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CASE REPORT

# Treatment of a broncho-esophageal fistula complicated by severe ARDS

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## Abstract

**Introduction** Broncho-esophageal fistula formation is a rare complication of tuberculosis, most often seen in immunocompromised patients.

**Methods and Results** In this paper, we report the case of a young non-immunocompromised refugee from Somalia diagnosed with open pulmonary tuberculosis complicated by extensive osseous involvement and a broncho-esophageal fistula with consecutive aspiration of gastric contents. The patient rapidly developed a severe acute respiratory distress syndrome (ARDS) requiring venovenous extracorporeal membrane oxygenation (ECMO) therapy for nearly 2 months. The fistula was initially treated by standard antituberculous combination therapy and implantation of an esophageal and a bronchial stent. Long-term antibiotic treatment was instituted for pneumonia and mediastinitis. 7 months later, discontinuity resection of the esophagus was performed and the bronchial fistula covered by an intercostal muscle flap.

**Discussion** This case illustrates that tuberculosis should always be suspected in patients from high-incidence countries in case of lung involvement and that an interdisciplinary approach including long-term intensive care management can enable successful treatment of tuberculosis with severe, near-fatal complications.

**Keywords** Broncho-esophageal fistula · Tuberculosis · ARDS · ECMO

## Case report

In November 2016, a 28-year-old male refugee from Somalia, who had been living in Germany for 1.5 years, was referred to our center. The patient had presented in a district hospital with abdominal pain, nausea and vomiting. In April 2016, he had been treated for atypical pneumonia of the right upper lobe in the same hospital. At that time, HIV, hepatitis B and C had been ruled out. The patient had not been tested for tuberculosis.

A computed tomography (CT) scan of the thorax and abdomen was suggestive of cavitary tuberculosis (TB) confined to the right upper lobe and spinal TB involving several vertebral bodies (Th 7, Th 9 with a paravertebral abscess, L 2 with bone fragments invading neuroforamina and the spinal canal, S 1 and S 2). In addition, an abscess of the left psoas muscle had to be noted (Fig. 1b, c). Instability of the spine was evident, but urgent surgical decompression was not required.

Respiratory secretions revealed acid-fast bacilli (Fig. 2a) that were identified as fully sensitive *Mycobacterium*

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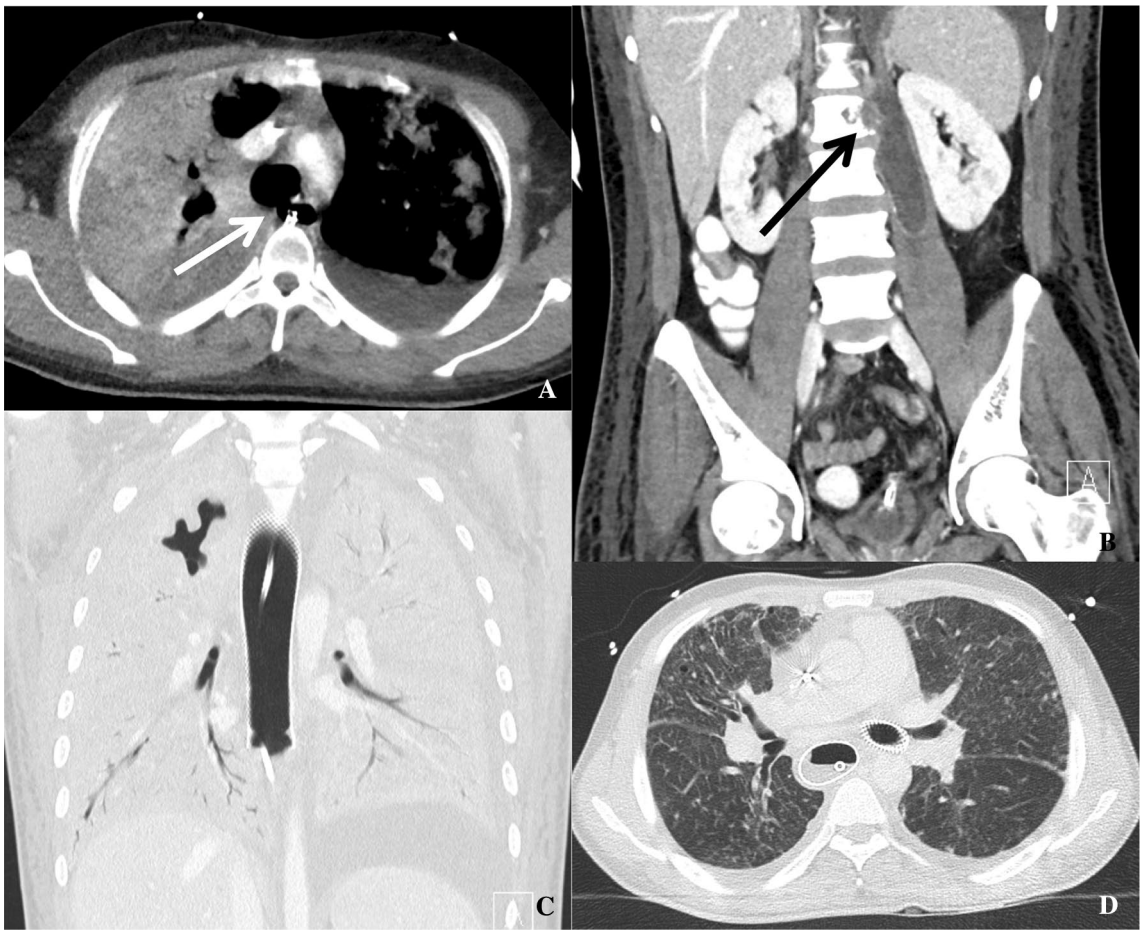


**Fig. 1** Computed tomography. **a** BEF formation (arrow), **b** an abscess of the lumbar spine with the abscess of the psoas muscle (arrow), **c** the maximum extent of ARDS (white lung) and the esophageal stent, **d** resolution of ARDS; the esophageal and bronchial stent are still in place

*tuberculosis* and standard combination antituberculous therapy (isoniazid, rifampicin, ethambutol, pyrazinamide) was initiated.

The following day, the patient developed rapid deterioration with respiratory insufficiency and was transferred to our intensive care unit (heart rate 128/min, respiratory rate 35/min, blood pressure 86/52 mmHg, Apache II score 15, SOFA score 7 on admission). A chest X-ray revealed considerably increasing bilateral pulmonary infiltrations. Antibiotic therapy with piperacillin/tazobactam was initiated to treat suspected pulmonary superinfection. With increasing hypoxic failure, endotracheal intubation was necessary the same day. We noticed an extensive insufflation of the patient's stomach and leakage of air via the naso-gastric tube in spite of correct position of the endotracheal tube. A broncho-esophageal fistula (BEF) reaching from the esophagus to the left main bronchus (Fig. 1a) was found to be the source of aspirate entering the bronchial system, causing severe disseminated inflammation with persisting elevated levels of CRP (Fig. 3).

Within a few hours, the patient developed a severe acute respiratory distress syndrome (ARDS) with rapidly decreasing tidal volumes and increasing hypoxia in spite of highly invasive ventilation [Horowitz index ($pO_2/FiO_2$) 65 mmHg]. As ultima ratio, a venovenous ECMO (extracorporeal membrane oxygenation) therapy using a bi-caval dual lumen catheter (AVALON Elite, Maquet, Rastatt, Germany) was initiated. A large, partially covered esophageal stent was inserted endoscopically to cover the fistula.

Weaning from the ECMO was possible over the course of 27 days under extensive antibiotic therapy. Percutaneous dilatational tracheotomy was performed to optimize weaning from the respirator. Only 6 days after explantation of the ECMO, respiratory function deteriorated again (Horowitz index 64 mmHg), requiring highly invasive ventilation and finally a second round of venovenous ECMO therapy. At the same time, the inflammatory parameters increased, indicating relapsing pneumonia. Simultaneous bronchoscopy and esophagoscopy demonstrated passage of methylene blue in both directions, broncho-esophageal and vice versa,

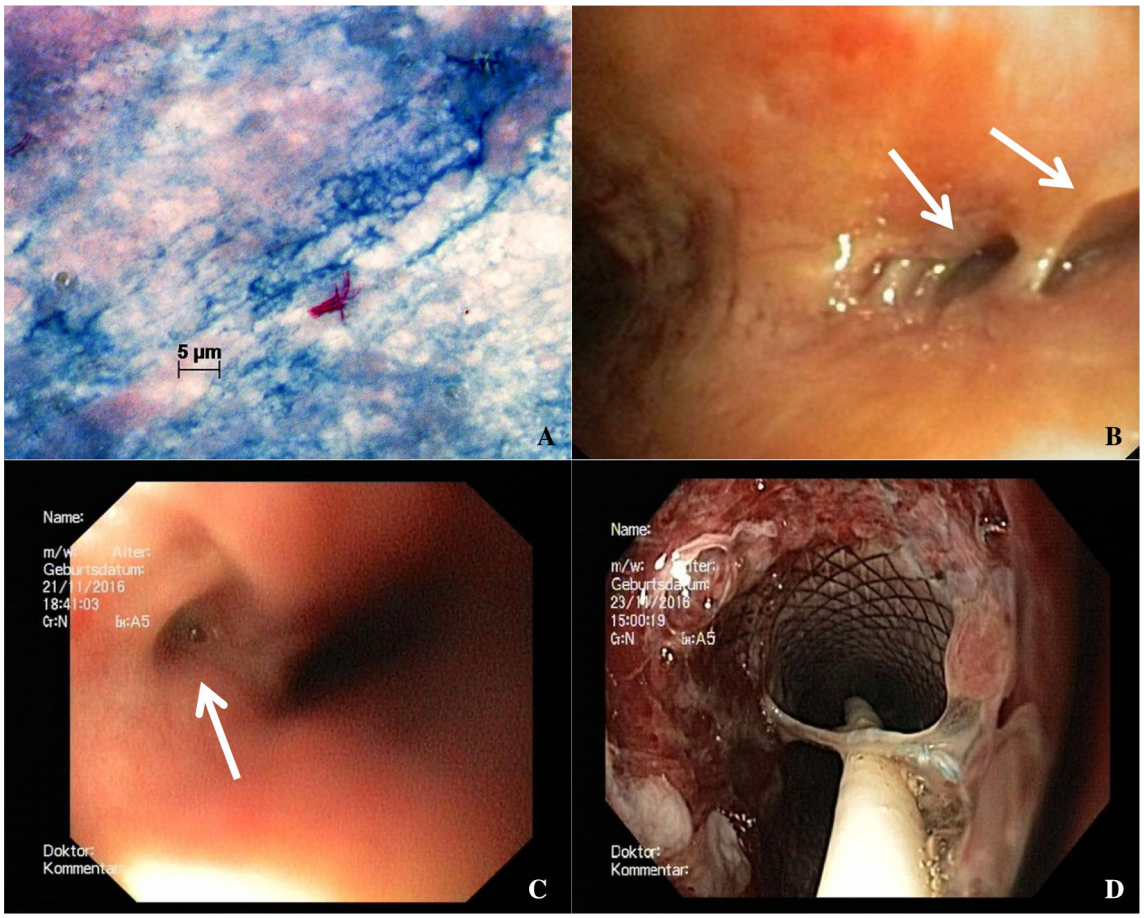


**Fig. 2** **a** Acid-fast bacilli in a sputum probe in Ziehl–Neelsen staining. **b** The bronchial opening of the fistula, which is shown in **c** in esophagoscopy. **d** The esophageal stent

confirming BEF persistence, although the esophageal stent was in correct position.

To prevent further leakage, an additional bronchial stent was implanted. From month 2 until month 6, we established long-term antibiotic therapy with piperacillin/tazobactam to prevent mediastinitis.

The patient suffered several further complications during the course of the prolonged hospital stay. Acute anuric renal failure with acute tubular necrosis requiring dialysis developed soon after admission. Urogenital manifestation of TB was ruled out. Bilateral hemorrhagic pleural effusions were continuously evacuated. PCR and a culture of the effusion were tested positive for *M. tuberculosis*. Furthermore, the patient suffered from severe chronical illness polyneuropathy and myopathy.

In repeated interdisciplinary case discussions with intensivists, thoracic, abdominal and orthopedic surgeons, pneumologists, infectiologists and nurses, there was consensus to postpone surgical therapy until stable recovery was achieved. Ethical issues concerning how long therapy should be continued in such a prolonged course of severe illness were also discussed.

The patient was ECMO dependent for another 26 days before weaning was achieved.

Decannulation of the tracheostoma was finally achieved by the end of March 2017 after 130 days of invasive ventilation. By the end of April 2017, the patient's renal function had recovered and dialysis could be terminated.

In June 2017, both the esophageal and the bronchial stent were explanted, a discontinuity resection of the esophagus with cervical end esophagostomy was performed and the bronchial fistula was covered by an intercostal muscle flap. The postoperative course was complicated by impairment of wound healing and formation of pleural empyema. However, by the end of August 2017, the patient had recovered and was finally discharged for rehabilitation. Antituberculous treatment was stopped after 9 months. Reconstruction of the continuity of the esophagus was performed in November 2017. Due to the complicated course, spinal stabilization was postponed for another 6 months.

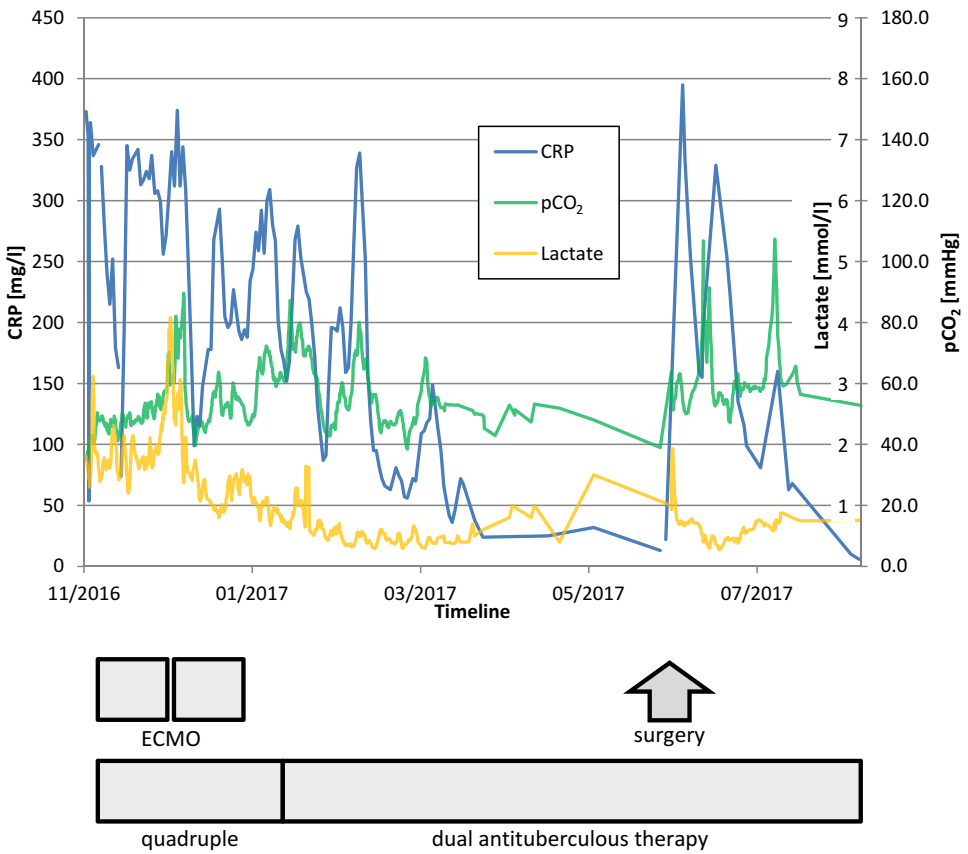


**Fig. 3** Course of CRP, $pCO_2$ and lactate. Note the increase of $pCO_2$ and lactate with every peak of inflammatory activity

## Discussion

There has been a change in the migration pattern into and within Europe in the last years, especially from countries with a higher prevalence of TB resulting in a higher risk for contracting the disease during migration and for the development of active TB [1]. In these patients, extrapulmonary TB manifestations such as miliary, meningeal and abdominal TB are associated with a higher risk of mortality [2].

Broncho-esophageal fistulas are a rare but potentially life-threatening complication of extrapulmonary TB. There are no studies comparing treatments and outcomes. Risk factors include immunosuppression [3, 4]. BEFs have been found more frequently in HIV-infected patients, probably due to a larger proportion of patients with lymph node TB [4]. BEFs secondary to TB in non-HIV patients, as seen in our case, are rare [5].

Four mechanisms are discussed in the development of TB-associated BEFs. In cases of active pulmonary TB, endobronchial involvement may be present in 10–40% of cases and may lead to fistula formation by erosion of bronchial ulcers into the esophagus [5, 6]. Esophageal ulcers in gastro-intestinal TB may perforate into the trachea or bronchi [5]. Rupture of caseonecrotic mediastinal lymph nodes into the esophagus and bronchus can lead to fistula formation. Furthermore, traction diverticula between the respiratory tree and the esophagus may develop [5, 6]. In our case, mediastinal lymphadenopathy was confirmed in the chest CT scan and was considered the most likely cause of the BEF formation.

Our patient initially had presented with abdominal pain, nausea and vomiting. He developed acute respiratory failure due to aspiration pneumonia and ARDS. The most characteristic symptom in cases of BEF is paroxysmal coughing particularly following ingestion of fluids; usually symptoms of lower respiratory tract infection are also present [6–8]. Other rather non-specific complaints may consist of wasting, retrosternal burning sensations or dysphagia [3, 6, 9]. In most cases, respiratory symptoms are mild and severe ARDS caused by aspiration pneumonia has only been previously described in one case report [10].

Traditionally, surgical repair has been advocated for the treatment of benign BEFs, but there has been a change of paradigm with antituberculous chemotherapy becoming the mainstay for the management of tuberculous BEFs [5]. Some authors recommend nasogastric feeding [4, 7, 8] to prevent further inflammation. In cases of severe stenosis or perforation, surgery may be required. Bronchoscopy performed in conjunction with esophagoscopy allows pre-operative analysis and planning for surgical correction [11].

Recently, endoscopic repair of BEFs with fibrin glue or hemoclipping has been reported [5, 6], there are even case reports about palliative closures of malignant fistulas using cardial septal occluder devices [12]. Surgical measures include lobectomy with primary closure of fistulas and reinforcement with intercostal muscle flaps [13] and even total gastrectomy with Roux-en-Y end-to-side esophagojejunostomy in case of perforation [11].

In our case, an esophageal stent was not sufficient for sealing the BEF, probably due to the pronounced inflammation and a persisting gastric paresis with high amounts of reflux. The combination of an esophageal and a bronchial stent with adequate antituberculous as well as anti-microbial chemotherapy under long-term ECMO support allowed the ARDS to resolve. The BEF, however, persisted, making surgical treatment inevitable.

7 months earlier, our patient had been treated for upper lobe pneumonia in a district hospital. Unfortunately, TB had not been investigated at that time. It is highly probable that the patient had already been suffering from pulmonary TB and that adequate therapy at this stage could have prevented the fistula formation and the severe course.

TB has become a rare disease in Western European countries. Nevertheless, the index of suspicion must still be high even for typical TB presentations, especially in patients with exposure to *M. tuberculosis* in endemic countries. Medical teams must be aware of the possibility of unusual presentations of TB to render early and interdisciplinary treatment. This case of a non-immunocompromised patient from a high-incidence country with severe ARDS requiring ECMO therapy due to a tuberculous BEF exemplifies that TB should always be suspected and actively investigated.

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## Compliance with ethical standards

**Conflict of interest** On behalf of all authors, the corresponding author states that there is no conflict of interest.

**Ethical approval** Treatment of the patient, preparation of the manuscript and discussion in the context of published literature comply with ethical standards and are in agreement with the Declaration of Helsinki.

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