

Case Report

Death by aorto-esophageal fistula due to disseminated tuberculosis: a case study

Joo-Young Na¹, Youn-Shin Kim², Yoo-Duk Choi³, Hyung-Seok Kim⁴, Jong-Tae Park⁴

¹Forensic Medicine Division, Gwangju Institute, National Forensic Service, Korea; ²Department of Forensic Medicine, Chosun University School of Medicine, Korea; ³Department of Pathology, Chonnam National University Medical School, Korea; ⁴Department of Forensic Medicine, Chonnam National University Medical School, Korea

Received February 4, 2015; Accepted March 30, 2015; Epub April 1, 2015; Published April 15, 2015

Abstract: Tuberculosis remains a serious public health problem worldwide, especially in Korea. Although tuberculosis is generally considered a non-fatal chronic disease, deaths have occurred. In this case study, a 68-year-old man was admitted to the hospital with dyspepsia, vomiting, and abdominal pain. Nine hours later, he suffered severe hematemesis and died despite cardiopulmonary resuscitation. A medico-legal autopsy was performed and an external examination revealed no external injuries. However, an internal examination revealed an aorto-esophageal fistula and a large amount of blood in the stomach. A histologic examination confirmed tuberculous mediastinitis with disseminated tuberculosis involving multiple organs, including the heart, lungs, liver, kidneys, and spleen. Both an aorto-esophageal fistula and sudden death due to tuberculosis infection are rare. This paper reports the case of a fatal aorto-esophageal fistula associated with disseminated tuberculosis.

Keywords: Aorto-esophageal fistula, tuberculosis, sudden death, autopsy

Introduction

Although aorto-esophageal fistulas (AEFs) are uncommon, they are usually fatal [1]. Primary AEFs are caused by pathologic conditions of the aorta or esophagus, such as aneurysm or cancer, while secondary AEFs are usually associated with foreign body ingestion, medical intervention (e.g., surgery), chemoradiotherapy, and biopsy. AEFs due to tuberculosis are extremely rare and are usually caused by tuberculous esophagitis [1, 2]. Tuberculosis itself remains a serious public health problem in Korea. Tuberculosis is generally considered a non-fatal chronic disease; however, lethal complications, such as those seen in this case, can occur. This paper presents a rare case of AEF due to disseminated tuberculosis that resulted in massive hematemesis and subsequent sudden death. This was confirmed with an autopsy and a histologic examination. This report suggests that an AEF secondary to tuberculosis was the cause of death.

Case report

A 68-year-old man presented to the hospital after experiencing dyspepsia, vomiting, and

abdominal pain for 1 day. Upon admission, his vital signs and laboratory tests were normal. He had a medical history of hypertension, cerebral infarction, and chronic renal disease but no history of tuberculosis. Approximately 9 hours later, he complained of nausea, began vomiting a large amount of blood, and subsequently died. A family member claimed medical malpractice and a medico-legal autopsy was required.

A medico-legal autopsy was performed within 24 hours. The external examination showed no external injuries except for those caused by medical procedures. However, the internal examination revealed adhesion of the aorta and the esophagus and a ruptured AEF. A defect in the tunica intima of the thoracic aorta and atherosclerotic plaque calcification in the tunica intima of the aorta were noted. The adhered connective tissue between the aorta and esophagus was thickened. A mucosal defect with hemorrhaging in the esophageal mucosa and a hemorrhage on the esophageal wall were also noted (**Figure 1**) and the stomach cavity contained a large amount of clotted blood. The

Death by aortoesophageal fistula due to disseminated tuberculosis

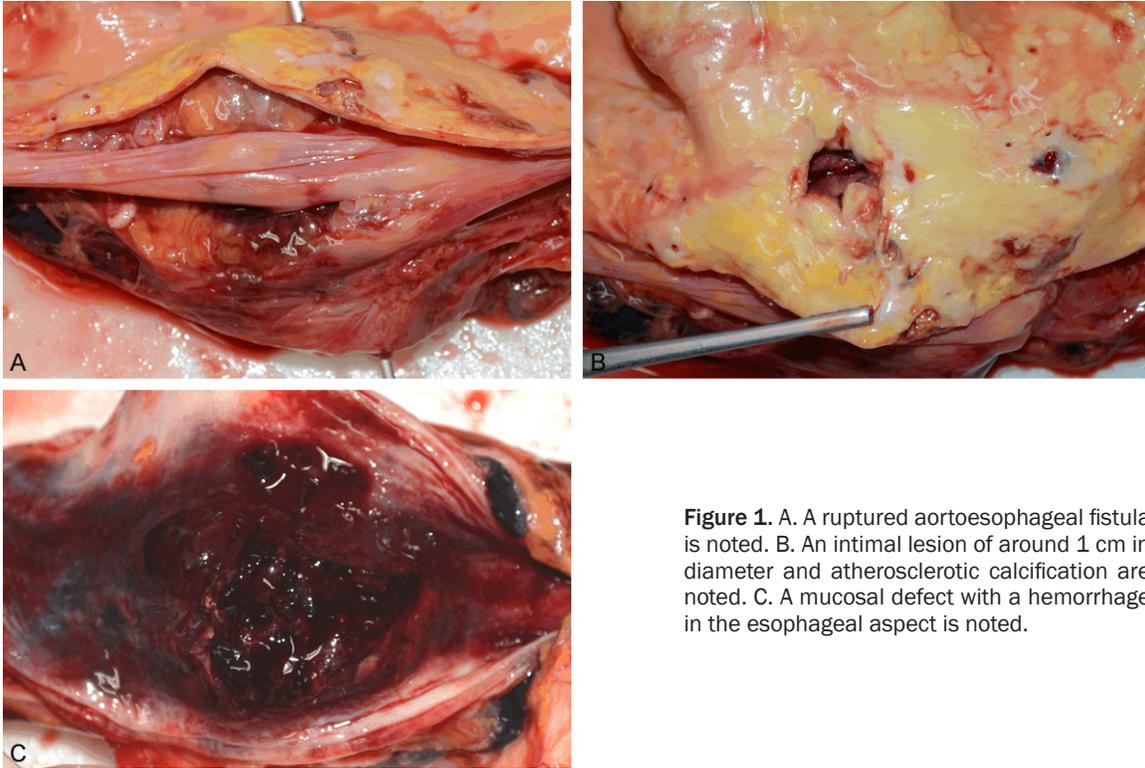


Figure 1. A. A ruptured aortoesophageal fistula is noted. B. An intimal lesion of around 1 cm in diameter and atherosclerotic calcification are noted. C. A mucosal defect with a hemorrhage in the esophageal aspect is noted.

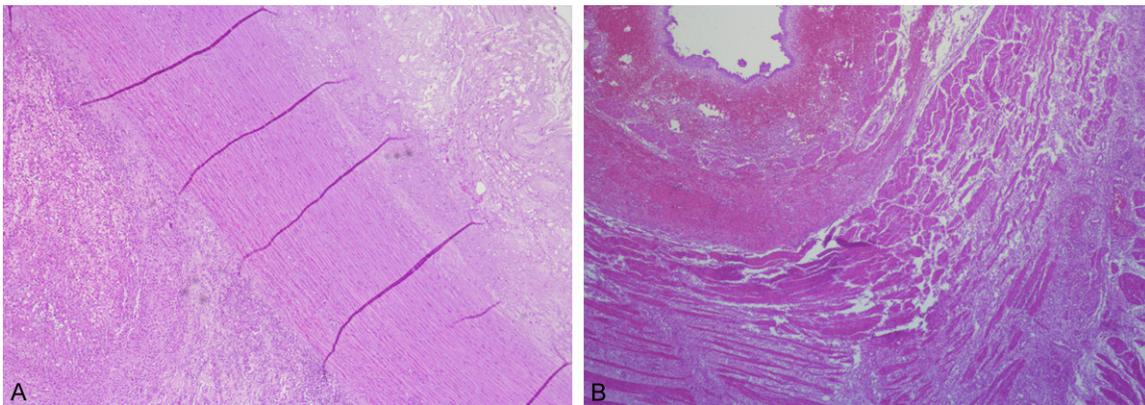


Figure 2. A. Atherosclerotic plaque and a massive inflammation (including granulomatous lesions within the giant cells and lymphocytes) in the adhered connective tissue between the esophagus and the aorta (including the tunica adventitia of the aorta) are noted. B. The esophageal wall (except mucosa) shows a hemorrhage and massive inflammation with epithelioid granulomatous giant cell lesions.

gross examination noted no other remarkable findings in any other internal organs.

The histologic examination confirmed a ruptured AEF with an aneurysmatic aortic pouch, massive inflammation with multiple caseating epithelioid granulomas within the giant cells, and lymphocytic infiltration suggestive of tuberculosis (**Figure 2**). The majority of these granulomatous inflammatory lesions were located in

the muscularis propria and serosa of the esophagus, the connective tissue between the esophagus and the aorta, and the tunica adventitia of the aorta. Esophageal mucosal lesions could not be thoroughly evaluated because of extensive structural damage and hemorrhaging. Microscopic examination of internal organs revealed disseminated tuberculosis in several other organs including the heart, lungs, liver, kidneys, and spleen (**Figure 3**). A paraffin-

Death by aortoesophageal fistula due to disseminated tuberculosis

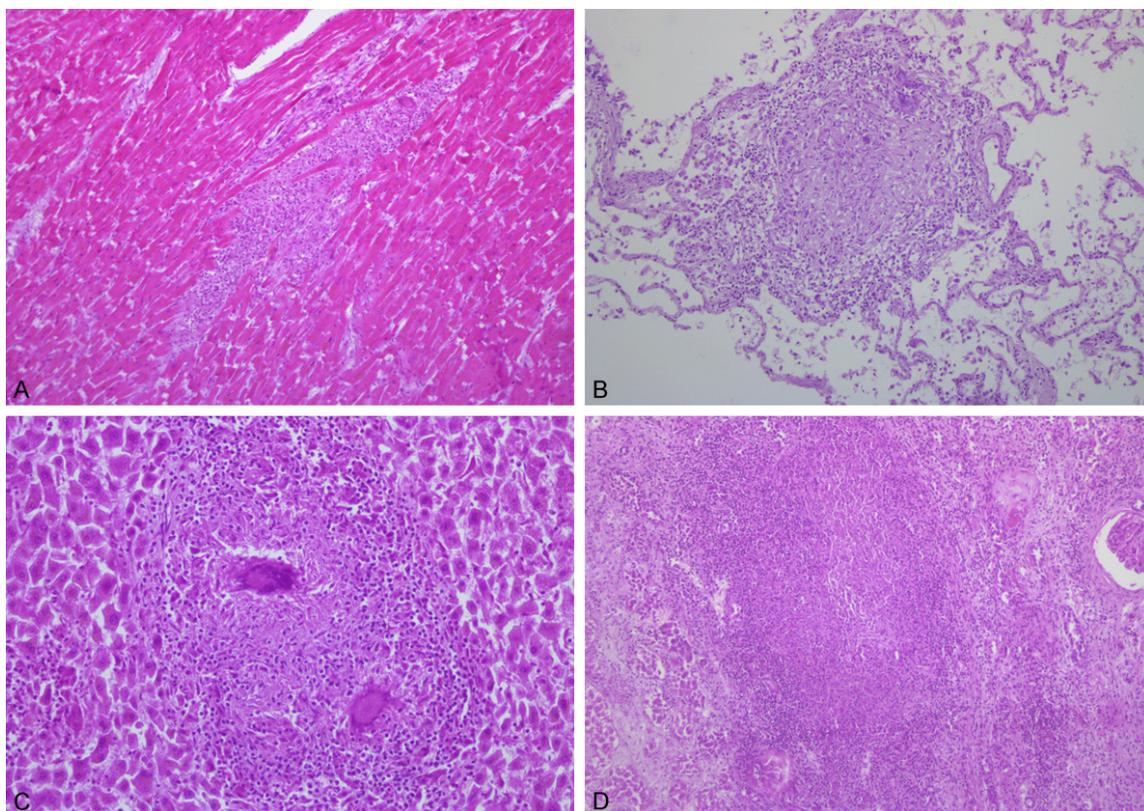


Figure 3. Multiple caseating epithelioid granulomatous inflammations within the giant cells were revealed in the various organs including the heart (A), lungs (B), liver (C), and kidney (D).

embedded tissue tested positive for mycobacterium tuberculosis using a polymerase chain reaction.

Toxicological tests were conducted on gastric content samples and blood samples from the heart. The samples were analyzed using gas chromatography-mass spectrometry. With the exception of chronic health medications, no significant drugs were noted in the toxicological analysis. Alcohol was detected; the blood alcohol concentration was 0.047% in the peripheral blood.

Discussion

AEFs are classified into two groups, primary and secondary. Primary AEFs arise from several underlying disease such as carcinoma, ulcers, infectious disease, foreign bodies, and complications from radiation. In contrast, secondary AEFs arise mainly from foreign bodies and medical interventions such as aortic surgery [1-3]. However, the most common causes of AEFs are thoracic aneurysms (51%), foreign body ingestion (19%), and esophageal carcinoma [4]. and,

although an AEF is rare, it can be fatal. A tuberculous-related AEF is extremely rare and is usually caused by tuberculous esophagitis; however, AEFs associated with tuberculous mediastinitis have also been reported [2]. In this case, the majority of the granulomatous inflammatory lesions were located between the esophagus and the thoracic aorta, primarily between the muscularis propria of the esophagus and the tunica adventitia of the aorta. However, as previously mentioned, the mucosa of the esophagus could not be thoroughly examined because of extensive structural damage and hemorrhaging. Therefore, in this case, both esophageal tuberculosis and tuberculous mediastinitis were potential causes of the AEF. However, given that the microscopic examination revealed disseminated tuberculosis in various organs, including the heart, it is likely that this AEF arose from tuberculous mediastinitis. In addition, the histological examination revealed that the other esophageal mucosae (except the fistula lesion) were tuberculosis free, and the microscopic examination revealed massive inflammation with necrosis in the connective

Death by aorto-esophageal fistula due to disseminated tuberculosis

tissue between the esophagus and the thoracic aorta further suggesting tuberculous mediastinitis. This finding is of interest given that a tuberculosis-related AEF is very rare and is usually caused by tuberculous esophagitis and not tuberculous mediastinitis [2].

Tuberculosis remains a serious public health problem worldwide, especially in Korea. Tuberculosis is generally regarded as a non-fatal chronic disease; however, deaths, such as the one in this case, sometimes occur. Since the 1960s, prosthetic aortic grafts have become the most common cause of aorto-gastrointestinal fistula; however, tuberculosis should also be considered in immunocompromised patients and in the countries with a high prevalence of tuberculosis [2]. In this case, the patient died in the hospital, and his family subsequently claimed medical malpractice. One study has shown that in 94% of cases, the main presenting symptom of aorto-gastrointestinal fistulas is gastrointestinal hemorrhage; however, a definitive preoperative diagnosis was only made in 36% of cases [5]. In addition, the survival rate for patients with an aorto-gastrointestinal fistula increased significantly when the time between the onset of bleeding and medical intervention was short [6]. Furthermore, preliminary symptoms such as an initial mild to moderate hematemesis (termed sentinel hemorrhage or herald bleed) occur in 44% of aorto-gastrointestinal fistula patients [5] and can be used as an indicator of a more serious, potentially fatal gastrointestinal hemorrhage. Steffes and O'Leary reported that 50% of patients with spontaneous aorto-gastrointestinal fistulas had longer than 24 hours after the sentinel hemorrhage to undergo an operation and an additional 29% had longer than 1 week [7]. This latent period between bleeding episodes of aorto-esophageal fistulas can be attributed to several factors such as clots occluding the fistula, hypotension, vasoconstriction in response to hypovolemia, and tamponade caused by increased esophageal intraluminal pressure [8]. However, this patient presented with dyspepsia, vomiting, and abdominal pain (not gastrointestinal bleeding) and experienced massive hematemesis shortly after admission.

This paper describes the unusual case of a fatal AEF rupture complicated by tuberculous mediastinitis associated with disseminated tuberculosis. The AEF was only identified as the

cause of death during the autopsy and tuberculous mediastinitis associated with disseminated tuberculosis was only revealed during detailed evaluations (e.g., broad microscopic examination). Although the cause of death was determined by gross examination during the autopsy, only the internal and histological examinations revealed that an unidentified infection and AEF pathophysiology also contributed to the cause of death. Although, AEFs are associated with a very high mortality rate due to massive exsanguinations, sudden death due to the rupture of an AEF associated with disseminated tuberculosis is very rare. However, in this case study, the authors were able to establish that the AEF was due to tuberculous mediastinitis during the autopsy. Although an AEF is rare, in cases of massive hematemesis, we recommend that it be considered as a potential cause of death. Tuberculosis should also be considered in such cases, especially in countries where the disease is endemic. In addition, full examinations during an autopsy should be performed to reveal other potential causes given that the diagnosis of such infectious diseases can only be made postmortem. This diagnosis has implications for practitioners and suggests that post-exposure prophylaxis is needed. Furthermore, an autopsy can unveil many hidden causes related to the death.

Acknowledgements

This study was supported by a grant from the Basic Science Research Program through the National Research Foundation of Korea (NRF) funded by the Ministry of Education, Science and Technology (Kim HS, NRF-2013R1A1A-2007621).

Disclosure of conflict of interest

None.

Address correspondence to: Dr. Jong-Tae Park or Dr. Hyung-Seok Kim, Department of Forensic Medicine, Chonnam National University Medical School, 5 Hak-dong, Dong-Gu, Gwangju, 501-757, Korea. Tel: +82-62-220-4090; Fax: +82-62-223-4250; E-mail: jtpark@jnu.ac.kr (JTP); veritas@jnu.ac.kr (HSK)

References

- [1] Egan C, Szontagh-Kishazi P, Flavin R. Aortic fistula after neoadjuvant chemoradiotherapy and esophagectomy for esophageal carcinoma: an

Death by aorto-esophageal fistula due to disseminated tuberculosis

- unusual cause of sudden death. *Am J Forensic Med Pathol* 2012; 33: 270-272.
- [2] Lee OJ, Kim SH. Aorto-esophageal fistula associated with tuberculous mediastinitis, mimicking esophageal Dieulafoy's disease. *J Korean Med Sci* 2002; 17: 266-269.
- [3] Yagi N, Akiyama H, Igaki N. Two cases of aorto-gastrointestinal fistula. *Intern Med* 1999; 38: 570-574.
- [4] Hollander JE, Quick G. Aorto-esophageal fistula: A comprehensive review of the literature. *Am J Med* 1991; 91: 279-87.
- [5] Peck JJ, Eidemiller LR. Aortoenteric fistula. *Arch Surg* 1992; 127: 1191-1193.
- [6] Kleinman LH, Towne JB, Bernhard VM. A diagnostic and therapeutic approach to aortoenteric fistulas: Clinical experience with twenty patients. *Surgery* 1979; 86: 868-880.
- [7] Steffes BC, O'Leary JP. Primary aortoduodenal fistula: A case report and review of the literature. *Am Surg* 1980; 46: 121-129.
- [8] Henry WJ, Miscall L. Aortic-esophageal fistula. *J Thoracic Cardiovasc Surg* 1979; 86: 868-880.