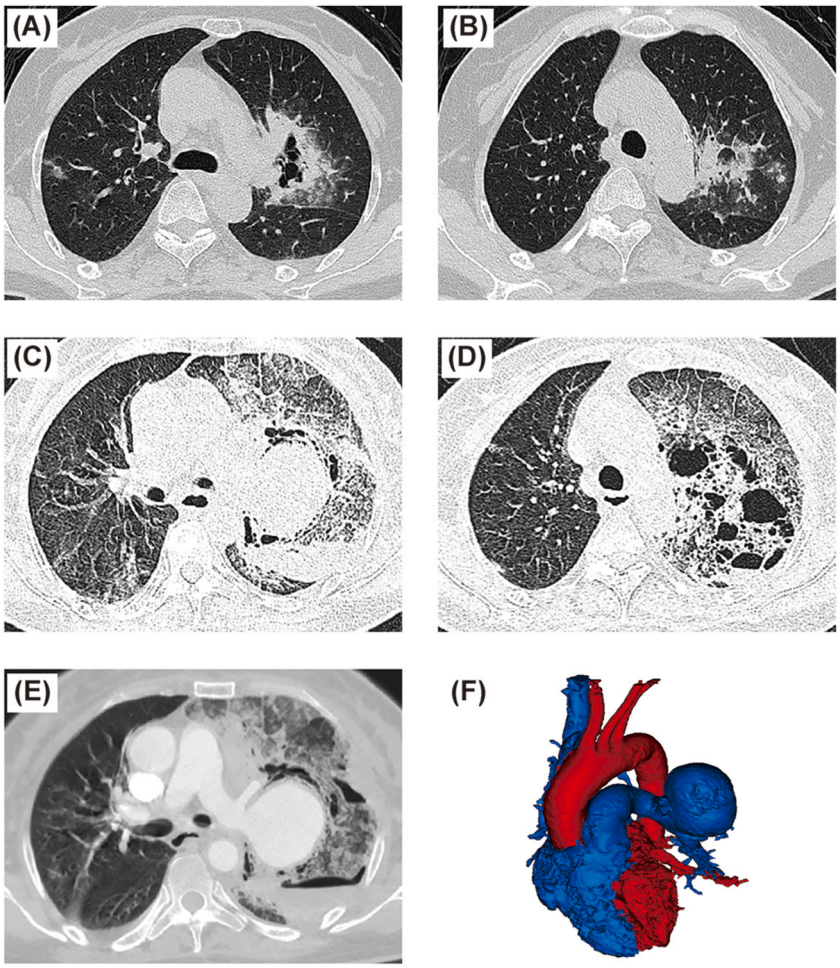

Fig. 1. computed tomography (CT) scans. (A, B) Initial chest CT images revealed bilateral pulmonary infection and regional multiple bullae, especially around the left pulmonary hilum. (C, D) A second chest CT demonstrated worsening of the left pulmonary infection, regional multiple bullae, pleural effusion on the left side and a left hilar mass. (E, F) Contrast-enhanced CT and three-dimensional reconstruction revealed an unexpected massive aneurysm of 5.6 × 4.9 cm in size at the left pulmonary hilar.

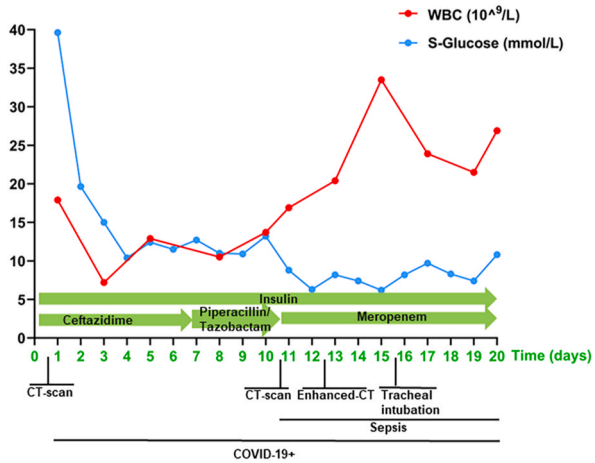

Fig. 2. Overview of the clinical course. The white blood cell count (red line) and serum glucose (blue line) was assessed by point-of-care testing. The duration of the applied antibiotic regimen is indicated by the arrow length. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

antibiogram (Table 1). Meanwhile, contrast-enhanced CT and three-dimensional reconstruction revealed an unexpected massive aneurysm of 5.6 × 4.9 cm in size at the left pulmonary hilar (Fig. 1 ef). Anticoagulation was discontinued due to the potential for increased bleeding risk from the aneurysm. A multidisciplinary consultation meeting (thoracic surgeons, respiratory physicians, endocrinologists, and radiologists) was organized to discuss further treatment options. Considering the patient's poor physical condition, treatment with surgical approaches was no longer suitable. The experts recommended an interventional approach with a covered stent of the aneurysm.

Unfortunately, her condition deteriorated rapidly with dyspnea and severe hypoxemia, and she was transferred to the intensive care unit (ICU) for intubation and ventilation on day 15 of hospitalization (Fig. 2). The patient subsequently experienced acute respiratory distress syndrome (ARDS) and septic shock. On day 20 after admission, her vital signs (continuous norepinephrine infusion) revealed a body temperature of 38.6 °C, a pulse rate of 133 beats/min, a blood pressure of 100/53 mmHg, a respiratory rate of 28 breaths/min, and an oxygen saturation of 86% with mechanical ventilation. The patient ultimately opted for hospice care.

3. Discussion

We report a case of fatal bloodstream infection of *Actinomyces odontolyticus* complicating severe COVID-19 that developed into life-threatening infectious PAA. Patients with severe COVID-19 are at increased risk of bacterial coinfections and developing bloodstream infections, often caused by gram-positive pathogens and multidrug-resistant bacteria (MDR) [8]. Actinomyces species are gram-positive, facultatively anaerobic, rod-shaped bacteria. These bacteria sometimes cause endogenous infection when tissue damage or excessive inflammation causes hypoxia and a decrease in local resistance [6]. *Actinomyces odontolyticus* infection is a rare and often fatal disease that frequently occurs in immunosuppressed patients [7]. In the present case, the patient was admitted to our hospital with infection-associated DKA. Meanwhile, the patient had received steroids for COVID-19. Moreover, the suspected portal of entry of the organism was the patient's various oral conditions, and blood culture testing was positive for *Actinomyces odontolyticus*. In conclusion, the patient had poor glycemic control and SARS-CoV-2 infection, causing a decrease in immunity and eventually leading to secondary bloodstream infection caused by *Actinomyces odontolyticus*.

In general, textbooks recommend high-dose penicillin (18–24 million U/day) intravenous therapy for 2–6 weeks followed by 6–12 months of oral penicillin for routine treatment of actinomycosis [9]. In our case, the primary reason for the poor prognosis is that the patient's condition deteriorated quickly, quickly progressing to refractory hypoxemia, ARDS, septic shock, and end-organ failure.

COVID-19 is considered a systemic vascular disease that primarily affects the respiratory tract but also damages the vascular endothelium, leading to endotheliitis [10]. SARS-CoV-2 binds to the angiotensin-converting enzyme 2 (ACE2) receptor to enter host cells, activating an inflammatory cascade and eventually impacting various organs and bodily functions [11]. The pathogenesis of PAA is very complex and may be idiopathic or may be related to infection, pulmonary artery (PA) injury, lung neoplasm, iatrogenic, pulmonary artery hypertension (PAH) or vasculitis [12]. Moreover, the most common cause of acquired PAAs or pseudoaneurysms is infections, including infections caused by pyogenic bacteria (e.g., *S. aureus*, *S. pyogenes*, *Klebsiella*, and *Actinomyces*), syphilis, tuberculosis, septic embolisms and viral or fungal pneumonia [12]. Most common germ infections, such as those caused by *Staphylococcus*, cause damage to all three layers of the vessel wall and lead to aneurysm formation [13]. Previous case reports have described pulmonary, coronary and popliteal artery aneurysms following SARS-CoV-2 infection associated with viral multisystem inflammatory syndrome [2,14–16]. *Actinomyces odontolyticus* infection-associated PAAs have not yet been reported. In this case, the patient had a history of DM for 9 years, and her diabetes was considered a chronic inflammatory disease. Moreover, the patient was diagnosed with an *Actinomyces odontolyticus* bloodstream infection, and SARS-CoV-2 coinfection also exacerbated the cytokine storm and subsequent multisystem inflammatory syndrome.

Aneurysm of the main pulmonary trunk is a rare entity that is usually asymptomatic [12]. In our case, the patient also did not present any specific symptoms and solely had respiratory symptoms such as cough, expectoration and respiratory distress. Enhanced CT revealed a massive PAA of 5.6 × 4.9 cm in size involved the main and proximal branches of the pulmonary arteries. The patient's CT showed multiple cavitary lesions adjacent to the PAAs or more peripherally; therefore, repeated endovascular seeding of the PA lumen with septic emboli or microemboli has been proposed as an important factor in the pathogenesis of PAAs in the infectious setting [17].

There are currently no clear treatment guidelines for PAA, and the optimal treatment of PAA remains uncertain. To prevent PAA rupture, surgical intervention (e.g., aneurysmorrhaphy, reconstruction with vascular prostheses and pulmonary allograft replacement) is recommended when the absolute diameter of the aneurysm is > 55 mm, in accordance with most institutions [18]. In the present case report, it was considered the critical condition accompanied by sepsis increased the risk of surgery. Endovascular treatment was the first therapy of choice for the patient; nevertheless, the patient ultimately opted for hospice care. Informed consent has been obtained for this case report.

4. Conclusions

In conclusion, this is the first atypical case of giant infectious PAA that developed during SARS-CoV-2 infection and *Actinomyces odontolyticus* sepsis. The choice of surgical intervention versus more conservative management of aneurysms should be determined by assessments of the patient's history and presentation.

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5. Consent to publish

Written informed consent was obtained from the bereaved family for publication of this case report and accompanying data and images.

Data availability statement

The original data of this study are available from the corresponding author upon reasonable request.

CRediT authorship contribution statement

Ling Wang: Writing – review & editing, Data curation, Conceptualization. **Wenyi Lei:** Writing – review & editing, Writing – original draft, Conceptualization. **Fan Qi:** Resources, Data curation. **Zheyuan Fan:** Writing – review & editing, Writing – original draft, Visualization, Software, Methodology, Investigation, Funding acquisition.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

References

[1] T. Ahmed, S.H. Lodhi, A. Al-Abdouh, T. Ahmed, A.W. Messerli, J.C. Gurley, Rapidly enlarging pulmonary artery aneurysm: an unusual complication due to prolonged mechanical cardio-respiratory support in COVID-19, Curr. Probl. Cardiol. 48 (2023) 101430, https://doi.org/10.1016/j.cpcardiol.2022.101430.
[2] C. Desnos, S. Boussouar, G. Hekimian, A. Redheuil, A. Combes, Spontaneous hemothorax in 4 COVID-19 ARDS patients on VV-ECMO revealing pulmonary artery aneurysms, Crit. Care 24 (2020) 638, https://doi.org/10.1186/s13054-020-03359-7.
[3] M. Gupta, A. Agrawal, A. Iakovou, S. Cohen, R. Shah, A. Talwar, Pulmonary artery aneurysm: a review, Pulm. Circ. 10 (2020) 2045894020908780, https://doi.org/10.1177/2045894020908780.
[4] M. Yüce, E. Filiztekin, K.G. Özkaya, COVID-19 diagnosis -A review of current methods, Biosens. Bioelectron. 172 (2021) 112752, https://doi.org/10.1016/j.bios.2020.112752.
[5] M. Xiang, X. Wu, H. Jing, V.A. Novakovic, J. Shi, The intersection of obesity and (long) COVID-19: hypoxia, thrombotic inflammation, and vascular endothelial injury, Front Cardiovasc Med 10 (2023) 1062491, https://doi.org/10.3389/fcvm.2023.1062491.
[6] E. Könönen, W.G. Wade, Actinomyces and related organisms in human infections, Clin. Microbiol. Rev. 28 (2015) 419–442, https://doi.org/10.1128/CMR.00100-14.
[7] Q. Huang, Z. Hong, Q. Hong, Cryptococcal meningoencephalitis with Actinomyces odontolyticus sepsis: a case report and literature review, BMC Infect. Dis. 23 (2023) 434, https://doi.org/10.1186/s12879-023-08391-w.
[8] V. Baskaran, H. Lawrence, L.E. Lansbury, K. Webb, S. Safavi, N.I. Zainuddin, T. Huq, C. Eggleston, J. Ellis, C. Thakker, et al., Co-infection in critically ill patients with COVID-19: an observational cohort study from England, J. Med. Microbiol. 70 (2021), https://doi.org/10.1099/jmm.0.001350.
[9] R. Floyd, S. Hunter, F. Abu Saadeh, C. McDonnell, P. McCormick, Pelvic actinomycosis, QJM 114 (2021) 587–588, https://doi.org/10.1093/qjmed/hcab048.
[10] Z. Varga, A.J. Flammer, P. Steiger, M. Haberecker, R. Andermatt, A.S. Zinkernagel, M.R. Mehra, R.A. Schuepbach, F. Ruschitzka, H. Moch, Endothelial cell infection and endotheliitis in COVID-19, Lancet 395 (2020) 1417–1418, https://doi.org/10.1016/S0140-6736(20)30937-5.
[11] L.-A. Teuwen, V. Geldhof, A. Pasut, P. Carmeliet, COVID-19: the vasculature unleashed, Nat. Rev. Immunol. 20 (2020) 389–391, https://doi.org/10.1038/s41577-020-0343-0.
[12] M. Kreibich, M. Siepe, J. Kroll, R. Höhn, J. Grohmann, F. Beyersdorf, Aneurysms of the pulmonary artery, Circulation 131 (2015) 310–316, https://doi.org/10.1161/CIRCULATIONAHA.114.012907.
[13] A.L. Duijnhouwer, E.P. Navarese, A.P.J. Van Dijk, B. Loeys, J.W. Roos-Hesselink, M.J. De Boer, Aneurysm of the pulmonary artery, a systematic review and critical analysis of current literature, Congenit. Heart Dis. 11 (2016) 102–109, https://doi.org/10.1111/chd.12316.
[14] M.R. Navaeifar, L. Shahbaznejad, A. Sadeghi Lotfabadi, M.S. Rezai, COVID-19-Associated multisystem inflammatory syndrome complicated with giant coronary artery aneurysm, Case Rep Pediatr 2021 (2021) 8836403, https://doi.org/10.1155/2021/8836403.
[15] K. Haq, E.G. Anyalechi, E.P. Schlaudecker, R. McKay, S. Kamidani, C.K. Manos, M.E. Oster, Multiple mis-C readmissions and giant coronary aneurysm after COVID-19 illness and vaccination: a case report, Pediatr. Infect. Dis. J. 42 (2023) e64–e69, https://doi.org/10.1097/INF.0000000000003801.
[16] R. Berchiolli, L. Torri, D. Adami, G. Bertagna, F. Canovaro, N. Troisi, Inflammatory popliteal aneurysm associated with SARS-CoV-2 infection, Eur. Rev. Med. Pharmacol. Sci. 27 (2023) 1708–1712, https://doi.org/10.26355/eurrev_202302_31414.
[17] H.S. Park, M.R. Chamarthy, D. Lamus, S.S. Saboo, P.D. Sutphin, S.P. Kalva, Pulmonary artery aneurysms: diagnosis & endovascular therapy, Cardiovasc. Diagn. Ther. 8 (2018) 350–361, https://doi.org/10.21037/cdt.2018.04.01.
[18] A.W. Hritani, F. Samad, S.C. Port, A.J. Tajik, Massive pulmonary artery aneurysm. Circulation, Cardiovascular imaging 12 (2019) e008677, https://doi.org/10.1161/circimaging.118.008677.