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Late AIDS presentation with tracheoesophageal fistula as an early complication of pulmonary-disseminated tuberculosis – a case report and review of the literature

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ABSTRACT:

- ***Background:*** Tracheoesophageal fistula (TEF) is a complex, challenging condition with a varying degree of acuity, pathogenesis, and therapeutic approaches. TEF is a pathological connection between the trachea and the esophagus that is associated with various underlying conditions.
- ***Case Report:*** A unique report of a TEF of tubercular origin, as a presentation of acquired immunodeficiency syndrome (AIDS) in a young patient with undiagnosed human immunodeficiency virus (HIV) infection, resolved with conservative therapy notwithstanding the extremely severe immunodeficiency and multiple opportunistic infections, is described and commented on the grounds of an updated literature review.
- ***Conclusions:*** There are few reports in the literature of HIV and tuberculosis infection-related TEF and/or bronchoesophageal fistula (BEF). Other reported causes of TEF in AIDS include infections caused by *Mycobacterium avium*-intracellulare, *Candida albicans*, *Nocardia* species, cytomegalovirus and herpes simplex virus. TEF caused by tuberculosis is an exceedingly rare complication and has been postulated to occur secondary to the rupture of caseous peribronchial lymph nodes into adjacent mediastinal structures with subsequent fistula formation. Most patients underwent conservative medical management, as in our case, with parenteral nutrition, with the help of a percutaneous endoscopic gastrostomy (PEG) tube, and parenteral antimycobacterial treatment and antiretroviral therapy (ART) with successful outcomes.
- ***Keywords:*** AIDS, Acquired immunodeficiency syndrome, HIV, Tuberculosis, Tracheoesophageal fistula, Bronchoesophageal fistula.

INTRODUCTION

Tracheoesophageal fistula (TEF) is a life-threatening condition due to an abnormal communication between the posterior tracheal wall and the anterior esophageal wall, associated with various underlying conditions, including malignancies, infections, inhalation injuries, and traumatic damage. TEF can manifest as an isolated congenital lesion, but it is more frequently associated with esophageal atresia at birth. Congenital TEF is mainly associated with esophageal atresia, while acquired TEF is less reported and can

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be caused by malignancies or other benign conditions.

Benign TEF occurs more commonly in the setting of prolonged mechanical ventilation *via* endotracheal tube or tracheostomy tube. Other conditions associated with TEF may include blunt trauma to the chest or the neck; traumatic airway injury, granulomatous mediastinal infections due to tuberculosis, stent-related injuries, and ingestion of foreign bodies or corrosive products.

The most common cancer associated with malignant TEF is esophageal cancer, with >10% of patients developing the condition during its clinical course[1].

TEF can develop in cancer patients due to tumors, tumor progression, or as a complication of treatment. This can lead to severe complications like aspiration, recurrent pneumonia, sepsis, and potentially fatal hemorrhage if major blood vessels are eroded. TEFs may manifest as persistent tracheal air leaks, abdominal distension (resulting from air entering the digestive tract), pulmonary aspiration injury, cough with swallowing, copious bronchopulmonary secretions, and respiratory distress.

Despite the high frequency of gastrointestinal complications in human immunodeficiency virus (HIV) infected patients, TEF and bronchoesophageal fistulas (BEFs) are extremely rare but serious complications in patients with acquired immunodeficiency syndrome (AIDS), typically caused by opportunistic infections like tuberculosis (TB) or cytomegalovirus (CMV) that form deep esophageal ulcers[2]. As a matter of fact, TB and CMV are the most common causes of spontaneous TEFs in the context of AIDS, creating ulcers that can erode into the trachea. *Candida* and Herpes simplex virus type 2 have also been implicated. A few other reported cases have occurred with infections caused by *Mycobacterium avium*-intracellulare and *Nocardia* species[3].

In susceptible individuals, a TEF can be challenging to diagnose due to the non-specific nature of symptoms and the potential for underlying conditions to mask the fistula. Diagnosis relies on a high index of suspicion, imaging techniques, and endoscopic procedures[4]. TEF may develop from direct tumor invasion or as a result of therapies, as radiation and chemotherapy, that can induce tumor necrosis and tissue breakdown, leading to fistulization[5].

A malignant TEF is usually an unfavorable prognostic feature, and the survival of such patients is frequently low. Management of malignant TEF deserves special attention, and the data about the impact of radiation treatment on outcome is not clear[6].

Acquired TEF, not secondary to malignancy, is considered a rather rare clinical entity; it has been reported[4-6] as a post-traumatic[5] complication in patients undergoing mechanical ventilation or following a tracheostomy and/or a severe local inflammatory process, and finally, it could be a late manifestation of a congenital TEF.

Early diagnosis and early surgical intervention, considered the treatment of choice, are still the key to successful management of non-malignant TEF.

We conducted a literature search of peer-reviewed articles in PubMed between 1991 and 2023 using the keywords “acquired TEF” and “TB” in order to report a narrative retrospective analysis of cases of TEF associated with tuberculosis in people living with AIDS, aiming to document and evaluate the presentation, treatment modalities, and outcome. Despite the introduction of highly active antiretroviral therapy (HAART) since the mid-1990s, cases of late-presenting AIDS with multiple opportunistic infections and neoplasms still occur, and TB remains a relevant co-infection where this disease is still endemic.

Despite the high frequency of gastrointestinal complications and opportunistic infections in people living with AIDS, TEF and BEF are rarely reported in these settings.

CASE REPORT

A 33-year-old female from Venezuela presented to the Emergency Department of our hospital on June 29, 2022, reporting worsening chest and abdominal pain for a few days, intermittent fever for several weeks and progressive dyspnea from minimal effort.

Her medical history was unremarkable; she stated that she had been living in Italy for two years and had not reported any health problems concerning her previous husband, from whom she had been separated for over 5 years. He has never used drugs, has never complained of organic disorders and has no known co-contacts with people with HIV and/or TB. Systemic physical examination showed an undernourished woman with generalized reduced muscle strength, shortness of breath, tachycardia, decreased muscle mass, pain on superficial abdominal palpation, and diffuse dry lung sounds.

Chest and abdominal computed tomography scanning (CT-scan) with contrast revealed mediastinal necrotic-colliquative lymphadenopathies, pericardial effusion (max thickness 1.7 cm), multiple, innumerable, micro-nodules at all lung lobes, multiple bilateral alveolar-interstitial thickening, and bilateral basal pleural effusion (Figure 1). There was evidence of a TEF with extra luminal spread of the incoming contrast medium in the mediastinal air collection, the latter in communication with the airway lumen: inhaled contrast medium tended to accumulate in the segmental bronchus for the apical segment of the right inferior lobe (Figure 1). Lymphadenopathy in the cephalo-duodeno-pancreatic lodge, a solid thickening of the right sub-umbilical rectus abdominis muscle (3.7 x 1.8 x 3.2 cm), and a minimal effusion in the hepatorenal recess and fluid layer between the loops in the hypogastric and pelvic region were also detected.

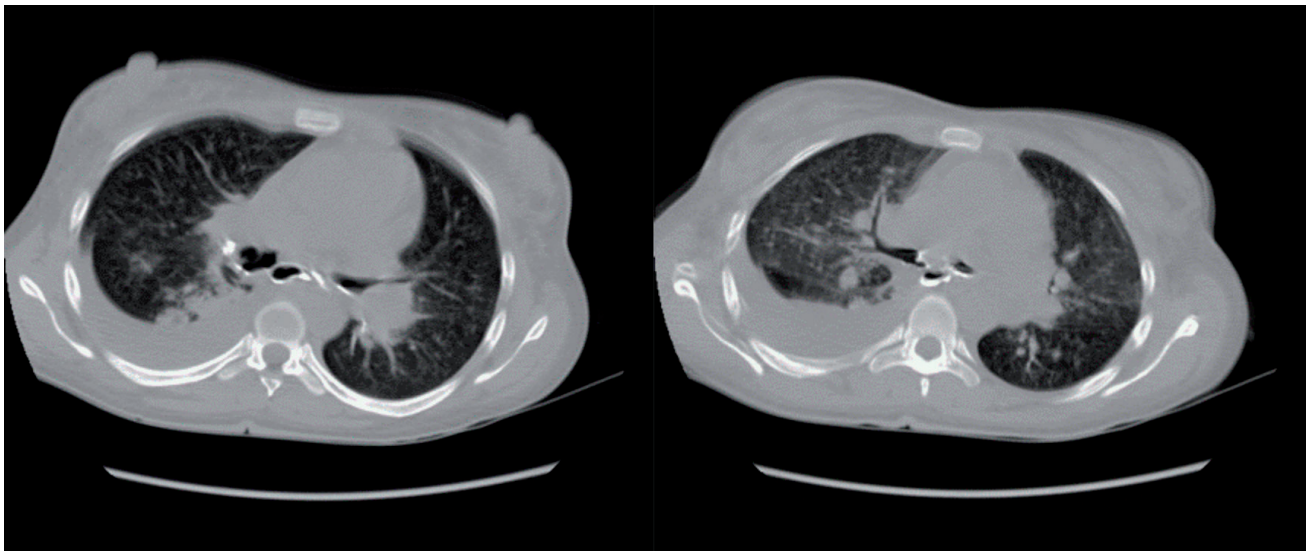

Figure 1. TEF: evidence of leakage of contrast medium entering the mediastinal air collection, in communication with the airway lumen. The contrast medium accumulates in the segmental bronchus of the apical segment of the superior left lobe.

An esophagoduodenoscopy (EGD) on day 2 documented the presence of normal-expandable esophageal walls with a regular course, the presence of esophageal candidiasis and evidence of a two-centimeter TEF in the middle esophagus, 30 cm from the dental arch.

Cardiac incontinence was observed during the retroversion maneuver.

A bronchoscopy on day 3 showed a subverted and irregular tracheal mucosa of the bronchial hemisystems, stratified by mucopurulent material, tenaciously adhered to the walls; spontaneous bleeding, with a picture of acute tracheobronchitis with structural subversion of the mucous membranes, and suspected TEF (Figure 2).

A bronchial histo-biopsy revealed the presence of fragments of bronchial mucosa, focally hyperplastic, the chorion of which is the site of intense chronic active and acute inflammation, as well as necrotic-purulent inflammation. A cytological examination of the broncho-alveolar lavage fluid appeared as almost exclusively blood material, mixed with rare dysplastic epithelial elements.

Admission laboratory tests are summarized in Table 1.

The different laboratory investigations have documented an HIV-positive status confirmed after two positive HIV tests and high-level CMV plasma DNAemia by quantitative polymerase chain reaction (PCR) technique (268,385 IU/mL). Screening tests for the hepatitis C virus and the hepatitis B virus were negative.

An extensive microbiological study on broncho-alveolar lavage fluid (BAL) yielded negative results for the detection of bacteria, viruses and fungi, *Cryptococcus neoformans* antigenemia, 1,3-beta-glucan antigen, galactomannan antigen and the detection of *Pneumocyctis jiroveci*-DNA; the search for *M. tuberculosis*-DNA by real-time (RT)-PCR assay, from sputum and BAL specimens, for the rapid diagnosis of TB was positive; a screening rapid genotypic assay to test susceptibility to rifampin resulted negative. The interferon gamma releasing (IGRA) serum assay was negative (quantiferon mitogen 3.53, quantiferon nil 0.838, TB1 – NIL 0.081, TB2 – NIL 0.055, mythogen – nil 2, QTF interpretation negative; quantiferon Ag T1 0.757, quantiferon Ag T2 0.783), probably because of the extremely severe underlying immunodeficiency.

Immunologically compromised individuals may have a diminished ability to mount a robust immune response, which is necessary for the IGRA to produce a positive result.

This reduced response can lead to a false-negative IGRA result, even if the individual is infected with *M. tuberculosis*. While IGRAs are valuable tools, they can produce false-negative results in individuals with weakened immune systems. Factors like the severity of immunosuppression, the stage of TB infection, and the type of IGRA used can also influence the test's accuracy.

A cardiological Doppler ultrasound documented a circumferential pericardial effusion.

Based on the results above, a diagnosis of pulmonary TB with dissemination to the mediastinal and abdominal lymph nodes, pericardium, and esophagus was established.

The patient was treated with oral isoniazid 300 mg/day, rifampicin 450 mg/day, ethambutol 1,000 mg/day, and pyrazinamide 1,200 mg/day for 8 weeks, followed by an additional 24 weeks of oral rifampin 450 mg/day and isoniazid 300 mg/day.

The immunovirological score at baseline was as follows: $CD4^+$ 28 cells/µL (8%), $CD8^+$ 259 cells/µL (71%), $CD4^+/CD8^+$ ratio 0.11, HIV-RNA 1,020,000 copie/mL copies/mL.

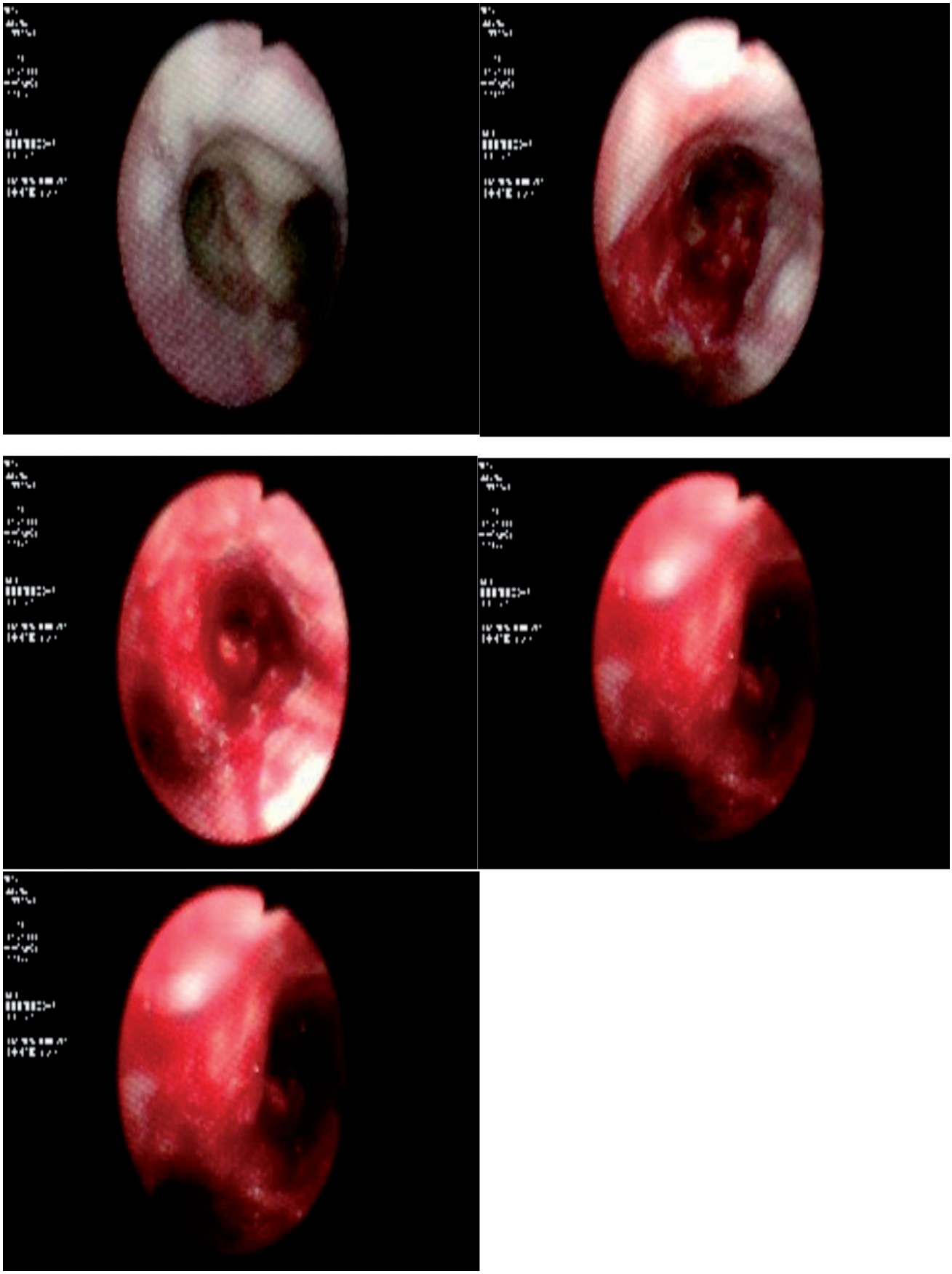

Figure 2. Images of the first broncoschopy showing vocal cords symmetrical and in axis, trachea in axis with preserved cartilaginous skeleton and enlarged median hull; the mucus covering the tracheal hull and the bronchial hemisystems appears irregularly subverted, stratified by mucopurulent material, tenaciously adhered to the walls with spontaneous bleeding. The picture shows acute tracheo-bronchitis with structural subversion of the mucous membranes and suspected TEF.

Table 1. Admission laboratory tests.

Tests	Results	Reference values
Leukocytes	5.5	(4-11 × 10^6/mL)
Neutrophils	4.6 (83.9%)	(2.0-8.0 × 10^6/mL)
Lymphocytes	0.5 (10.4%)	(1-5-3.5 × 10^6/mL)
Hemoglobin	8.2	(12-16 g/dL)
Hematocrit	24.1%	(36-46%)
NLR	9,000	
PLR	792,000	
Ferritin	1,780	(11-307 ng/ mL)
Cholinesterase	2,126	(3,930-11,500 U/L)
Albumin	1.8	(3.5-5 g/dL)
Lactate dehydrogenase	392	(50-248 U/L)
Serum folate	5	(3-20 ng/mL)
C-reactive protein	254.3	(0-5 mg/L)
Procalcitonin	1.117	(<0.1 ng/mL)

NLR, neutrophil/lymphocyte ratio; PLR, platelet/lymphocyte ratio.

Simultaneously with the anti-TB treatment, the patient received intravenous treatment with ganciclovir for 28 days and antifungal treatment with fluconazole for 28 days.

A prophylaxis against SARS-CoV-2 infection was promptly offered with tixagevimab plus cilgavimab.

An initial ART regimen with dolutegravir (DTG) 50 mg BID plus lamivudine (3TC) 300 mg, and abacavir (ABC) 300 mg was started 4 weeks after the introduction of the anti-TB therapy, through a naso-gastric tube (NGT).

A check of the viroimmunologic score 4 and 12 weeks after the start of ART documented the following results: HIV-RNA 504 copies/mL and 30.1 copies/mL, $CD4^+$ 77 (11%) and 152 (11%), $CD8^+$ 561 (77%) and 970 (69%), $CD4^+/CD8^+$ 0.14 and 0.15, respectively.

In the follow-up chest CT scan, performed after three months of antimycobacterial therapy (Figure 3), TEF was no longer detected, while small areas of consolidation in the right lung, some bilateral micronodules, some bilateral cylindrical bronchiectasis, a mild right pleural effusion and adenopathy in the hilum of the mediastinum were observed.

A control video bronchoscopy (Figure 4) performed three months after anti-TB therapy was started, showed a whitish punctate formation on the mucosa of the left corniculate cartilage, the trachea appeared patent and in line with pink mucosa and the presence of some roughness on the surface, scarring results of the previous TEF, and at the level of both bronchial hemisystems, the explorable bronchial branches appeared covered by hyperemic mucosa and granulomatous-like reliefs were observed in particular on the mucosa of the main bronchi.

The patient was then discharged in improved clinical conditions and with the resolution of the TEF, and she is still being followed up on HIV disease.

DISCUSSION

TEF is an abnormal, pathological connection between the esophagus and trachea, which can be a major source of significant morbidity and mortality. TEF is more often congenital and commonly occurs with esophageal atresia. TEF may also be acquired in adulthood due to esophageal cancer or lung cancer, infection (such as TB), or trauma from a medical procedure, and may lead to severe and fatal pulmonary complications.

In the past, the most common cause of acquired benign TEF and BEF was from granulomatous mediastinal infection, more commonly TB.

Possible mechanisms underlying the development of such fistulae include rupture of caseonecrotic subcarinal lymph nodes into the esophagus and trachea, erosion of primary tracheal ulcers into the esophagus, or development of traction diverticula between the respiratory tree and the esophagus.

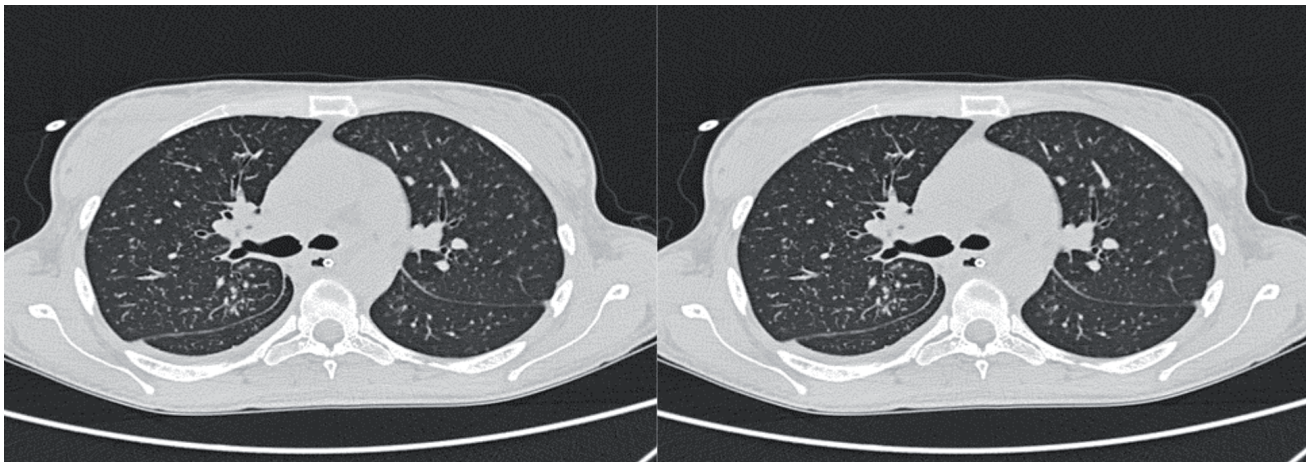

Figure 3. TEF was not detected, while the presence of small areas of consolidation in the right lung, some bilateral micronodules, some bilateral cylindrical bronchiectasis, a mild right pleural effusion and adenopathy at the mediastinal hilum were observed.

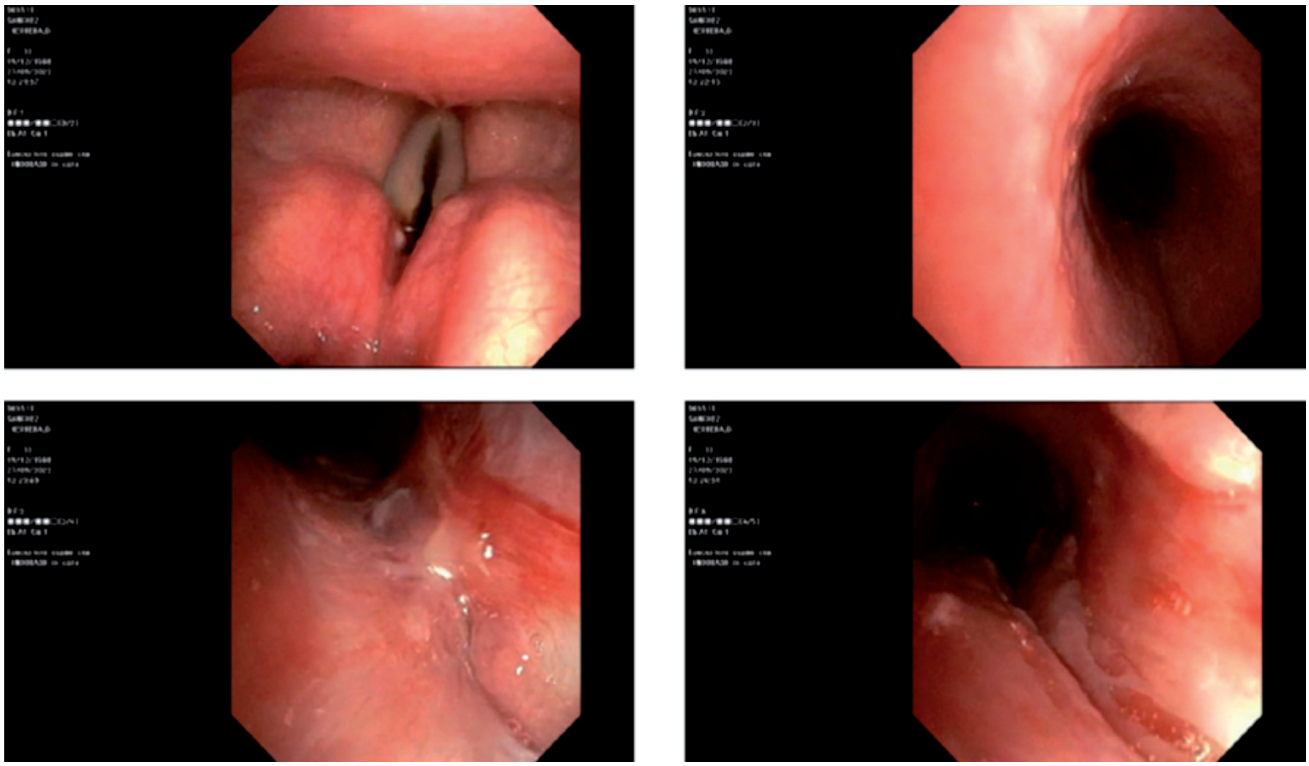

Figure 4. Before the patient was discharged, bronchoscopy showed the presence of a punctiform whitish formation on the mucosa of the left corniculate cartilage. The trachea appeared permissive and aligned, displaying a pink mucosa with some surface roughness. The cartilaginous skeleton was preserved, and the median carina appeared mobile with respiration. Scarring from the previous esophago-tracheal fistula was evident. At the level of both bronchial hemisystems, patency of the explorable bronchial branches is noted, which appear covered by hyperemic mucosa; the presence of granulomatous-like reliefs is observed, present in particular on the mucosa of the main bronchi.

TEF is a morbid condition, and surgical correction (esophageal bypass and esophageal stenting) is required because spontaneous closure is rare. It is a rare occurrence in immunocompromised hosts, and among people with HIV; only a few cases of TB-associated TEF have been described to date[7-11].

Esophageal involvement by TB is rare in both immunocompetent and immunosuppressed individuals; as a matter of fact, the esophagus is the organ least likely to be infected by TB, usually resulting from extension from adjacent structures or by hematogenous spread from a distant site. Esophageal TB is rare but appears to be increasing, especially in endemic areas and in immunosuppressed individuals. TB can occur in any segment of the esophagus, but is more common in the middle third just proximal to the tracheal bifurcation or carina, probably because of the concentration of lymph nodes around the carina.

Coughing while eating or drinking suggests the development of a TEF. CT is mandatory for documentation of the secondary nature of the disease.

A narrative review[7-11] of TB-associated TEF cases in people living with AIDS documented the publication from 1990 to 2018 of 8 cases (7 males, one female; median age 39 years, range of age 27-54 years) in 5 reports[7-11]. Five patients recovered after conservative therapy, one patient died on the 50th hospital day, and two patients signed out of the hospital and have been lost to follow-up (Table 2).

We have also discovered ten cases of BEF (6 males, 4 females, median age 32 years, range of age 19-48 years) due to TB in people with HIV, described in 8 articles[12-20] published between 1991 and 2017.

All these patients recovered after conservative treatment, mainly based on anti-TB therapy and parenteral nutrition; only two patients underwent surgical treatment. After diagnostic tracheoscopy and esophagoscopy with identification of the size and form of the fistula, indications for endoscopic or conservative treatment were determined (Table 3).

Endoscopic stenting *vs.* surgical repair has been discussed by many authors. Rosario et al[8] preferred endoscopic management in a person with HIV, while Shah et al[20] pointed out the risks related to endoscopic/stenting procedures in the presence of granulomatous lesions.

From Spain, Mosquera Klinger et al[11] reported the stent migration in the presence of an underlying CMV-tuberculous infection.

From France, Couraud et al[21] alerted to the need for concomitant management of both esophageal and tracheal edges of TEF.

Saikia MK et al[22] described their surgical repair of TEF based on an intercostal muscle flap and local glue application.

Hungarian authors[23] described that high-frequency ventilation of the trachea proved useful in trachea reconstruction after TEF.

Table 2. Tracheoesophageal fistula (TEF) due to tuberculosis in the setting of HIV disease.

References, age, sex	$CD4^+$ ($/mm^3$), Main presentation	HIV-RNA (copies/mL)	Esophagography	EGD	Thoracic CT scan	Diagnosis	Treatment	Outcome
de Silva et al[7], 1990, USA; 53 y/M	Fever, cough, odynophagia, and dysphagia of 3 weeks duration	N.A.	Esophagitis, esophago-mediastinal communication	A 4-mm-diameter ulcer 28 cm from the incisors. Examination of a biopsy specimen of the ulcer revealed squamous mucosa with acute and chronicinflammation and numerous acid-fast organisms	Mediastinal adenopathy, nodal air	Examination of a biopsy specimen of the ulcer revealed AFB	Anti-TB chemotherapy	Died on the 50th hospital day
de Silva et al[7], 1990, USA; 42 y/M	Fever, chills, cough, night sweats, and chest pain of 2 weeks duration	N.A.	Esophageal ulcer with mass effect, and wa BEF	Not done	Mediastinal adenopathy	AFB were found in the sputum	Anti-TB chemotherapy	The patient signed out of the hospital
de Silva et al[7], 1990, USA; 27 y/M	Fever, cough, weight loss, chest pain, and odynophagia of 3 weeks duration	N.A.	A 2-cm-diameter deep ulcer in the midesophagus, eso- phagomediastinal communication	Not done	Not done	One month earlier, pulmonary tuberculosis had been diagnosed	Anti-TB chemotherapy	The patient signed out of the hospital
Rosario et al[8], 1996; 33 y/M	A recent history of coughing-up food immediately after ingestion	100, N.A.	Not done	Fistulous tract arising 5 cm above the carina; a fistulous connection between the esophagus and the trachea	Not done	Not done	An esophageal stent and a NGT were placed	Recovered
Devarbhavi et al[9], 2003, India; 37 y/M	Diarrhea, dysphagia	N.A.	Irregularity proximal third, ulcer middle third	3-cm ulcer over submucosal swelling at 30 cm from incisor teeth	Mediastinal lymphadenopathy	Not done	Not done	Recovered
Devarbhavi et al[9], 2003, India; 32 y/M	Dysphagia, neck swelling	N.A.	Ulcer middle third	3-cm excavated ulcers with edges at 27 cm	Mediastinal lymphadenopathy	Not done	Not done	Recovered
Pagano et al[10], 2007, Italy; 54 y/F	Cough, wasting, low-grade fever, weakness and lymphadenopathy	51, 16,000	Not done	Two sublaryngeal TEF identified by EGD, confirmed by bronchoscopy	Not done	Lymphnodes and pulmonary	PEG, parenteral/ enteral nutrition, iv anti-TB chemotherapy, ART	Recovered
Mosquera Klinger and Holguín Cardona[11], 2018, Colombia; 39 y/M	Fever, dry cough of a three-week duration, which worsened after the ingestion of food or fluids	N.A.	Not done	TEF with an orifice with a diameter of 2 cm and marked inflammatory changes at 30 cm from the dental arches	Not done	N.A.	Esophageal SEMS→ OTSC®; anti-TB, ART	Recovered

DOT, direct observed therapy; SEMS, self-expanding metal stent; OTSC®, the over scope clip; PEG, percutaneous enterogastric tube; NGT, naso-gastric tube; EGD, esophagoduodenoscopy; iv, intravenous; ART, antiretroviral treatment; N.A., not available; AFB, acid-fast bacilli; ART, antiretroviral therapy.

Table 3. Bronchoesophageal fistula (BEF) due to tuberculosis (TB) in the setting of HIV disease.

References, age, sex	Main presentation	CD4+ (/mm³), HIV-RNA (copies/mL)	Esophagography	EGD	Bronchoscopy	Thoracic CT scan	Diagnosis	Surgical intervention	Treatment	Closure time	Outcome
Allen et al[12], 1991, England; 38 y/M	An 8 week history of fever, weight loss and malaise	N.A.	A fistula from the upper esophagus into the right paratracheal mass at a lower level into the right main bronchus	N.A.	N.A.	A complex mass originating above the sternal notch and contained pockets of gas	Necrotic tissue with granulomas and AFB. MTB was isolated from cultures	Not necessary	NGT feeding, tubercular chemotherapy	1 month	Recovered; however, 1 month later he was readministered because of a new BEF
Porter et al[13], 1994; England; a 24 y/F, Ugandan	A 1-week history of fever, dry cough, and dysphagia	20/mm³	Two BEFs	An ulcerated lesion at 30 cm	Widened carina, suggesting enlarged subcarinal nodes	Confirmed two BEFs		Not necessary	NGT feeding, tubercular chemotherapy	4 and 9 months	Recovered
Porter et al[13], 1994; England; 19 y/M, Ugandan	A 2-month history of dysphagia, cough weight loss, fever	20/mm³	A BEF at the sixth thoracic vertebra	BEF opening at 25 cm	N.A.	Pleuro-pericardial effusions, adenopathy	Not done	Not necessary	NGT feeding, tubercular chemotherapy	2 weeks	Recovered
Porter et al[13], 1994; England; 38 y/M, West Indian	An 8-week history of fever, sweats, and a rash on the back, weight loss	20/mm³	Two BEFs from the upper esophagus to the right main bronchus via paratracheallymph nodes	N.A.	N.A.	A large mediastinal mass, including pockets of gas	Lymph-node biopsy specimens: non-giant-cell granuloma, and AFB	Not necessary	NGT feeding, tubercular chemotherapy	4 months	Recovered
Asnis et al[14], USA; Argentina	A 1-week history dyspnea, and fever	20	A BEF below the level of the carina, into the right bronchial tree	N.A.	A 7-mm opening in the right main-stern bronchus below the main carina	Bilateral infiltrates, mediastinal adenopathy, and an air pocket corresponding to the level of the BEF	MDR TB was cultured from sputum, bronchoscopic washings	Not necessary	Parenteral nutrition, tubercular chemotherapy	1 month	Recovered

Continued

Table 3 ***(Continued)*****.** Bronchoesophageal fistula (BEF) due to tuberculosis (TB) in the setting of HIV disease.

References, age, sex	Main presentation	CD4+ (/mm3), HIV-RNA (copies/mL)	Esophagography	EGD	Bronchoscopy	Thoracic CT scan	Diagnosis	Surgical intervention	Treatment	Closure time	Outcome
Dronda et al[15], 1995, Spain; 27 y/F	Dysphagia, cough provoked by swallowing	52	Not done	N.A.	Two BEFs in the right main bronchus and a third in the left subcarinal area	Infiltrates in the middle lobe and hilar enlargement	MT was isolated from the sputum	The patient underwent endoscopic bronchial surgery	The patient refused NGT feeding	3 months	Recovered
Vartian and Septimus[16], 1996; Texas-USA; 40 y/M	Fever, weight loss, and cough, while he was drinking li quids	44/mm3	Two BEFs: one area above the carina, and the second extended from the subcarinal area and communicated with the right mainstem bronchus	N.A.	N.A.	Mediastinal infiltration, lymphadenopathy, and pneumomediastinum	Dual infection with MTB and CMV	Not necessary	NGT feeding, tubercular chemotherapy	2 months	Recovered
Ravera[17] 1997, Uganda; 37 y/M	Night sweats, retrosternal burning, vomiting after meals	N.A.	Fistula communicated with bronchi	A BEF at the middle third of the esophagus	N.A.	A slide wide of the upper mediastinum and calcified mediastinal adenopathy	Sputum cultures grew MTB	Not necessary	Tubercular chemotherapy	N.A.	Recovered
Ravera[18], 1998, USA; 29 y/F	A 3-day history of fever, chills, and cough	39	A right-BEF	Not done	N.A.	Right lower and middle lobe infiltrates, right hilar adenopathy	Sputum cultures grew MTB	Not necessary	NGT feeding, tubercular chemotherapy	2 months	Recovered
Alexander[19], South Africa; 27 y/F	Cough exacerbated by ingestion of liquids and solids	N.A.	Two BEFs	BEFs were noted in the main bronchi below the carina	BEFs were noted in the main bronchi below the carina	Bilateral bronchiectasis	N.A.	Surgery was undertaken (Ivor-Lewis's procedure)	NGT feeding	2 weeks	Recovered

AFB, acid-fast bacilli; ZN, Zhiel-Neelsen; NA, not available; MTB, Mycobacterium tuberculosis; MDR TB, Multidrug-resistant TB; CMV, cytomegalovirus; BEF, bronchoesophageal fistula; TBEF, tuberculous bronchoesophageal fistula; NGT, nasogastric feeding tube.

Italian authors[24] reported a lethal case of AIDS-related TEF secondary to a dual *Candida* and CMV infection.

Moreover, a key role is played by clinical, laboratory, and instrumental differential diagnosis when multiple opportunistic infections are expected or are present (like in our case), and/or an underlying cancer lesion may be of concern.

Other authors[25] underlined the role of CT virtual bronchoscopy to drive both diagnosis and treatment of TEF, but the many pitfalls of both diagnosis and management of TEF had already been recognized since the 1960s.

CONCLUSIONS

When reporting an extremely rare case of TEF in a young late AIDS presenter, we emphasize the importance of prompt management of all associated disorders, which can serve as clinical confounders in these highly vulnerable patients, as well as our success with conservative antimycobacterial, antifungal, antiviral, and nutritional treatments in this challenging context. Although primary repair is recommended for people living with AIDS with a TEF/BEF, medical therapy has resulted in the mainstay of management of TB-associated TEF and/or BEF, with complete healing of the fistula with standard drug regimen alone usually leading to complete cure.

For TEFs caused by advanced cancer[26,27], or in very fragile individuals such as patients with AIDS and/or tuberculosis disease where surgery is not feasible and is not an option, due to the high clinical risk and/or the diffusion of tuberculosis infection, interventions like airway stenting can provide a minimally invasive option to close the fistula, relieve obstruction, improve breathing, palliate symptoms, and enhance quality of life[26,27].

Authors' Contributions:
A. Mastroianni: conceptualization, writing – original draft preparation, review and editing.
R. Manfredi: supervision, review and editing.
V. Vangeli: data curation, formal analysis, methodology.
G. Guadagnino: data curation, formal analysis.
L. Chidichimo: data curation, formal analysis.
L. Berardelli: data curation, formal analysis.
S. Greco: writing – original draft preparation, review, and editing.

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Written informed consent has been obtained from the patient for the publication of this case report.

Conflict of Interest:
All authors declare they have no personal and financial relationships with other people or organizations that could influence (bias) their work.

Ethics Approval:
Not required due to the nature of the study.

Data Availability:
Data are available on request from the authors.

AI Disclosure:
The authors declare they have not used artificial intelligence or assisted technologies in the production of the article.

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