IDCases 38 (2024) e02078

Contents lists available at ScienceDirect

IDCases

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Case report

Mediastinal abscess and bacteremia due to *Streptococcus dysgalactiae* complicated by aorto-esophageal fistula leading to death with massive bleeding in a 70-year-old Japanese man with gastric cancer

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ARTICLE INFO

Keywords:
Mediastinal abscess
Streptococcus dysgalactiae
Aorto-esophageal fistula

ABSTRACT

Streptococcus dysgalactiae can lead to bacteremia in elderly individuals with underlying conditions, primarily from cellulitis. Although rare, mediastinal abscesses can develop from anatomical anomalies, post-thoracic surgery, esophageal rupture, or inflammation in the oral cavity or neck. Aorto-esophageal fistula, a life-threatening condition causing severe bleeding, typically arises from thoracic aortic aneurysms with atherosclerosis. We present a case of recurrent *Streptococcus dysgalactiae* bacteremia complicated by mediastinal abscess and aorto-esophageal fistula in a patient undergoing treatment for gastric cancer. Initial imaging suggested lymph node metastasis, with a diagnosis of abscess only confirmed at autopsy. Although the exact etiology of the abscess was unclear, we highly suspect the recurrent *Streptococcus dysgalactiae* bacteremia contributed to its development via hematogenous spread. Autopsy also revealed progression of the mediastinal abscess into the esophagus and aorta, leading to the formation of a fistula, massive hemorrhage, and ultimately, the patient's death. While uncommon, a mediastinal abscess should be recognized as a potential cause of aorto-esophageal fistula.

Introduction

Aorto-esophageal fistulae are a rare but devastating complication of underlying vascular disease, prior surgery, or esophageal pathology [1–5]. Infections leading to these types of fistulae are rarely reported in the literature. We present a case of *Streptococcus dysgalactiae* bacteremia leading to a spontaneous mediastinal abscess in the cervicothoracic region. Autopsy findings confirmed our clinical suspicion that the mediastinal abscess was likely the underlying reason for the patient's aorto-esophageal fistula, which resulted in massive bleeding and unfortunately, death of the patient.

Case

A 78-year-old man with a past medical history of type 2 diabetes mellitus, hypertension, dyslipidemia, sick sinus syndrome (requiring pacemaker placement) and chronic kidney disease presented to our hospital with a one-day history of fevers and chills. Two years prior to admission, he was evaluated by the Hematology service for a new diagnosis of anemia (hemoglobin level: 8.0 g/dL). Laboratory workup suggested iron deficiency, and although a bone marrow biopsy was recommended, the patient declined and opted for medical management. Approximately three months prior to admission, he reported fever and dyspnea. Further investigation revealed his hemoglobin level had declined to 5.3 g/dL. An upper gastrointestinal endoscopy confirmed the diagnosis of advanced gastric cancer (cT3N3M0 Stage IIIb). The patient was scheduled for outpatient surgery, but before this could happen, he returned to the hospital with complaints of dyspnea and fever, leading to admission for concern of sepsis. On admission, his temperature was 38.5 °C, and two sets of blood cultures grew *Streptococcus dysgalactiae,* subspecies *equisimilis*.

Initially there was suspicion for infective endocarditis. However, the

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https://doi.org/10.1016/j.idcr.2024.e02078
Received 8 May 2024; Received in revised form 5 September 2024; Accepted 6 September 2024
Available online 7 September 2024

patient's examination did not reveal a new murmur or peripheral embolic phenomena, and transthoracic echocardiography showed no evidence of valvular vegetations. Additionally, rheumatoid factor was negative at 15 IU/mL, and his blood cultures cleared quickly. Therefore, he did not clinically meet criteria for endocarditis, prompting a workup for other potential causes of the bacteremia. Contrast-enhanced computed tomography (CT) of the chest, abdomen, and pelvis was negative for abscess or any findings suspicious for infection. The patient was treated with a 14-day continuous intravenous infusion of penicillin G (24 million units daily) for *Streptococcus dysgalactiae* bacteremia of unknown origin and responded well to the therapy. After completing treatment for bacteremia, he underwent distal gastrectomy, with resultant negative margins for malignancy. His postoperative course was uneventful, and he remained well for several weeks.

One month after discharge, the patient re-presented to the emergency department with a one-day history of fevers, chills, and malaise. He denied chest or abdominal pain and reported no new exposures or events since his last discharge, such as sick contacts, new sexual partners, substance use, or dental treatments. Upon admission, he was alert and oriented, with the following vital signs: Japanese Coma Scale I-1; body temperature, 38.8 °C; pulse, 91 beats/min; blood pressure, 138/72 mmHg; respiratory rate, 26 breaths/min; and SpO2, 95 % on room air. Physical examination was significant only for petechial hemorrhages isolated to the toes. Laboratory tests indicated an elevated inflammatory response, with white blood cells at 7700/μL (normal range: 4000–11,000/ μL), with neutrophil predominance and an elevated CRP at 9.10 (normal range: < 0.5 mg/dL). Liver transaminases, albumin, electrolytes, and creatinine were normal. Contrast-enhanced CT revealed thickening of the upper thoracic esophageal wall and a solid lesion near the esophagus (Fig. 1). Given the patient's history, initial concerns were for gastric or esophageal cancer with lymph node metastasis.

As the patient met criteria for sepsis, intravenous ampicillin/sulbactam (3 g every 6 h) was started immediately upon admission. The following day, upper gastrointestinal endoscopy revealed grade M gastroesophageal reflux disease with edematous mucosa throughout the esophagus, and biopsies were negative for malignancy. Blood cultures obtained at admission again detected *Streptococcus dysgalactiae* subspecies *equisimilis* (minimum inhibitory concentration [MIC] to penicillin G ≤ 0.12 mcg/mL) and subsequent cultures after antibiotic administration remained negative.

A repeat workup for infective endocarditis, including transthoracic and transesophageal echocardiography, showed no evidence of valvular vegetations. However, the case was still classified as confirmed infective endocarditis by the 2023 Duke-International Society for Cardiovascular Infectious Diseases Criteria. This classification was based on one major criterion - recurrent bacteremia with the same organism over a short period of time – along with four minor criteria: appearance of petechial hemorrhagic spots on the toes, elevated rheumatoid factor (22 IU/mL), fever (38.8 °C), and the presence of a pre-existing cardiac condition or device (pacemaker). The antibiotic regimen was changed to a combination of penicillin G (24 million units per day) and gentamicin (3 mg/kg per day), with a tentative plan to continue penicillin G for 4 weeks and gentamicin for 2 weeks.

After the initiation of antibiotics, the patient had an uneventful course until the 33rd day of hospitalization, when he suddenly vomited a large amount of blood, leading to immediate cardiopulmonary arrest. Despite resuscitation efforts, he could not be revived and passed away. A pathological autopsy was conducted to help elucidate the source of the recurrent *Streptococcus dysgalactiae* bacteremia and determine the cause of the massive bleeding. The autopsy revealed the presence of an aorto-esophageal fistula (Fig. 2) and an abscess (Figs. 3 and 4) in the mediastinum, near the middle of the thoracic esophagus. The lumen was covered with fibrin (Fig. 5a), and relatively enlarged and reactive lymph nodes were scattered around it (Fig. 5b). An organized thrombus (Fig. 5c) was also noted, indicative of a chronically formed lesion. Gram stains of the tissue surrounding the abscess were negative for bacterial forms. The abscess was primarily situated from the muscularis propria to the submucosa of the esophagus (Fig. 4).

Clinically, the solid lesion seen on the initial CT (Fig. 1) was suspected to be an early sign of a mediastinal abscess, possibly seeded during the initial or recurrent bacteremia episodes. However, it could not be definitively concluded that the abscess had originated from the esophageal epithelium, and no other foci of infection were identified, making it challenging to determine the exact cause of the abscess based solely on the pathological findings. Additionally, the progression of tissue necrosis indicated that the source of the bleeding was an aorto-esophageal fistula, formed by the extension of the mediastinal abscess toward the aorta (Fig. 6). Pathologically, there were no signs of gastric cancer metastasis or recurrence, and no cardiac valvular abnormalities were identified.

Discussion

Streptococcus dysgalactiae is part of the Lancefield C or G group streptococci and exhibits β-hemolytic properties. It is a normal inhabitant of the pharynx, gastrointestinal tract, vaginal flora, and skin. Recently, *S. dysgalactiae* has attracted attention as a cause of pharyngitis, cellulitis, and bacteremia [6–8]. When bacteremia occurs, cellulitis is the most common underlying etiology (41 %), followed by unknown causes (26 %), with endocarditis and deep abscesses being rare (3 %)

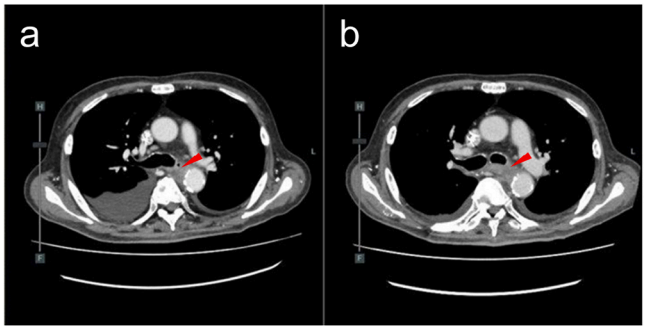

Fig. 1. The solid lesion (the arrow head) of the middle mediastinum revealed by the CT. a. Computed tomography 2 months prior to admission. b. Computed tomography at this present admission. In Fig. 1b, there is a solid lesion near the esophagus and the thoracic aorta of the middle mediastinum. In Figs. 1a and 1b, there are slight lesions at the same site.

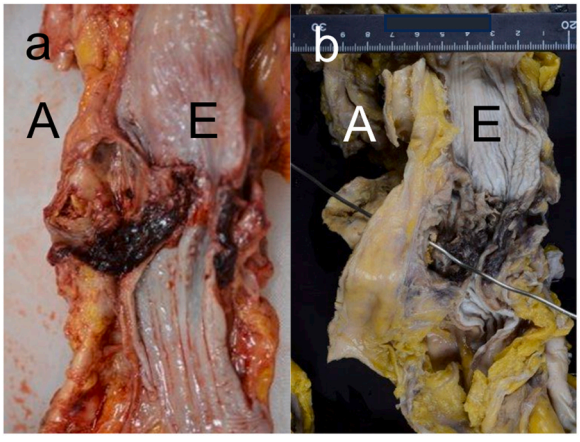

Fig. 2. The raw (a) and formalin fixed organs (b) of the aorto-esophageal fistula confirmed macroscopically at autopsy. The upper side of the figure is the cranial side. Aortoesophageal fistula confirmed by sonde. A: the wall of the aorta. E: the wall of the esophagus.

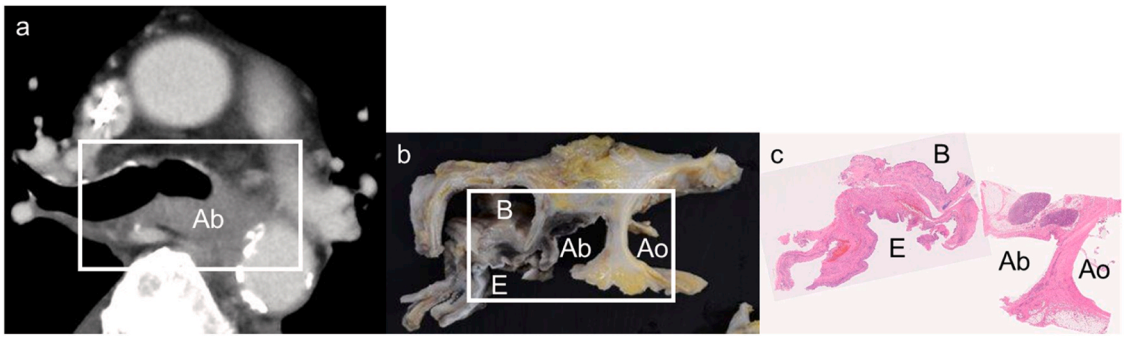

Fig. 3. The correspondence between the imaging (a), macroscopic (b), and pathological (c, hematoxylin and eosin stain (HE), 10 ×), findings of the middle mediastinum. The rectangle in (a) indicates the region of (b), and the one in (b) indicates the region of (c). The abscess (Ab) was located between the aorta (Ao) and the esophagus (E). B: the bronchus.

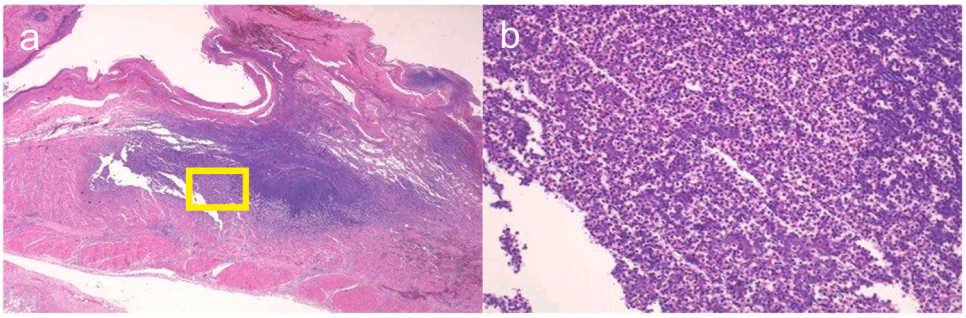

Fig. 4. The abscess located mainly from the muscularis propria to the submucosa of the esophagus. The rectangle in (a, HE, 50 ×) indicates the region of (b, HE, 200 ×).

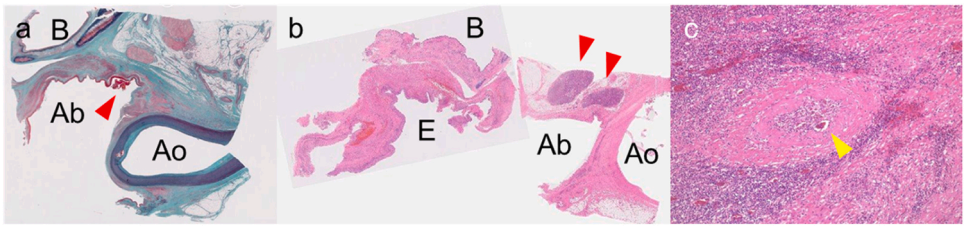

Fig. 5. The pathological findings indicating that the lesion has been formed chronically. a (Elastica Masson stain, 10 ×). lumen covered with fibrin (the red arrow head). b (HE, 10 ×). reactively enlarged lymph nodes scattered around the abscess (the red arrow head). c (HE, 100 ×). the organized thrombus (the yellow arrow head). Ab: the abscess. Ao: the aorta. B: the bronchus. E: the esophagus.

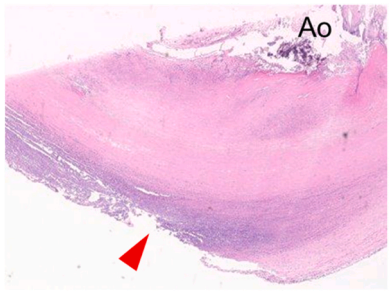

Fig. 6. The abscess with necrotic tissue extending from the adventitia to the intima of the aorta. HE, 20 ×. It suggests that the aorto-esophageal fistula had progressed from the esophageal side to the aortic side. Ao: the cavity of the aorta.

[8]. Risk factors for *S. dysgalactiae* bacteremia include male sex, advanced age, and chronic medical conditions [6,8]. Although groups B, C, F, and G streptococci are generally more resistant to penicillin than group A streptococci [9], antibiotic treatment is similar to that of oral streptococci. When managing native valve endocarditis, as was done with our patient, either penicillin G or ceftriaxone for four weeks is recommended, with adjunctive gentamicin for two weeks in the setting of elevated MIC values [10]. Given the patient's MICs were not elevated, the use of gentamicin, in retrospect, may not have been necessary. Recurrence occurs in 3–9 % of cases, primarily in skin and soft tissue infections [11].

Mediastinitis and mediastinal abscess are deep infections which most commonly occur after cardiac surgery, esophageal perforation, or descending infection from the neck. The microorganisms responsible vary depending on the underlying cause, with typical skin flora (staphylococcal and streptococcal species) and Enterobacteriaceae most common following cardiac surgery. When esophageal perforation is the cause, gut flora, including viridans streptococci, are frequently implicated. Descending necrotizing mediastinitis often involves normal flora from the oral cavity, upper respiratory tract, ears, and eyes [12]. Hematologic seeding of the mediastinum leading to infection and abscess is rare [13–15]. While streptococci are common pathogens in mediastinitis and abscess formation, *Streptococcus dysgalactiae* as a cause has rarely

been reported [16,17]. Diagnosis is challenging, with a significant number of cases (20 %) diagnosed only after autopsy [18].

Aorto-esophageal fistulae generally carry a poor prognosis due to massive hemorrhage into the gastrointestinal tract [1]. They are classified as primary or secondary, depending on the underlying condition leading to their development. Primary fistulae are associated with esophageal or aortic disease, whereas secondary fistulae are post-surgical, such as after thoracic endovascular aortic repair (TEVAR) for aortic disease. Just as with mediastinitis and abscess, diagnosis is challenging, often only being found at autopsy [19]. Clinical criteria, known as Chiari's Triad - sentinel arterial bleeding, chest pain, and hemorrhage - are rare in combination (11–28 %) [3]. Imaging is helpful, but even when advanced testing such as contrast-enhanced CT, angiography, and endoscopy are performed, fistulae can be missed [1,4,5]. Surgery is the only definitive treatment, but mortality rates are high (55–77 %) [1,20].

Our patient, with advanced age and multiple chronic medical conditions, was at high-risk for invasive infection from streptococcal species, though he did not present with a typical inciting event such as cellulitis. Initially labeled as recurrent *Streptococcus dysgalactiae* bacteremia of unknown origin, he was treated twice with appropriate pathogen-directed antibiotics. At autopsy, however, a mediastinal abscess was found, which was not visualized on imaging during his admission. The absence of positive cultures from the specimen prevents a definitive conclusion that *Streptococcus dysgalactiae* was the causative agent of the mediastinal abscess. Nevertheless, the recurrence of bacteremia and the absence of other infectious sources strongly suggest its involvement in the formation of the abscess, which subsequently led to recurrent bacteremia. While the pathological findings did not identify a clear entry point for the abscess, a CT scan at the onset of the initial bacteremia revealed a minute solid lesion in the mediastinum, possibly an early sign of abscess formation from transient bacteremia related to the gastric cancer lesion (prior to resection).

In this case, commonly recognized causes of mediastinal abscess, such as spread from nearby organs, were absent. Predicting the development of an aorto-esophageal fistula was challenging, and neither contrast-enhanced CT nor upper gastrointestinal endoscopy yielded a diagnosis. The difficulty in diagnosis and the fatal clinical course are characteristic of this disease. The finding of a mediastinal abscess leading to an aorto-esophageal fistula, presumably due to *S. dysgalactiae* , is exceedingly rare. This case is significant as multiple rare microbiological and pathological conditions are presented which culminated in a devastating outcome for the patient.

Conclusion

We present a case of *Streptococcus dysgalactiae* leading to recurrent bacteremia, mediastinal abscess, and eventual progression to an aorto-esophageal fistula. Initially, the mediastinal lesion was presumed to be a lymph node metastasis, but autopsy confirmed it as a mediastinal abscess. While the exact etiology of the abscess remained unclear, it was likely the result of hematogenous spread from *Streptococcus dysgalactiae* bacteremia. Histopathological findings confirmed the progression of the mediastinal abscess into the esophagus and aorta, leading to the formation of a fistula and subsequent massive bleeding. Although rare, a mediastinal abscess should be considered as a potential cause of aorto-esophageal fistula.

CRediT authorship contribution statement

Yoshiya Sugano: Writing – original draft. **Akihito Yoshida:** Writing – review & editing. **Wataru Uegami:** Writing – review & editing. **Takaaki Kobayashi:** Supervision. **Tadashi Eguchi:** Writing – review & editing. **Nicholas Van Sickels:** Writing – review & editing. **Kazuya Oshima:** Writing – original draft.

Authors' contributions

KO, YS, AY, WU, NVS and TE wrote a first draft of the manuscript. TK critically revised and revised the manuscript. All authors read and approved the final paper.

Consent

The patient's family's written consent was obtained.

Ethical approval

The local ethical committee approval does not apply in this case.

Funding

None.

Conflict of interest

No disclosure.

Acknowledgements

None.

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