

Endoscopic management of recurrent tracheoesophageal fistula induced by chronic use of nonsteroidal anti-inflammatory drugs: A case report and review of the literature

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Tracheoesophageal fistula (TEF) is frequently congenital and requires surgical correction. TEF can also occur secondary to malignant esophageal tumors or benign diseases and these cases are managed by endoscopic means, such as closing the defect with metallic stents. Although esophageal injury can occur secondary to nonsteroidal anti-inflammatory drugs (NSAIDs), TEF secondary to chronic NSAIDs use has not been described in the literature.

We report the case of a male patient with refractory migraine and chronic use of NSAIDs, with a history of esophageal stenosis presenting with acute-onset total dysphagia. Upper gastrointestinal endoscopy and CT-scan revealed TEF located at 25 cm from the incisors. An esophageal stent was placed endoscopically, and 6 weeks a second stent was placed in a stent-in-stent manner to allow removal of both stents. Endoscopic control after the removal of the stents showed the persistence of the fistula, so a third stent was placed as a rescue therapy.

Against medical advice, the patient continued to use OTC painkillers and NSAIDs in large doses. Three months later, he was readmitted with total dysphagia and recent-onset dysphonia. CT scan revealed a new fistula above the already placed stent. A second metallic stent was endoscopically placed through the old stent to close the newly developed fistula. The patient was discharged on the third day with no complications and he remains well at 6 months follow-up.

Due to small cases studies, recurrent TEF remains a therapeutic challenge. Endoscopic therapy is usually an effective solution, but complex cases might require multiple treatment sessions.

Key words: tracheoesophageal fistula – nonsteroidal anti-inflammatory drugs – esophageal stent.

INTRODUCTION

Tracheoesophageal fistula (TEF) is usually congenital, but it can also appear secondary to benign or malignant conditions. Malignant esophageal tumors are the most common cause of secondary TEF [1]. Other benign diseases which can cause TEF are tracheostomy, long-term mechanical ventilation, trauma, mediastinal infections and esophageal surgery or stenting [2].

Pill-induced esophageal injury is a common disorder, especially among older patients, with a high prevalence for esophagitis, but ulcers, strictures and aorto-esophageal fistula secondary to nonsteroidal anti-inflammatory drugs (NSAIDs) use have also been described in the literature ³. There are, however, no reports of TEF secondary to NSAIDs.

The treatment of TEF is mostly endoscopical, consisting in esophageal and tracheal stenting or a combination between stenting and closure of the defect with glue [1].

Surgical approach has a high risk of complications [2] and should only be reserved for patients in whom endoscopic management has failed.

CASE REPORT

A 68-year old man with a history of refractory migraine and chronic NSAID ingestion (over 2 g per day ibuprofen) was admitted in our unit for total dysphagia. He had a history of benign esophageal stenosis and had undergone several bougie dilations over the past 20 years at another hospital. He had been diagnosed with recurrent migraine few years earlier and was currently taking carbamazepine (600 mg daily) as well as several over-the-counter NSAIDs and painkillers. Clinical examination revealed pallor, cachexia, cough with muco-suppurative expectoration and pulmonary rales. Laboratory studies showed mild anemia (Hb 9.5 g/dL), inflammatory syndrome (CRP 71.81 mg/L), hypokalemia (3.3 mmol/L) and cholestasis (GGT 5 times ULN).

Following admission, an upper GI endoscopy was performed which revealed a tracheoesophageal fistula located at approximately 25 cm from the incisors (Fig. 1).

A CT scan was performed, confirming the tracheoesophageal fistula, located at 11 cm below

the upper esophageal sphincter, with a diameter of 5 mm and a length of 6 mm. Other findings were enlarged mediastinal lymph nodes, hepatic hemangiomas and a suprarenalian adenoma, with no evidence of mediastinal masses.

We decided to place a 10 cm long, 18 mm-wide, partially covered, self-expandable metal stent (Wallstent, Boston Scientific) to close the fistula under endoscopic and fluoroscopic control. The patient was given intravenous antibiotics and was discharged home after three days.

He was scheduled for stent removal after 6 weeks. When he returned for endoscopic control and stent removal, he had already gained 7 kilo-

grams and was feeding normally. Of note, the patient had continued to use OTC medication (NSAIDs and various pain-killers) for his migraine.

A larger diameter stent was placed (12 cm/23 mm, fully covered – Wallstent, Boston Scientific) in a stent-in-stent manner and an attempt to remove both stents was undertaken 5 days later. Both stents were removed using a rat-tooth grasping forceps but endoscopic control after stent removal showed the persistence of the fistula (Fig. 2) which led to placement of a new metal stent (6 cm/18 mm, partially covered, Guangzhou Medical). The patient was discharged on the next day.



Figure 1. Endoscopic view of the first tracheoesophageal fistula.

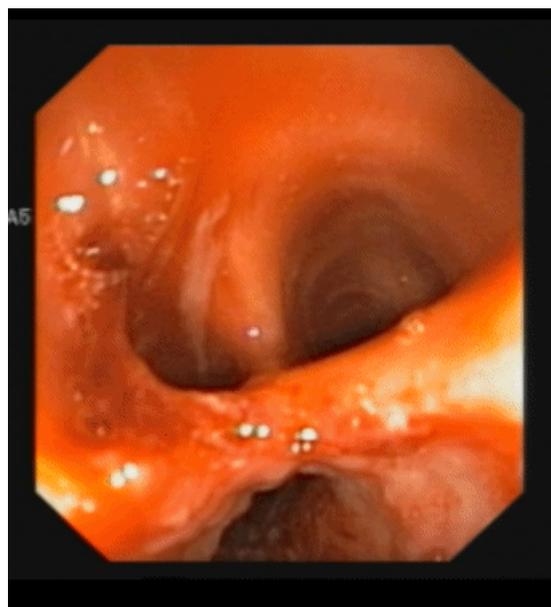


Figure 2. Endoscopic view of the first tracheoesophageal fistula after removing the esophageal stent.

Three months later, the patient was readmitted with total dysphagia, dysphonia and mucous expectoration. CT scan revealed a new fistula (Fig. 3) above the already placed stent and pneumonia of the lower left lobe. Antibiotics were started and a second metallic stent (15 cm/18 mm, partially

covered, Guangzhou Medical) was placed through the old stent to close the second fistula (Fig. 4). The patient completed a 7-day course of intravenous antibiotics and was discharged with minimal dysphagia with a follow-up visit scheduled at 3 months.



Figure 3. CT-scan view of the second tracheoesophageal fistula above the esophageal stent.



Figure 4. Radiological view after placing the second esophageal stent.

LITERATURE REVIEW

We conducted a Pubmed search using the following keywords in the title or abstract of potentially relevant papers: “nonsteroidal*”, “NSAID*”, “antiinflammatory agents, nonsteroidal” from the MeSH Database; “fistula*”, “esophageal fistula*”. We identified 73065 papers containing either “fistula” or “esophageal fistula” in their abstract and 76779 papers on NSAIDs. There were 71 results retrieved by our search using both types of keywords, most of them case reports of gastrocolic fistulas or postoperative fistulas, but no reports of esophageal fistulas secondary to NSAID use were identified after the abstracts of these studies were reviewed.

DISCUSSION

TEF can be congenital or acquired. Acquired fistula can be either benign, caused by prolonged intubation, secondary to caustic agents or secondary to infections or more commonly malignant, due to carcinoma of the esophagus. NSAIDs usually cause gastrointestinal injuries, but can rarely induce esophageal injury, among which ulcers and strictures are most commonly found [4]. No case report has yet been published about TEF secondary to NSAIDs. The exact mechanism by which these drugs can induce esophageal injury is unknown. Two mechanisms have been proposed, one related to the depletion of prostaglandins, based on the belief that they play as a protective agent in the mucosa and the other related to pepsin. NSAIDs make the esophageal mucosa barrier more permeable to pepsin, which may injure the collagen membrane [5].

Whereas treatment for malignant TEF is palliative, benign fistulas can be managed surgically or endoscopically with curative intent [6]. For our patient, the multidisciplinary consultation opted for the placement of an esophageal metallic stent due to his poor nutritional status and his chronic abuse of NSAIDs that might impede healing after surgery.

There are several endoscopic techniques for closing a TEF, with a rate of successful closure of the fistula in 87-100% [7]. Depending on the size, the degree of esophageal stenosis and the airway stenosis, different strategies could apply. For a small defect without airway stenosis an esophageal stent is the best option. For patients with bigger

defects, airway stenosis and without esophageal stenosis a double stenting is recommended¹. In our case the patient had a small fistula with no airway compression so we opted for an esophageal stent without tracheal stenting. After removing the esophageal stent at 6 weeks interval, we observed the persistence of the fistula so we decided to place a stent as a definitive treatment in this patient. Although closure of the first fistula was successful, the patient developed a second fistula 9 months later 1 cm proximal to the upper border of the metallic stent, probably through a combined mechanism (ongoing NSAID consumption and decubitus by the preexisting stent) [8]. This required placement of a second stent, also in a stent-in-stent manner, to ensure fistula closure. We decided to place the stent in the esophageal lumen as opposed to the tracheal side of the fistula because there were no signs of airway compression.

Multiple types of esophageal stents are currently available. Silicone stents can be easily removed and are very flexible, but have a greater risk of migration, whereas self-expandable metallic stents (SEMS) are easy to deploy but are more difficult to remove [6].

A new type of esophageal stent made from biodegradable materials is now also available on the market. It is made of woven polydioxanone monofilament and it starts to dissolve after 11 weeks [9].

Due to the small series of patients described in these studies of benign acquired TEF, we consider that treatment should be individualized based on the size and location of the fistula and the functional status of each patient.

Although there is an association between NSAIDs and esophageal injury, this is, to our knowledge, the first report of a recurring tracheoesophageal fistula secondary to chronic NSAIDs use, despite complex endoscopic therapy.

Recurrent TEF constitutes a therapeutic challenge and endoscopic treatment is a feasible treatment option in this case.

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Abbreviations: TEF: tracheoesophageal fistula; NSAIDs: non-steroidal anti-inflammatory drugs; OTC: over the counter.

Fistula esotraheală (FET) este, de obicei, o patologie congenitală și necesită tratament chirurgical. FET poate apărea secundar tumorilor maligne esofagiene

sau afecțiunilor benigne și aceste cazuri sunt rezolvate, cel mai des, prin tehnici endoscopice, cum ar fi închiderea defectului cu stenturi metalice. Deși afectarea esofagului poate apărea secundar consumului de AINS, fistula esotraheală secundară AINS nu a fost descrisă până în prezent în literatura de specialitate.

Prezentăm cazul unui pacient cu migrenă refractară, consumator cronic de AINS în doze ridicate, cu istoric de stenoză esofagiană secundară, care s-a prezentat cu disfagie totală apărută brusc. Endoscopia digestivă superioară și examenul CT au evidențiat FET localizată la 25 cm de arcada dentară. S-a montat un stent esofagian pe cale endoscopică și peste 6 săptămâni un al doilea stent a fost montat prin tehnica stent-in-stent pentru a permite extragerea ambelor stenturi. Controlul endoscopic după extragerea stenturilor a evidențiat persistența fistulei, așa că un nou stent a fost plasat cu viză definitivă.

În ciuda sfaturilor medicale, pacientul a continuat consumul de AINS și analgezice în doze mari. Trei luni mai târziu pacientul a fost reinternat pentru disfagie totală și disfonie recentă. Examenul CT a evidențiat o nouă fistulă deasupra stentului anterior. Un al doilea stent metalic a fost poziționat endoscopic prin stentul anterior pentru a închide și fistula nou apărută. Pacientul a fost externat 3 zile mai târziu fără complicații, și s-a menținut asimptomatic și la controlul de la 6 luni postprocedural.

Fistula esotraheală este o patologie rară, fiind dificil de tratat. Terapia endoscopică este o soluție eficientă, dar cazurile complexe pot necesita mai multe sedințe terapeutice pentru a oferi o soluție definitivă.

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