

Esophageal pulmonary fistula and malignancy

VITORINO MODESTO DOS SANTOS¹⁾, LISTER ARRUDA MODESTO DOS SANTOS²⁾

¹⁾*Department of Internal Medicine, Armed Forces Hospital and Catholic University of Brasília–DF, Brazil*

²⁾*Department of General Surgery, State Worker's Hospital, São Paulo–SP, Brazil*

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Dear Editor,

We read with major interest the recent article of high quality by Cameniță *et al.* published in this Journal focusing on the morphological profiles of esophageal carcinomas obtained from 46 surgically treated cases [1]. Esophageal carcinoma is the seventh most common cancer and the sixth cause of death associated with cancers. Besides low socioeconomic status, tobacco smoking, alcohol consumption, and diet are synergic risk factors. Predominantly affect males of older age groups, are often found in the lower segments of organ measuring 5 to 10 cm of major diameter, causing stenosis (50%), and often presenting infiltration, protrusion, and ulcerated macroscopic aspect [1]. Squamous cell carcinoma (SCC) and adenocarcinoma are the two more common histological patterns of esophageal cancers, which usually evolve aggressively, are late-diagnosed, and with different morphological and behavioral profiles. Worthy of note, most of the esophageal carcinomas are classified as poorly differentiated tumors in stage III, and the main histological type (90%) is SCC, with a more elevated incidence in developing countries [1]. The authors highlighted their following findings: more frequent invasion of the neighboring structures (T4); predominance of a poorly differentiated pattern; uniform distribution of SCCs along the esophagus; less than 20% of distant metastasis (more often detected in the SCCs; and a more accentuated trend to high stages of the SCCs [1]. Although more frequently invading the structures surrounding the esophagus, there was no description of fistulae.

Based on the findings of this well-planned Romanian research, we decided to add comments on data of studies about the esophageal respiratory fistula, a scarcely reported entity that can be congenital or acquired [2–4]. Acquired esophageal respiratory and esophageal aortic fistulae are found in late stages of predisposing conditions, after invasive procedures, or chemoradiotherapy complications [2–4]. Half of the cases have a malignant cause and up to 15% of advanced esophageal cancers give origin to fistulae, 52–57% are tracheal, 37–40% bronchial, and 3–11% pulmonary [2–4]. Tuberculosis, syphilis, histoplasmosis, actinomycosis, and candidiasis are more rare causes [3]. Common manifestations of esophageal respiratory fistula are productive cough, mid-thoracic pain, dysphagia, sentinel hemorrhage, and repeated episodes of aspiration pneumonia [2–4]. Confirmatory data depend on images of fluoroscopy with oral Barium contrast, computed tomography (CT), besides esophagoscopy or bronchoscopy to verify the anatomic site [2–4]. Mechanisms include tracheal direct invasion by cancer, erosion of the airway by metastatic lymph nodes, inflammatory tissue necrosis of esophagogastrostomy, and chemoradiotherapy-induced necrosis; main risk factors are bulky tumors of the mid-thoracic esophagus, elevated C-reactive protein or carcinoembryonic antigen, young age, and necrotizing stenosis [2]. These fistulas are uncommon in esophageal cancer but pose challenges to management; their first treatment options are jejunal tubes and fully covered self-expanding metal stents [2–4]. The mean survival time without treatment in fistula due to malignancy is one to six weeks [4]; video-assisted thoracoscopic procedures favor the elimination of infected tissues or effusions. Antimicrobials must be active against Gram-positive and anaerobic bacteria, as well as fungi; but the management is usually palliative, aiming to get an improvement in the quality of life with the focus on nutritional depletion, respiratory insufficiency, and pulmonary sepsis [2–4].

Ghosh *et al.* recently reported a 56-year-old woman with esophageal pulmonary fistula due to an unsuspected esophageal cancer that clinically evolved mimicking a lung abscess [4]. Sputum exam showed mixed flora and Piperacillin–Tazobactam and Clindamycin were used. Based on manifestations and images of plain chest radiography, she unsuccessfully underwent this antibiotic therapy before the contrast-enhanced CT and endoscopy showed the esophageal malignancy and the fistula in communication with the cavity at right lower pulmonary lobe. Further oral contrast administration revealed a defect at the right lateral wall of the esophagus leaking the contrast within the lung cavity, confirming the esophageal pulmonary fistula. Gastrointestinal endoscopy yielded biopsy samples of ulcerated

lesions in the mid esophagus. A moderately differentiated SCC was diagnosed in stage IVB (T4b N2 M1), and the option was for palliative Cisplatin-based chemotherapy plus radiotherapy [4]. The authors emphasized the hidden malignant esophageal fistula in the differential diagnosis. The lack of esophageal symptoms propitiated initial misdiagnosis and late correct diagnosis, but after abscess drainage and self-expandable esophageal stent the outcome was favorable. On longstanding follow-up, she had no residual pulmonary cavity [4].

Similar scenery was related to a never-smoker 46-year-old woman with an initial diagnosis of pulmonary abscess by *Klebsiella* spp. refractory to the antibiotic treatment [3]. Plain chest radiographs showed condensations and cavities in the right pulmonary lower lobe, and she underwent Amoxicillin and Clavulanic Acid unsuccessfully. Her clinical condition deteriorated, with convulsive episodes and right hemiparesis, respiratory failure, and death. Necropsy revealed enlarged lymph nodes in mediastinum, a right lung tumor with cavities, an esophageal pulmonary fistula, and cerebral metastasis that caused the neurological changes. Immunohistochemistry study was negative for cytokeratin (CK)5/6, CK10, CK14, p63, thyroid transcription factor-1 (TTF-1), and synaptophysin (Syn); while the CK7 and CK20 positive were consistent with primary lung cancer. Esophageal cancers display CK10 and CK14 positive and negative CK7 and CK20 [3]. The final diagnosis was a high-grade poorly differentiated carcinoma with a large cell variant. The authors highlighted the never-smoker status of a patient with pulmonary cancer, besides the role of complete autopsy studies to establish the correct *causa mortis* in challenging cases [3].

Malignant esophageal pulmonary fistula evolving unsuspected or misinterpreted can give origin to diagnostic pitfalls, in special because clinical and imaging findings may mimic a lung infection. Commentaries on these challenging conditions scarcely reported may contribute to enhance the awareness of health care workers avoiding the occurrence of misdiagnosis with poor outcomes of late diagnosis.

Conflict of interests

The authors had full freedom of manuscript preparation and there is no conflict of interests.

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Corresponding author

Vitorino Modesto dos Santos, Professor, MD, PhD, Department of Internal Medicine, Armed Forces Hospital, Estrada do Contorno do Bosque s/n, Cruzeiro Novo, 70630–900 Brasília–DF, Brazil; Phone #55–6132330812, Fax #55–6132331599, e-mail: vitorinomodesto@gmail.com

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