Successful Medical Treatment for Aortoesophageal Fistula after Thoracic Endovascular Aortic Repair

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Aortoesophageal fistula is a fatal disease that requires surgical treatment. Due to the patient's wishes, we chose medical treatment for aortoesophageal fistula after thoracic endovascular aortic repair for a pseudoaneurysm in the distal anastomotic site after total aortic arch replacement. Satisfactory early and long-term outcomes were obtained with complete fasting and appropriate antibiotics.

Key words: Aortoesophageal fistula, Thoracic endovascular aortic repair, Antibiotic treatment

INTRODUCTION

Aortoesophageal fistula (AEF) is a fatal disease that requires surgical treatment. Here, we report a case in which antibiotic treatment was successfully used for a patient who developed AEF after thoracic endovascular aortic repair (TEVAR) for an aneurysm in the distal anastomotic site after total aortic arch replacement.

CASE REPORT

The patient was a 70-year-old male who was transferred to our hospital for treatment of a pseudoaneurysm that had developed in a anastomotic site (Fig. 1A) one year after total aortic arch replacement performed at another hospital using an elephant trunk procedure for a true aortic aneurysm. TEVAR was performed with the GORE-TAG thoracic endoprosthesis (TAG; W.L. Gore, Flagstaff, AZ). The patient was discharged from hospital 5 days after TEVAR with no endoleak shown by computed tomography (CT).

The patient was readmitted to hospital due to dysphagia and fever 19 days after TEVAR. He had a high WBC count of 9.8×10^3 /μL and a high CRP level of 12.60 mg/dL. CT showed air density in the aneurysm and posterior mediastinum (Fig. 1B). Esophagography showed leakage of contrast media in the mediastinum (Fig. 1C). Esophagoscopy revealed a fistula 28 cm from the incisor and invading adipose tissues (Fig. 1D), and AEF was diagnosed. The patient was fasted and given an antibiotic, meropenem hydrate (MEPM), intravenously at a dose of 4 g/day. We planned esophagectomy, graft replacement and omentopexy, but the patient declined this treatment. Therefore, fasting, intravenous hyperalimentation and treatment with antibiotics were continued. Blood culture was negative, but MEPM-sensitive *Stenotrophomonas maltophilia* (*S. maltophilia*) were detected in 3 sputum cultures. Therefore, MEPM was administered for 26 days. Three weeks of strict food fasting were used to avoid the concern of transesophageal infection from oral ingestion.

Esophagoscopy on day 21 after readmission confirmed fistula disappearance and scarring (Fig. 2A). Based on an improved inflammatory response (WBC 5.4×10^3 /μL, CRP 0.55 mg/dL) and disappearance of air density on CT (Fig. 2B), ingestion of a liquid diet was started, and MEPM was replaced with oral rifampicin (450 mg/day) and levofloxacin (500 mg/day). The patient was discharged from hospital on day 51 after readmission. Rifampicin and levofloxacin are still being administered 6 years after readmission, although CT showed reduced aneurysm and CRP was < 0.03 mg/dL. Consent for publication was obtained from the patient and written in the medical record.

DISCUSSION

This report is a rare case of a patient who survived medical treatment without surgical intervention for an AEF after TEVAR. AEF is difficult to treat and has the highest mortality among TEVAR-treated diseases. AEF occurs in 1.9% of cases after TEVAR [1]. Okita *et al.* [2] suggested that one-stage open radical surgery provides a better outcome for AEF compared with conservative treatment, and in a multicenter analysis of AEF as a complication after TEVAR, Czerny *et al.* [3] found no one-year survival without esophagectomy. We are also confident that open radical surgery is best for treatment of AEF, but the current patient declined this treatment.

There are various pathogenic bacteria in patients with AEF; however, approximately 20% of these are detected in blood culture. Multivariate analysis [4] showed that long-term administration of antibiotics for

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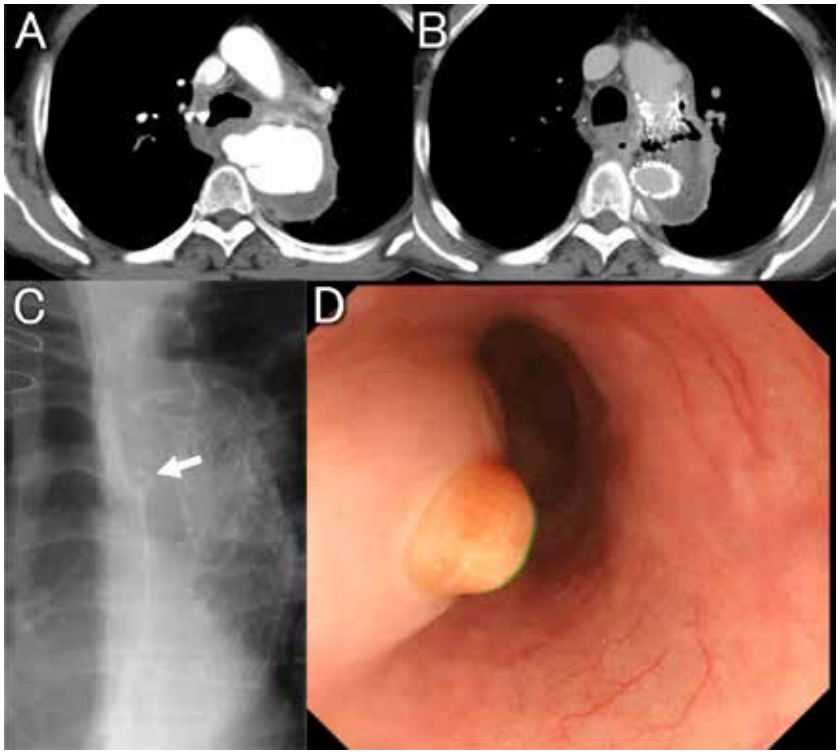

Fig. 1 A. Computed tomography (CT) showed a pseudoaneurysm in the distal anastomotic site. B. CT after TEVAR showed air density in the aneurysm and posterior mediastinum. C. Esophagography after readmission showed leakage of contrast media (white arrow). D. Esophagoscopy showed adipose tissues in the esophageal fistula.

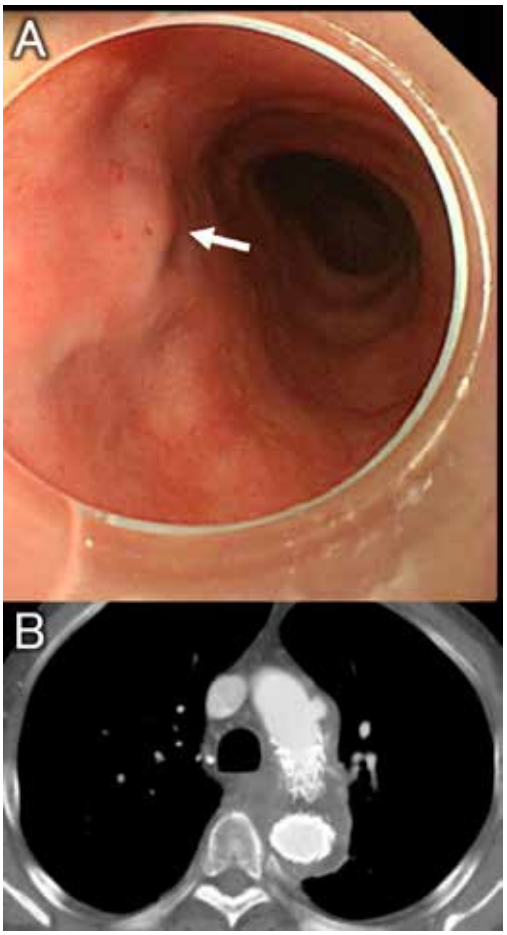

Fig. 2 A. Esophagoscopy showed disappearance and scarring of the esophageal fistula (white arrow). B. CT showed disappearance of air density in the aneurysm and posterior mediastinum.

AEF treatment significantly decreased aorta-related death. Although, microbial detection is required to select antibiotics with high sensitivity, TEVAR does not allow sampling from the surgical field and it is difficult to detect pathogenic bacteria. AEF is likely to complicate with aphagia; therefore, there is a possibility that bacteria refluxing from the esophagus are included in the sputum, and these oral bacteria are probably pathogenic. Therefore, in addition to early administration of broad-spectrum antibiotics, frequent conduct of sputum culture is recommended to allow selection and administration of appropriate agents.

AEF has a very serious course. Conservative treatment with antibiotics alone may not be life-saving, and invasive treatment may be required [3, 5]. Akashi *et al*. suggested that esophageal removal, vascular graft replacement, and omental filling are necessary to save the patient's life and that treatment should not be completed with TEVAR alone [6]. There are no cohorts that have received antibiotic therapy as first-line treatment without surgical intervention. Therefore, we believe that patients with AEF should undergo surgery and we strongly recommended surgery to our patient, but he declined surgery. We note that the long-term results of radical surgery are poor, with a 5-year survival rate of only 42.4% found by Yamazato *et al*. [7]. Infection control with preoperative antibiotics is important in surgery for AEF [2], and since our patient refused surgery, strong and broad-spectrum antibiotics were used as an empiric approach from the beginning of treatment.

Staphylococcus aureus is the most common cause of AEF after aortic treatment, followed by hemolytic streptococcus. A variety of other bacteria, including Escherichia coli, Pseudomonas aeruginosa, fungi, enterococci, and pneumococci, may also be involved [8]. Meropenem, vancomycin and fluconazole are the most common antibiotics used to prevent graft or stent infection. Therefore, graft replacement and esophagectomy can achieve a favorable prognosis for patients with AEF, but strong, broad-spectrum antibiotic therapy may be required to prevent sepsis after surgery [9]. Since our patient had refused surgery, strong broad-spectrum antibiotic use was initiated as an empiric approach. We were aware that *S. maltophilia* is a concern as the most commonly reported carbapenem-resistant Gram-negative pathogen. A sputum culture revealed *S. maltophilia*, but de-escalation of antibiotics was not performed because possible infection by multiple strains not detected in the culture could not be ruled out. We were concerned that de-escalation of antibiotics targeting only *S. maltophilia* might exacerbate infection by other undetected strains or lead to bacteremia, with potentially disastrous results. Therefore, surveillance cultures were strengthened, and as a result, carbapenem-susceptible *S. maltophilia* was detected in three sputum cultures.

Cure with complete fasting and antibiotic treatment in our case may have occurred because of stable hemodynamics and systemic conditions, a small fistula with esophageal penetration, adipose tissues in the mediastinum between the esophagus and descending aorta, and administration of appropriate antibiotics. It is also possible that fasting may induce microbial drainage into the esophagus.

We recognized that the mainstay of oral antibiotic treatment for *S. maltophilia* infections was trimethoprim-sulfamethoxazole (TMP-SMX), and this remains the current drug of choice. However, in this case, obtaining tissue cultures from the surgical field was not possible, and we suspected that other bacterial species would be latent. Oral administration of a combination of rifampicin and levofloxacin is often selected as broad-spectrum antibiotic empiric therapy after surgery for infected aortic aneurysm and graft infection, and we chose life-long oral administration of these antibiotics.

We continued careful follow-up for the occurrence of adverse reactions such as emerging drug-resistant pathogens, diarrhea, liver, and renal dysfunction. Antibiotics after surgery for AEF are continued for 4 to 8 weeks, with the goal of a negative inflammatory reaction. After this period, it may be possible for antibiotics to be discontinued [10], but other reports suggest that oral antibiotics should be continued life-long [11, 12]. We have experience indicating that graft infections due to aortobronchial fistula can recur up to 3 years after surgery if suppressive antibiotics are stopped. Thus, we believe that patients with this infection should be treated with life-long antibiotic therapy. In the current case, 12 years have passed since TEVAR, with no side effects or recurrence of infection under continuous oral administration of rifampicin and levofloxacin. Thus, satisfactory early and long-term outcomes were obtained in this case, but further follow-up is required.

CONFLICT OF INTEREST

The authors declare that there are no conflicts of interest associated with this manuscript.

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