

Clozapine-Induced Colonic Obstruction Requiring Surgical Treatment

Eran Lavi MD, Louis Rivkin MD, Moshe Carmon MD and Petachia Reissman MD FACS

Department of Surgery, Shaare Zedek Medical Center, and Hebrew University-Hadassah School of Medicine, Jerusalem, Israel

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Clozapine is an atypical antipsychotic drug that is commonly used in the therapy of patients with treatment-resistant schizophrenia. The use of clozapine has been limited because of its potential adverse reactions, mainly leukopenia and agranulocytosis [1]. Constipation is another side effect of clozapine, affecting 14% of patients [2]. The mechanism of constipation is most likely the anticholinergic and antiserotonergic effects of the drug.

Complete colon obstruction due to fecal impaction is an extremely rare complication and only a few reports of clozapine-induced mechanical bowel

obstruction have been published to date in the English-language medical literature. We present, to the best of our knowledge, the first case of a clozapine-induced large bowel obstruction resulting in abdominal compartment syndrome requiring surgical intervention.

PATIENT DESCRIPTION

A 62 year old man presented to the emergency room with severe abdominal pain and distension of 24 hour duration. His last bowel movement was on the day of admission. His medical history included a 40 year history of schizophrenia that had been managed with clozapine for 16 years prior to admission. Six months before the present admission his clozapine dose was increased from 350 to 400 mg/day. He had a history of mild constipation, with a bowel movement every 1–2 days for the past year. He kept a normal diet, but drank prune juice every day to maintain bowel movements. He had no history of previous abdominal surgery except for an inguinal hernia repair.

Upon admission, the patient was dyspneic and in pain, with a temperature of 38°C and pulse rate of 125/minute. He had diffused abdominal tenderness and marked distension, with hyperactive high-pitch bowel sounds. Rectal examination revealed several fecalomas. Laboratory studies showed a slight leukocytosis (10.9 white blood cells/ml), neutrophilia (71%), and elevated serum lactate (3.2 mmol/L), with elevated creatinine due to acute renal failure. Blood gas examination revealed metabolic acidosis.

Abdominal X-ray showed distended loops of small and large bowel, with air fluid levels, and fecal impaction of the entire rectum and colon. Computed tomography showed similar findings [Figure]. Due to the above findings, as well as a very low urine output and measurement of intraabdominal pressure of 45 mmHg, the diagnosis of large bowel obstruction with abdominal compartment syndrome was made.

Emergency laparotomy was performed, revealing a large bowel obstruction secondary to massive fecal impaction involving the entire colon. Decompression of the colon was done via cecotomy. A loop transverse colostomy was constructed and the abdomen was closed primarily. After surgery, the patient was transferred to the intensive care unit. Five days later the patient developed respiratory and hemodynamic decompensation, with another elevation of intraabdominal pressure. Relaparotomy for abdominal decompression was performed, the abdominal wall was left open and a “Bogota bag” (a sterile nylon bag of Hartmann’s solution) was sewn to the edges of the fascia. The Bogota bag was replaced after a week with a Vycril mesh and 2 weeks later a split-thickness skin graft was placed. Despite a series of antibiotic-resistant hypergastric feeding and has good colostomy function. He underwent slow weaning and is planned for rehabilitation.

COMMENT

Drug-related large bowel obstruction due to fecal impaction is not unusual



Abdominal CT showing dilated small and large bowel loops with widespread fecal impaction.

but the need for surgery in such a condition is extremely rare.

Fecal impaction of the rectum and sigmoid colon is a common problem in elderly patients, many of whom are treated with constipating drugs like opiates or tricyclic antidepressants that slow the colonic transit time. However, in the vast majority of these patients, mechanical disimpaction with cleansing enemas will solve the problem. The unusual case described here represents an extreme form of massive fecal impaction involving the entire colon, causing complete colonic obstruction with abdominal compartment syndrome requiring laparotomy with construction of a colostomy.

Mild or chronic constipation has also been reported in patients treated with clozapine, as well as the link between clozapine treatment and bowel obstruction. Levin et al. [3] described a 43 year old man treated with clozapine who presented with vomiting and abdominal distension. Laparotomy revealed large bowel obstruction due to severe fecal impaction affecting the entire colon. A total colectomy and protective ileostomy was performed. The patient died 3 weeks later due to refractory septic shock. Hayes and Gibler [4] reported a case of aspiration of vomitus secondary to constipation and bowel obstruction

leading to the death of a 29 year old man treated with clozapine. In a survey of the Medline literature from 1950 to 2007, Palmer and collaborators [5] found 29 cases of clozapine-induced severe gastrointestinal hypomotility, as well as an additional 73 cases reported in the Australia-New Zealand pharmacovigilance database. A 27% mortality rate among the 102 patients in these two groups was noted! Gastrointestinal hypomotility was shown to be dose dependent with daily mean doses of 428 mg/day in these patients [5].

No specific guidelines for the prevention and treatment of clozapine-induced constipation have been published. However, from the literature review we conducted, it is recommended that physicians avoid prescribing concomitant constipating medications. Clozapine doses should be as low as possible. Patients should be warned about the risk of constipation. We suggest a high fiber diet and high fluids intake to lower the risk of constipation. When symptoms of constipation occur treatment with a laxative may be required.

The case presented here was extremely unusual due to the severe abdominal compartment syndrome that developed secondary to the large bowel obstruction. Initial treatment with disimpaction of fecaloma followed by transverse

colostomy was not sufficient and a second laparotomy with the use of a Bogota bag was required. In summary, increased awareness of the potential risk of constipation and associated symptoms in patients treated with clozapine is warranted. Physicians should monitor bowel function in these patients, particularly in the period following an increase in dosages. Prophylactic treatment with laxative and clozapine dose reduction may be appropriate when symptoms of constipation occur.

Correspondence:

Dr. E. Lavi

Dept. of Surgery, Shaare Zedek Medical Center,
P.O. Box 3235, Jerusalem 91031, Israel
Phone: (972-54) 545-0280
Fax: (972-2) 666-6253
email: lavi.eran@gmail.com

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