A case series of 3 patients with acute colonic pseudo-obstruction after vincristine administration

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Abstract

Acute colonic pseudo-obstruction (ACPO) or Ogilvie's syndrome is characterized by acute colonic dilatation in the absence of mechanical obstruction. It usually occurs in hospitalized patients with acute illness or following surgical procedures, but several medications such as cytotoxic chemotherapy can also induce ACPO. We report three cases of patients with Ogilvie's syndrome after induction therapy with vincristine-containing chemotherapy. Conservative management failed in all three cases. Awareness for this syndrome is necessary when administrating vincristine, because delay in diagnosis may lead to colonic ischaemia and perforation. (Acta gastroenterol. belg., **2020**, 83, **660-662**).

Keywords : acute colonic pseudo-obstruction, Ogilvie's syndrome, vincristine.

Introduction

Acute colonic pseudo-obstruction (ACPO) is a rare disorder of gastrointestinal motility, in which patients present with symptoms of mechanical obstruction of the colon without an underlying obstructive lesion (1,2). It may be caused by autonomic dysfunction with increased sympathetic activity and/or reduced parasympathetic tone. Best known predisposing factors are severe illness, trauma, surgery, delivery, sepsis and acute ischemic heart disease, yet a large amount of conditions and therapies are associated with ACPO (2,3,4). If the colonic dilatation progresses and remains, ischemia and perforation can occur (2).

Case reports

Case report 1

The first patient, a 29-year old male diagnosed with a Philadelphia-negative common B-cell acute lymphoblastic leukaemia, was started with vincristine-containing induction chemotherapy. He noted constipation 2 days after his first chemotherapy administration. Oral polyethylene glycol (PEG) and an enema were given, without success. Four days after chemotherapy initiation he visited the emergency department with abdominal pain and bloating. On clinical examination, his abdomen was tense and tender. CT showed dilatation of the whole colon up to 8 cm with caecal dilatation exceeding 12 cm (Figure 1A). Mechanical obstruction was excluded

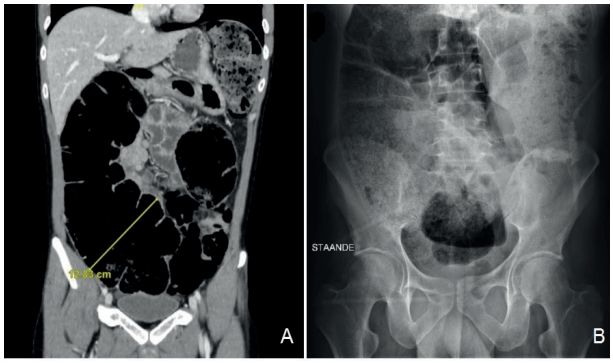

Figure 1. — (A) CT shows a distended colon with a caecal diameter of > 12 cm. (B) Reoccurrence of colonic distention after endoscopic decompression, for which a new colonoscopy with desufflation was performed.

and a sigmoidoscopy with desufflation was performed with placement of a rectal decompression tube, with good clinical effect. This tube dislocated the next day, with reoccurrence of abdominal distention and pain. X-ray investigation showed again distention of the ascending colon exceeding 11 cm (Figure 1B). A new decompression procedure was performed. Afterwards, one intravenous neostigmine infusion of 2 mg was given, whilst monitoring the patient for arrhythmia. Profuse diarrhoea occurred, and the patient returned to normal peristalsis. Chemotherapy was continued after 2 weeks, with a lowered dose of Vincristine.

Case report 2

A 25-year old male suffering from a B-cell acute lymphoblastic leukaemia as well, presented with ACPO 6 days after induction chemotherapy with vincristine. Progressive abdominal dilatation had occurred, with secondary nausea and vomiting. Radiological investigations showed dilatation of the colon, mostly affecting the caecum, and dilatation of the small bowel with multiple

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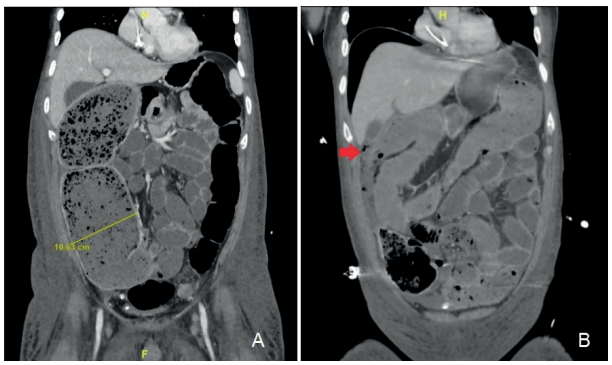

Figure 2. — (A) CT at presentation showed manifest dilatation of the caecum and ascending colon, filled with faecal residue. (B) CT scan shows signs of colonic perforation with free infradiaphragmatic air and free intra-abdominal fluid with inlying air bubbles (red arrow).

air fluid levels. Conservative management was started to no avail and pharmacological therapy with neostigmine was initiated after 2 days. A 2 mg bolus of neostigmine was injected intravenously on two consecutive days with cardiac monitoring, with recovery of normal peristalsis afterwards. A lowered dose of Vincristine was administrated in his later chemotherapy infusions, whilst being watchful for new symptoms. Furthermore, oral PEG was associated to prevent constipation and a possible recurrence of Ogilvie's syndrome.

Case report 3

A 56-year old male HIV patient was treated with vincristine induction chemotherapy for a newly diagnosed HHV8-related extracavitary primary effusion lymphoma. Five days after administration of chemotherapy, peristalsis halted. X-ray showed mostly signs of small bowel obstruction, with multiple air-fluid levels. On CT a manifest dilatation of the caecum and ascending colon was seen (Figure 2A). This dilatation progressively diminished towards the distal colon. No signs of mechanical obstruction were noted. Conservative management with fluids and electrolyte correction was started. A nasogastric tube was placed to relieve the patient, and an endoscopic desufflation was performed. Nevertheless, the day after this sigmoidoscopy a caecal blow out necessitated urgent surgery. On CT scan signs of perforation were present (Figure 2B). Laparotomy showed 2 perforations : one in the caecum, one in the ascending colon. A right sided hemicolectomy was performed, and an ileostomy was placed. Due to the post-operative cachexia and immobilization, further chemotherapy was repeatedly postponed. His lymphoma appeared rapidly progressive. He died 4 months after surgery.

Discussion

ACPO is an uncommon syndrome with clinical symptoms of mechanical obstruction such as marked gaseous abdominal distention, abdominal pain, nausea and vomiting (1,2). Radiology shows a dilated colon, mostly affecting the caecum, with a transition zone usually near the splenic flexure (1). There are no obstructing anatomical lesions. Colonic ischemia and perforation can develop, with an incidence of perforation of 15-20%, and a high mortality risk of 40-50% (1,2). Risk of perforation seems to be heightened in cases of colonic dilatation beyond 12 cm, or when symptoms persist beyond 6 days (1,4).

Conservative management should be started when ACPO is suspected : fluid repletion, correction of electrolyte abnormalities, proximal gastro-intestinal decompression (fasting, nasogastric suction) and placement of a decompressive rectal tube if the distension extends to the sigmoid and rectum. Furthermore, any possible underlying cause should be treated and medications that delay gut motility should be discontinued. Daily abdominal imaging is advised in order to assess the progression of ACPO and to exclude possible perforation (1,2).

If the symptoms persist 48-72 hours despite conservative therapy, pharmacological treatment or endoscopic decompression are indicated. Acetylcholinesterase inhibiting drugs like neostigmine can be administered either subcutaneously or intravenously to promote colonic contractility. Intravenous administration requires cardiac monitoring because of possible bradycardia. Other adverse events such as nausea, abdominal cramping, excessive salivation and bronchospasm are described. An alternative treatment strategy is endoscopic decompression, to quickly resolve the complaints of bloating or abdominal pain, and to prevent an impeding perforation because of excessive dilatation of the colon. Often a rectal decompression tube is left in place after desufflation, to ensure ongoing decompression after the procedure. In case of partial or absent clinical response to these interventions, treatment strategies can be repeated or switched. Sometimes this remains ineffective. In these cases percutaneous endoscopic colostomy should be considered. When signs of perforation or ischaemia are present, immediate surgery is necessary (1,2).

We describe three cases of patients with a typical presentation of Ogilvie's syndrome after vincristine-containing induction chemotherapy. Vincristine is an alkaloid chemotherapy, inhibiting migration of microtubules, primarily being used in acute lymphocytic leukaemia and Hodgkin and non-Hodgkin lymphoma. Neurotoxicity is a well-recognized side effect and may be a trigger for the autonomic imbalance theorized in ACPO. The combination of vincristine with other chemotherapy which may slow transit is a risk factor for the development of Ogilvie's syndrome (3,5,6). Patients suffering from haematological malignancies often combine other risk factors as well, such as immobility, cachexia, infectious events, and steroid- and opioid usage.

In our cases obstipation was one of the first clinical signs, followed by progressive abdominal bloating and

pain. Radiological imaging uniformly showed dilatation of the caecum, with variable degrees of faecal stasis in the more distal colon and dilatation of the small bowel, sometimes with air-fluid levels. No mechanical causes for obstruction were found. In all three cases non-medical treatment proved insufficient. Endoscopic decompression with placement of exsufflation tubes was efficient in relieving symptoms, but it did not induce peristalsis in the two patients in whom it was performed. The administration of neostigmine was more successful in our cases. No adverse events were observed. Neostigmine was evaluated for the treatment of Ogilvie's syndrome in three prospective trials (7,8,9). It was significantly more effective compared to placebo, with success rates up to 94% and recurrence up to 27% (1,2). Sometimes a preference of pharmacological treatment over colonoscopy is suggested, because the latter may increase the risk of perforation (2). Yet, there are no prospective trials comparing pharmacologic therapy directly with endoscopic decompression. Most evidence and guidelines still consider both treatment strategies equally as treatment for Ogilvie's syndrome after failure of conservative management (1,2,10). In our third patient caecal blow-out necessitated urgent surgery. If dilatation remains, perforation can occur, necessitating surgery and often placement of an ileal stoma (2). Recurrent Ogilvie's syndrome may be prevented with polyethylene glycol (1,2). Sgouros et al. performed a prospective study in which the effect of PEG was evaluated on the relapse rate of Ogilvie's syndrome after initial resolution with neostigmine or endoscopic decompression. Despite the small number of patients, no recurrence was observed in the patients who received PEG in comparison to placebo (11).

To conclude, alertness for Ogilvie's syndrome is needed in patients when administering vincristine. As constipation and paralytic ileus are other side effects, the differential diagnosis between ACPO and these pathologies should be made. Early diagnosis and correct management are important to prevent evolution to ischaemia or perforation, which is associated with high morbidity and mortality.

Conflict of interest

None.

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