Distal intestinal obstruction in CF patients

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Abstract

Distal intestinal obstruction syndrome (DIOS) - the incomplete of complete intestinal obstruction by intestinal contents in the terminal ileum and proximal colon- is frequently seen in cystic fibrosis (CF) patients. Diagnosis is based on suggestive symptoms of abdominal pain in the right lower quadrant, a palpable mass on examination and signs of obstruction on plain radiography. Treatment consists of intensive laxative treatment with oral laxatives and enemas. Surgery only serves as the last resort for patients not responding to medical therapy, because of the well-known high rate of peri- and postoperative morbidity of surgery in CF patients. In this article we present 3 cases of DIOS, followed by a review of the relevant literature. (Acta gastroenterol. belg., **2015**, 78, **49-52**).

Key words : cystic fibrosis, mucoviscidosis, obstruction.

Report of cases

Case 1

A 50-year-old man with a long history of CF was referred to the emergency ward after presenting with recent signs and symptoms of intestinal subobstruction, together with increasing cough and dyspnea. His extensive medical history included colonization of the lower airways by Pseudomonas aeruginosa and Staphylococcus aureus, chronic pancreatitis with pseudocysts, exocrine pancreatic insufficiency and diabetes mellitus. His surgical history included ethmoidectomy. Examination demonstrated abdominal tenderness in the right fossa. He was unsuccessfully treated with nasogastric decompression and enemas and underwent a CT scan which showed an inspissated mass in the caecum. The patient was prepared for a total colonoscopy that showed a mucus plug impacted in the appendix which was removed. The previous obstruction was resolved by the preparation for the colonoscopy. After further antibiotic treatment for a pneumonia, the clinical course was favourable.

Case 2

A 24-year-old man with CF presented at the consultation with relapsing pain in the right fossa since a few weeks. His medical history included bilateral bronchiectasis, colonisation of the lower airways with Pseudomonas aeruginosa and Stenotrophomonas maltophilia, exocrine pancreatic insufficiency and chronic rhinosinusitis. His surgical history included inguinal hernia repair. Examination demonstrated a palpable mass in the right fossa. Computed tomography showed a thickened wall of the ascending colon. The patient was prepared for a colonoscopy with oral polyethylene glycol. Colonoscopy showed a prolapse of the appendix into the caecum which was filled with a white mass removed during this procedure. Hereafter, the clinical course was favourable.

Case 3

A 34-year-old woman with CF was hospitalized for reasons of chronic persisting abdominal pain in the right fossa. Her medical history included bilateral bronchiectasis, colonization of the lower airways with Pseudomonas aeruginosa and Staphylococcus aureus, exocrine pancreatic insufficiency and pseudomembraneous colitis. She was prepared for a colonoscopy with oral polyethylene glycol. Impaction of thick and viscous faecal material was noticed in the terminal ileum and the caecum. During this procedure, a laxating fluid was administered locally through the scope. A control colonoscopy a few days later was normal and complaints subsided.

Discussion

Cystic fibrosis (CF), also known as mucoviscidosis, is an autosomal recessive genetic disorder and the most common genetic lethal disease within the Caucasian population. CF is caused by a mutation in the gene for the protein cystic fibrosis transmembrane conductance regulator (CFTR). CFTR is an ABC-transporter–class ion channel that conducts chloride ions across epithelial cell membranes. Mutations of the CFTR gene lead to malfunctioning of chloride ion channel function with subsequent dysregulation of epithelial chloride- and sodium-transport in the lungs, pancreas and other organs resulting in cystic fibrosis (1). CF is mainly characterized by progressive pulmonary disease and exocrine pancreatic insufficiency. The last decades, great progress is made in the treatment and survival of CF patients due to better and more aggressive use of antibiotics and intensive nutritional support. Hence, less severe manifestations of CF, such as the intestinal obstruction syndromes gain in importance. Meconium ileus at birth, distal intestinal

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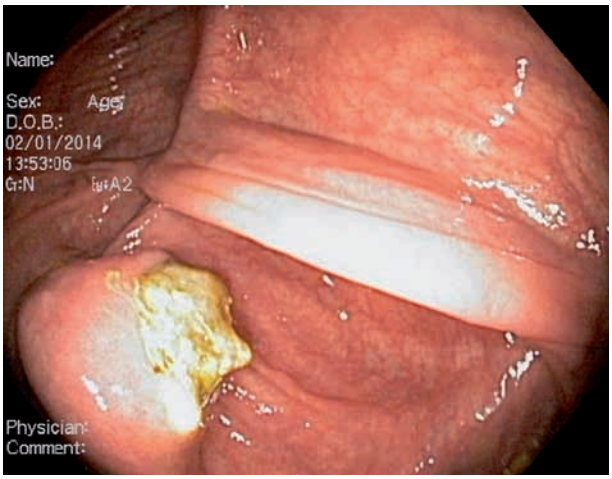

Fig. 1. — Case 1 : mucus plug impacted in the appendix.

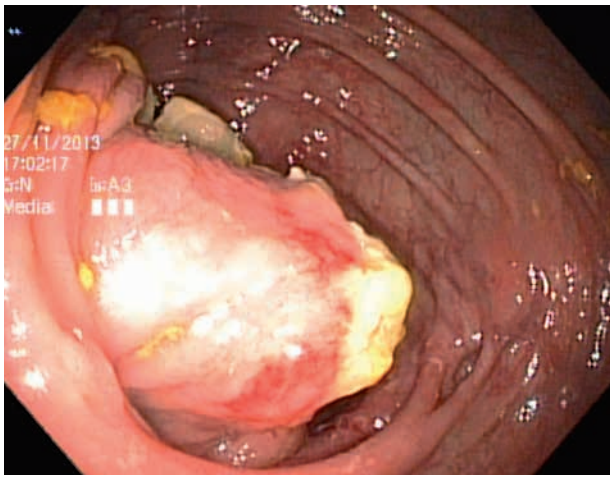

Fig. 2. — Case 2 : prolapse of the appendix with impacted mucus plug.

obstruction syndrome and constipation are an interrelated group of intestinal obstruction syndromes with a variable severity of obstruction that occurs in cystic fibrosis patients (2). Studies on the incidence and prevalence of DIOS and constipation are difficult to compare because definitions vary. The guidelines stated by the European society for Pediatric Gastroenterology, Hepatology, and Nutrition (ESPGHAN) CF Working Group define DIOS as an acute, complete or incomplete, fecal obstruction in the ileocaecum, whereas constipation is defined as gradual fecal impaction of the total colon (3). Using these definitions, both the incidence (2.2-6.2 episodes per 1000 patient-years) and lifetime prevalence (7-8%) of DIOS in childhood is low (4-6). There is a progressive increase in adult patients with a reported incidence of 23.3 episodes per 1000 patients-years and lifetime prevalence of 14-16% (5-7).

Chloride secretion, together with an inhibition of sodium absorption, is the driving force for fluid secretion into the lumen in both intestinal and respiratory epithelium. In CF, defective CFTR-function leads to reduced chloride and fluid secretion. Moreover, an up-regulation of the epithelial sodium channel caused by loss of down-regulation of CFTR enhances sodium and fluid absorption from the luminal mucus (8-10). There are several factors associated with a higher risk for DIOS. DIOS is mainly seen in patients with genotypes associated with severe phenotypes : the majority of patients with DIOS are indeed pancreatic insufficient and DIOS in patients with adequate pancreatic function is rare . Moreover, inadequate dosage of pancreatic enzymes is a known risk factor in the etiology of DIOS (3,4,7,11). A possible explanation for the association between pancreatic insufficiency and DIOS could be that unabsorbed fat entering the distal ileum inhibits gastric emptying and also prolongs intestinal transit through activation of the ileal brake, and could in this manner induce DIOS (8,12,13). Another risk factor for DIOS is intestinal inflammation. In the majority of CF patients, intestinal inflammation is present which is suggested by capsule endoscopy or by elevated fecal calprotectin levels (14,15). Ileal biopsies from both meconium ileus and DIOS patients also show signs of intestinal inflammation, especially in the myenteric ganglion cells and myocytes[16). It is possible that this inflammation delays intestinal transit time and promotes in this way the development of intestinal obstruction. Intestinal dysmotility is also seen as a risk factor for DIOS. In the general CF-population, prolonged intestinal transit time is described. Constipation is seen in 42 percent of individuals with DIOS (12). Another risk factor for DIOS is lung transplantation. About 10 to 20% of CF lung transplant patients develop one or more DIOS episodes early in the post-transplant period. Dehydration, immobility, transient postoperative ileus and opiate use in combination with other predisposing factors such as adhesions due to previous abdominal surgery, may lead to fecal impaction in the ileocaecum and eventually complete intestinal obstruction in selected patients (2,8,17,18). Further reported risk factors for the development of DIOS are a previous history of meconium ileus or intestinal obstruction, infection and CF related diabetes mellitus (2,8).

DIOS typically presents with abdominal pain generally located in the right lower quadrant with a palpable mass on examination. The onset is usually acute, patients are constipated and symptoms progressively increase and complete obstruction with vomiting is possible (2,8). Plain radiography of the abdomen usually reveals faecal impaction in the right lower quadrant and in complete obstruction, multiple air-fluid levels in the dilated small bowel are seen (19). When considering DIOS, it is important to distinguish this diagnosis from other common

causes of abdominal pain in CF. The differential diagnosis between impending DIOS and severe constipation may not always be possible (12,20). In constipation, the onset of symptoms is usually more gradual and the stool is distributed more divided throughout the entire colon. However, the initial approach to treatment (laxatives) is similar in both. Intussusception is seen in approximately 1% of CF patients, is usually located in the ileocaecum and can subside spontaneously (8). Fibrosing colonopathy may present quite similar to DIOS with symptoms of abdominal pain, distention, vomiting and constipation. However, these symptoms usually do not respond to the initial medical management of DIOS and the patient may progress to subacute and later acute obstruction (21). Other differential diagnoses include appendicitis, appendicular abscess or mucocoele, volvulus and ovarian problems (12). In the majority of cases, the history combined with a palpable mass in the right lower quadrant and supported by a characteristic plain abdominal radiography is sufficient to establish the diagnosis of DIOS. Additional radiologic imaging, with an abdominal ultrasound or a CT scan, can aid in the diagnosis (19).

Because of the lack of randomized controlled trials, treatment of DIOS remains until present largely empirical. Initial management consists of intensive laxative treatment with oral laxatives and/or enema or polyethylene glycol lavage (2,4,6-8). For patients with impending DIOS, or for those with complete DIOS but who are not vomiting, the general recommendation is to start with an oral laxative (polyethylene glycol given at a dose of 2 grams/kg/day with a maximum of 80 to 100 grams/day) with or without an enema and restoration of adequate hydration. When this first line of treatment failes, or in a more severe episode of DIOS, intestinal polyethylene glycol lavage with a balanced electrolyte osmotic solution is started orally or via nasogastric tube (2,8). For patients presenting with vomiting or other evidence of complete intestinal obstruction, a hyperosmolar enema like sodium meglumine diatrizoate (Gastrografine) can be used. This enema consists of 100 ml of gastrografine diluted in 400 ml water and is administered under fluoroscopic guidance to visually confirm clearance of the obstruction as the enema refluxes retrograde through the ileocaecal junction. However serious complications are possible such as fluid shift from the circulation to the bowel leading to shock, perforation and necrotizing enterocolitis (2,8,22,25,26). Only few patients do not respond to the medical management described above or develop evidence of intestinal ischemia. In this case, surgical laparotomy and decompression is indicated. Surgery serves only as the last resort because of the high peri- and postoperative morbidity in CF-patients, due to a combination of bad nutritional state, diminished lung function capacity and chronic use of corticosteroids (23). The most common operative technique is open disimpaction. This technique consists of manual disimpaction of the stool into the colon while administering warm isotonic sodium chloride solution mixed with mineral oil through a nasogastric tube (23,24). If this technique failes, an appendectomy with placement of an appendicostomy for irrigation is necessary. After solubilization, the stool is milked distally into the colon or evacuated through the appendicostomy (22,23). When all previous operative techniques fail, enterotomy, placement of a temporary obstruction-relieving stoma or primary resection and re-anastomosis serve as last resort (23). Because most DIOS patients have more than one episode, continuation of the laxative treatment with polyethylene glycol after the first DIOS episode must be considered. Dehydration and fat malabsorption (coefficient of fat absorption < 85%) should be avoided to prevent recurrence. Finally, in transplantation patients, pretransplant bowel preparation with polyethylene glycol and early postoperative start of enteral feeding seems appropriate, as does adequate use of pancreatic enzymes and polyethylene glycol (2,8,23).

Summary

DIOS is the complete or incomplete obstruction caused by faecal impaction in the ileocaecum in CF patients. The typical presentation consists of abdominal pain in the right lower quadrant with a palpable mass on examination. Plain radiography, ultrasound and CT-scan can aid in the diagnosis. Medical therapy with oral and rectal laxatives is usually effective. Only selected cases need surgery which is associated with at higher peri- and postoperative morbidity.

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