

Probiotic intake unmasking a gastro-pleural fistula

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Abstract. – OBJECTIVE: Gastropleural fistula represents a rare clinical event often resulting in an iatrogenic complication of gastrointestinal surgery. Clinical presentation is insidious, patients complain of chronic and non-specific respiratory symptoms and may be conservatively treated for lung infections for several months until detailed tests finally reveal the correct diagnosis.

PATIENTS AND METHODS: We describe a case of a healthy patient with an unexpected diagnosis of empyema due to a gastropleural fistula.

RESULTS: A 51-year-old man with a past history of splenectomy for cyst was admitted because of high fever and cough. A chest radiography and CT-scan revealed a left-side pneumonia complicated with pleural empyema. Broad spectrum empirical antibiotics and pleural drainage did not significantly improve the clinical picture. While the need for a surgical complex thoracic approach becomes a collective awareness, questions about causes of empyema and its unfavorable evolution in our patient did not initially find a common satisfactory answer. It was only by the identification of probiotics bacteria in the pleural fluid that a gastropleural fistula was suspected, and then, it was confirmed by CT-scan and by digestive endoscopy. A combined thoraco-abdominal surgical treatment was therefore scheduled, leading to progressive improvement till total healing.

CONCLUSIONS: Although gastropleural fistula is rare, it is necessary to include this pathological condition in the differential diagnosis of a persistent complicated pneumonia, because early diagnosis and, consequently, surgical management, may significantly impact on the prognosis of these patients. In our case, the detection of probiotics bacteria in the pleural fluid helped us to suspect and to look for the fistula.

Key Words:

Probiotic, Pneumonia, Fistula.

Introduction

Gastropleural fistula is a very rare communication between the gastrointestinal tract and the pleural cavity, sometimes representing a complication of gastrointestinal surgery^{1,2}. The diagnosis is based on radiological exams, such as CT scan after oral administration of Gastrografin (which allow to highlight the acquired communication between air and digestive systems) and by endoscopic investigations (that allow the identification of the fistula ostium).

Here we describe a case of gastropleural fistula in a patient that previously undergone splenectomy; the diagnosis was relieved by the evidence of orally administered probiotics inside the pleural fluid.

Case Description

A 51-year-old man was admitted to the Internal Medicine Department because of high fever (>39°C) for 5 days, resistant to amoxicillin/clavulanate therapy, associated with angry cough, chest pain and dyspnea after moderate physical activities.

In past history, the patient only referred a splenectomy with partial diaphragmatic resection because of a massive splenic cyst five years before, and surgery for back localized melanoma four years before (actually, negative follow up). No drug allergies, he denied vaccination for flu virus and capsulated germs. No history of smoking or cardiovascular events, no diabetes mellitus.

At the admission, the patient presented tachycardia and fever, normal blood pressure, and mild dyspnea with normal peripheral oxyhemoglobin saturation. At the physical examination of the thorax, vesicular murmur was absent at the left lower field. The electrocardiogram showed sinus

tachycardia. Chest X-ray showed a left pleural effusion associated with a hypodiaphanous lung parenchymal area. Laboratory tests showed an increase in C-reactive protein values (PCR, 147 mg/l) and neutrophilic prevalence of leukocytosis (white blood cells $21 \times 10^9/L$, neutrophils 80%). Blood and urine culture tests were negative, as well as atypical germ serologies and Quantiferon Test.

For bacterial pneumonia we started empirical antibiotic therapy with piperacillin/tazobactam and azithromycin, adding oral probiotics for prophylaxis of intestinal dysbiosis.

Unfortunately, no improvement was observed in the following days. High fever persisted, and the patient developed moderate hypoxic-hypocapnic respiratory failure. A chest CT-scan excluded signs of pulmonary embolism and confirmed the massive left pleural effusion with atelectasia with a suspicion of empyema. An upgrade of antibiotic therapy was prescribed (meropenem 1 g x3/day and linezolid 600 mg x2/day). At the same time, we decided to place pleural drainage. The pleural fluid resulted an exudate, while the cultures of pleural liquid were positive for *Roseomonas spp.*; the search of *Mycobacterium tuberculosis* (Ziel Nilsen staining and Polymerase Chain Reaction) resulted negative. Moreover, repeated blood and urine culture tests persisted negative.

After 10 days, blood tests showed only a mild laboratory improvement (PCR 58.1 mg/l, procalcitonin negative) but fever persisted (until 39°C) as well as the neutrophilic leukocytosis (white blood cells $20 \times 10^9/L$, neutrophils 81%). A new chest CT-scan showed on the left side a fluid collection with air bubbles and reactive signs of thickening of the pleural sheets (lung abscess/necrotizing pneumonia). So, we decided to perform a thoracoscopic toilet removing a remarkable amount of necrotic material located in the left pleural cavity. At surgery, the diaphragm was not explorable because of huge and firm adhesions at this level. In detail, the lung parenchyma was in strict contact with left hemidiaphragm and was affected by a necrotizing pneumonia at the level of the left lobar lobe. No pulmonary resection was indicated at this time.

Cultures of the pleural samples identified the presence of *Candida glabrata* but also *Lactobacillus gasseri*, *Lactobacillus spp.*, and *Bifidobacterium breve*. Due to these findings, we added Caspofungin. At the same time, the presence in the surgical sample of the same active probiotic bacteria orally administered led us to

assume the presence of a digestive-pleural fistula. This hypothesis was confirmed thanks to a specific CT-scan with oral administration of Gastrografin and by a gastroscopy that showed an ulcer of the gastric fundus with a fistula ostium (Figure 1).

Since this diagnosis, a combined thoraco-abdominal surgical treatment was scheduled. By a midline laparotomy, after gaining access to the left diaphragmatic region, we found a 3 cm diaphragmatic defect just lateral to the left crura with a strangulated sliding herniation of the gastric fundus. The hernia sac was reduced in abdomen and revealed a transmural necrosis of the herniated gastric fundus. The necrotic gastric wall was resected (Figure 2) and a handsewn gastric repair was performed. A redo-mini-thoracotomy was finally performed to better drain the pleural cavity from empyema associated to the gastro-pleural fistula. At surgery, the pleural cavity was completely damaged by the persistent gastric acids edged up from the stomach through the fistula. A partial pleurectomy was performed to remove necrotic pleura, and 2 pleural drains were left to treat at best the pleural empyema.

The postoperative course was uneventful. The nasogastric tube was removed on postoperative day (POD) 3. The patient started a liquid diet on POD 4 and a normal diet on the POD 6. The abdominal drain was removed in the POD 5. The two thoracic drains were removed on PODs 4 and 7. Antibiotic therapy was stopped on POD 8. The patient was discharged home on POD 9. At the

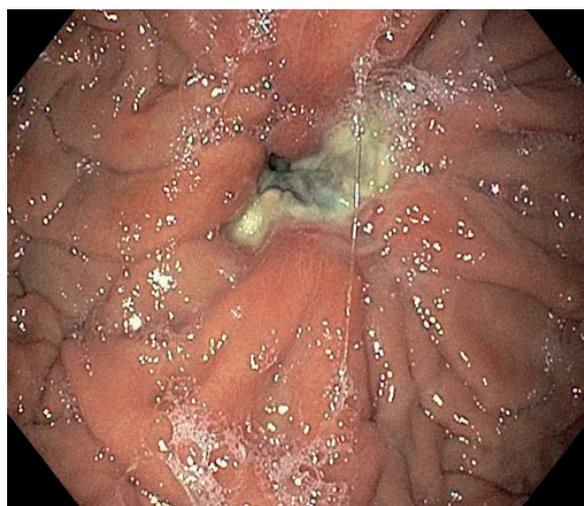


Figure 1. Endoscopy image showing an ulcer of the gastric fundus with drainage of purulent material from the ostium of the fistula.

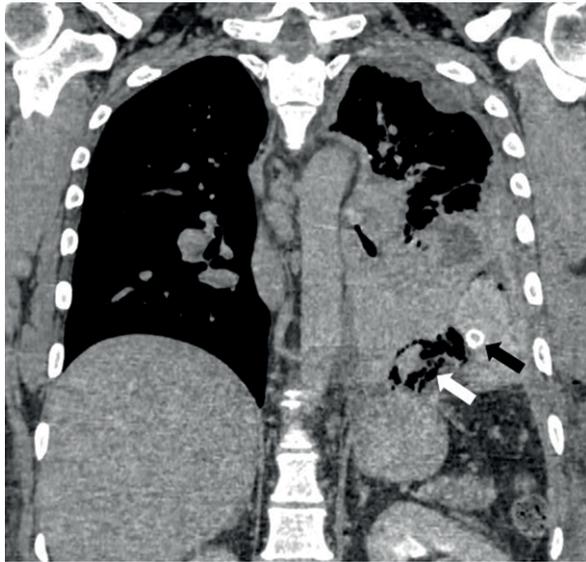


Figure 2. Chest CT scan showed the presence of an insidious gastro-pleural fistula (*white arrow*) causing a pleural empyema and necrotizing pneumonia resistant to pleural drain (*black arrow*) and antibiotics.

three months follow-up visit, the patient was in good clinical conditions, with no gastro-intestinal symptoms and a chest/abdomen CT-scan did not detect any sign of pleural/abdominal effusion.

Discussion

This represents a peculiar case, where clinical reasoning led to an unexpected but fortunately crucial diagnosis.

In this young and healthy patient (except only for a previous not-traumatic splenectomy), a necrotizing pneumonia complicated by pleural empyema that did not improve despite multiple antibiotics, pleural drainage, and a thoracoscopic toilette had unavoidably triggered questions about causes and eventual predisposing factors. In our case, the finding of orally assumed probiotic bacteria in the pleural cavity represented the key element leading us to the hypothesis that there was a connection between gastrointestinal tract and pleural cavity. Therefore, it is plausible that the presence of the fistula represented the *primum movens* of the whole pathophysiological process.

As reported from the literature, gastro-pleural fistulas are very rare. Their occurrence may be related to trauma, gastrointestinal herniation in the thoracic cavity, such as for intrathoracic

perforation of the stomach in hiatal hernia or traumatic diaphragmatic hernia^{1,2}, malignancy, or iatrogenic surgical complication. At this regards few cases¹⁻⁶ have been described after bariatric surgery or following pneumonectomy or oesophagogastrrectomy. The first case of gastro-pleural fistula was described by Markowitz and Herter in 1960² as a complication of esophageal hiatal hernia.

Mechanisms responsible for the development of these fistulae are not clearly understood; for bariatric surgery, it is likely that postoperative leaks may cause the formation of an abscess, subsequently leading to a communication between stomach and pleural cavity⁵.

So far, only one case of gastro-pleural fistula has been reported after splenectomy, in particular, in a twelve-years old boy undergoing the surgical procedure for splenic abscess⁷. In our patient, the pathogenesis of gastro-pleuric fistula was not clearly understood. We speculated that after the splenectomy with diaphragm resection, a small diaphragm defect led to a chronic herniation of the gastric fundus. This post-surgical diaphragmatic hernia remained asymptomatic until the strangulation with ischemia of the gastric wall gave rise to the gastro-pleuric fistula.

In consideration of the insidious clinical presentation, usually diagnosis may be very difficult and can be delayed. Patients often complain of chronic and non-specific respiratory symptoms and may be conservatively treated for lung infections for several months until more detailed tests finally reveal the correct diagnosis¹. Our patient underwent splenectomy five years before and did not complain of any particular symptoms since this episode.

A first chest CT scan showed the presence of left side empyema, but initially failed to demonstrate the presence of gastropleural communication. Only a high index of suspicion, in our case strongly supported by the finding of probiotics in pleural fluid, led to perform more specific and appropriate exams, such as CT scan with Gastrografin and upper endoscopy, and not to leave the diagnosis unmissed.

In our patient, probiotics had not a pathogenic role but help us to reveal the diagnosis of fistula, despite some cases of infective endocarditis due to *Lactobacilli* and *Bifidobacterium breve* have been reported^{8,9}. We have to remember that presence of *Candida* species in pleural cavity, as in our patient, is also considered a clue to suspect perforation of the gastrointestinal tract even if

currently few data in the literature reported the link between *Candida* and gastro-pleural fistulas⁹. In particular, the most important retrospective study about pleural empyema revealed that in 5.4% of patients (7/128) the empyema was caused by gastro-pleural fistula and 5 of these 7 patients were culture-positive to *Candida*¹⁰.

Conclusions

Therefore, we indicated that in patients with empyema, even if very rare, presence of a gastro-pleural fistula should be taken into account especially in subjects with a history of previous surgery. In our case, the detection of probiotics bacteria in the pleural fluid helped us to suspect and to look for the fistula.

Conflict of Interest

The Authors declare that they have no conflict of interests.

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