Colobronchial Fistula: An Unusual Complication after Peritonectomy and Hyperthermic Intra-peritoneal Chemotherapy (HIPEC)

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Abstract. Background: Cytoreductive surgery (CRS) and hyperthermic intraperitoneal chemotherapy (HIPEC) is an innovative approach to peritoneal carcinomatosis. Due to the complexity of the combined procedure, high rates of potentially life-threatening complications have been reported. This is the first report of colobronchial fistula following CRS and HIPEC. Case Report: A 70-year-old woman underwent CRS and HIPEC for papillary well-differentiated peritoneal mesothelioma. During the postoperative course, recurrent pneumonia occurred and bacteria of intestinal origin were isolated from expectorated sputum. Water-soluble contrast studies revealed direct communication between the left colon flexure and the bronchial tree. After appropriate medical and supportive therapies, the patient underwent resection of the splenic flexure and immediate anastomosis with complete recovery. Conclusion: Colobronchial fistula is a rare and potentially lethal complication of CRS and HIPEC. A suggestive clinical picture and contrast studies allow conclusive diagnosis to be made. Surgery is a safe and effective therapeutic option.

The combination of cytoreductive surgery (CRS) and hyperthermic intra-peritoneal chemotherapy (HIPEC) has reportedly resulted in improved long-term survival for selected patients affected by peritoneal carcinomatosis (1). These promising results have prompted many centres worldwide to start peritoneal surface malignancy programs. However, CRS and HIPEC is a complex procedure, related to high rates of potentially life-threatening adverse events (2). In this context, the identification of risk factors for postoperative complications is of the utmost relevance in order to improve their prevention and successful resolution. Even the early recognition and appropriate management of the most unusual complications is needed to minimize treatment-related mortality and to maximize survival and quality of life results.

This paper reports a case of colobronchial fistula following CRS and HIPEC in a patient affected by papillary well-differentiated peritoneal mesothelioma (PWDPM).

Case Report

A 70-year-old woman, with peritoneal mesothelioma and an unremarkable past medical history, was referred to the Milan National Cancer Institute. She had undergone paracentesis at another hospital and mesothelial tumour cells were found at cytological examination. Abdominal exploration was performed at our institution, revealing massive peritoneal involvement of the pelvis, epigastric area and both right and left sub-diaphragmatic regions. Total parietal and diaphragmatic peritonectomy, stripping of the Glisson liver capsule, omentectomy, splenectomy, hysterectomy and bilateral salpingo-oophorectomy were needed to remove all the visible tumour. HIPEC was performed to treat the microscopic residual disease for 90 minutes at 42.5°C, according to the closed-abdomen technique with cisplatin (160 mg) and doxorubicin (60 mg). Pathological examination revealed PWDPM. The postoperative course was uneventful, apart from functional gastric paresis which resolved spontaneously. The patient was discharged on the 28th postoperative day.

One month after discharge, the patient experienced serious dyspnoea and cough with dark blood-coloured sputum. Physical examination revealed peripheral cyanosis, bilateral
bronchial breath sounds and rales. Blood oxygen saturation on room air was 85% and an arterial blood gas analysis revealed a pO2 of 59 mm Hg. Leucocytosis (14,300/ml), neutrophilia (84.3%) and an elevated PCR (310 mg/l) were noted. Bilateral pneumonia was diagnosed on chest x-ray and the patient was admitted to the hospital. The analysis of expectorated sputum identified *Escherichia coli* and *Pseudomonas suppurans*. Based on sputum study results, the patient was treated with metronidazole (500 mg three times a day), levofloxacin (500 mg once a day), difluconazole (400 mg once a day), teicoplanin (400 mg once a day). The patient was discharged 18 days after the resolution of the respiratory symptoms.

On the 104th postoperative day, the patient was again admitted to our institution due to respiratory failure. The finding of abundant feculent sputum, along with the identification of mixed colic bacterial flora in the expectorated sputum, prompted us to submit her to computed tomography (CT) scan. The study revealed the presence of air in the left posterior recessus costodiaphragmaticus in direct continuity with the peritoneal cavity. A further study of the large bowel with water-soluble contrast enema visualized a direct communication between the left colon flexure and the bronchial tree of the left lower lobe (Figure 1).

The patient was initially managed conservatively with antibiotic therapy (meropenem 1,000 mg three times a day, teicoplanin 400 mg once a day, difluconazole 400 mg once a day, metronidazole 500 mg three times a day) and total parenteral nutrition. After 35 days, the clinical picture of pneumonia resolved but a further contrast study documented the persistence of the colobronchial fistula. Therefore the patient underwent surgical exploration, resection of the left colic flexure with immediate transverse-descending colon anastomosis and repair of the diaphragmatic breach. The patient was finally discharged on the 22nd postoperative day. Forty months from CRS and HIPEC, the patient is currently alive with no evidence of neoplastic disease, nor any signs or symptoms related to the colobronchial fistula.

### Discussion

To the best of our knowledge, this is the first report of postoperative colobronchial fistula in a patient undergoing CRS and HIPEC. The development of a fistula between the bronchial tree and abdominal organs is an uncommon event and colobronchial fistulae are likely the rarest ones within this group (3). Nowadays, the incidence of such disease entities has been reduced by the introduction of antibiotic therapy and surgical prophylaxis. Sub-diaphragmatic abscesses (4), Crohn’s disease (5), large bowel carcinoma (6), appendicitis (7) and previous colon surgery (3) are the clinical conditions most often associated with colobronchial fistulae.

The splenic flexure is the most frequently involved colon segment due to its cranial location, the direct contact with diaphragm and the absence of the liver that plays a protective role towards the right hemi-diaphragm (5). Unobserved surgical injury of the left hemi-diaphragm during peritonectomy, damage to the serosal surface of the splenic flexure during splenectomy, or a combination of these two factors may explain the occurrence of the colobronchial fistula in this patient. Besides the mechanical trauma due to the laser-mode electrosurgery, other potential etiologic factors could be taken into account, such as the increased intra-abdominal temperature and pressure during closed-abdomen HIPEC (2). Of interest, a case of colobronchial fistula following debulking surgery for pseudomyxoma peritonei has been recently published (8). However, it should be noted that such a limited surgical approach is radically different from the aggressive surgical cytoreduction performed in our patients.

Generally, the presence of a colobronchial fistula does not imply the presence abdominal symptoms. The clinical picture is rather characterised by recurrent pulmonary infections, respiratory failure and cough with dark and feculent sputum, since the pressure gradient between the abdominal cavity and the chest determine the transit of faecal material from the large bowel to the bronchial tree and the occurrence of pneumonia. (3-8) The patient reported herein did not show symptoms of enteric perforation. In the early postoperative period, clinical and radiological evidence of...
pleural effusion and basal parenchymal infiltrates were detected. However, this clinical picture is frequent after stripping of the diaphragmatic peritoneum and HIPEC, as a result of the surgical and thermal trauma (9).

The diagnosis of colobronchial fistula is often insidious. The execution of physical and microbiological analyses of the expectorated sputa may be of help. The evidence of faecal material (vegetal fibres, friable material, cellular detritus) and isolation of Gram-negative bacteria of the colonic flora can raise the clinical suspicion of enterobronchial fistula. Antibiotic therapy may weaken or even completely resolve the symptoms related to pulmonary infection, although they often re-present later (5, 10). This often results in diagnostic delay ranging in the literature from 4 to 12 months (5, 10). This was the case with our patient, as she presented with typical symptoms of colobronchial fistula about one month after the surgery. The definitive diagnosis was obtained only three months later by means of radiological studies that demonstrated the contrast medium passage from the splenic flexure to the bronchial tree.

Colobronchial fistula often requires surgical treatment with resection of the involved colic segment and sometimes pulmonary lobectomy (7, 10). In fact, conservative therapy with antibiotic administration and total parenteral nutrition seldom obtains spontaneous resolution of the fistula. Preoperative nutritional status should be evaluated and total parenteral nutrition may play a major role in providing bowel rest to allow recovery in malnourished patients. In the case described herein, conservative treatment was able to resolve the pulmonary infection and to ameliorate patient conditions. The persistence of the fistula supported a surgical option. A combined endoscopic approach involving digestive endoscopy, broncoscopy and the application of fibrin sealing is an interesting option which has been used in the treatment of oesophagus-bronchial fistulae (11).

PWDPM is an exceedingly uncommon variety of peritoneal mesothelioma with uncertain malignant potential. Good long-term prognosis is generally described. However, high recurrence rates and transformation into truly malignant and potentially lethal mesothelioma have been reported supporting the rationale of an aggressive approach with CRS and HIPEC (12).

In conclusion, colobronchial fistula is a rare and potentially life-threatening complication of CRS and HIPEC which may be related to extensive disease involvement and aggressive peritonectomy of the sub-diaphragmatic regions. Its occurrence should be suspected when recurrent pneumonia and isolation of Gram-negative bacteria of intestinal origin in the expectorated sputum occur. Appropriate contrast radiological studies are needed for diagnosis. Surgical management, possibly integrated by medical and supportive therapy, seems to be the treatment approach of choice.

References


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