Focal parietal necrosis of the sigmoid due to atypical neuroleptics : a case report

Arnaud Devresse, Philippe Maldague, Bruno Coulier, Frédéric Pierard, Isabelle Gielen

Department of Gastroenterology, Diagnostic Radiology, Visceral Surgery, Clinique St Luc, Bouge, Namur, Belgium and Department of Pathology and Genetics, Loverval, Belgium.

Abstract

We present the case of a 26-year-old man with schizoid personality disorder who suffered from a very focal and transparietal necrosis of the sigmoid after an overdose of atypical neuroleptics. This is a singular, rather unknown and potentially lethal side effect of these drugs.

The physiopathology of this complication is multifactorial. (Acta gastroenterol. belg., **2012**, 75, **263-265**).

Key words : necrosis, sigmoid, atypical neuroleptics, adverse event.

Presentation of case

A 26-year-old man with schizoid personality disorder took an overdose of his usual heavy treatment of neuroleptics. Five days later he was admitted with complaints of constipation, abdominal pain, nausea and an episode of green vomit.

His treatment included Trazodone (antidepressant of the triazolopyridine class) 100 mg twice a day, Clotiapine (atypical neuroleptic of the dibenzothiazepine class) 40 mg once a day, Lamotrigine (antiepileptic of the phenylthriazine class) 200 mg once a day, Lorazepam (benzodiazepine) 2,5 mg twice a day, Escitalopram (selective serotonin reuptake inhibitor) 10 mg once a day, Quetiapine (atypical antipsychotic of the dibenzothiazepine class) 300 mg thrice a day and Zuclopenthixol (a typical antipsychotic of the thioxanthene class) 200 mg once every 2 weeks. No NSAIDs, no antibiotics, no illegal drugs (including cocaine) had been taken in the past days.

The patient had no history of peptic ulcer, thromboembolism, constipation, dyslipidemia, diabetes and was not a smoker.

At physical examination, there was an elective pain in the left inferior quadrant without defense. Vital signs were normal. Laboratory tests revealed white cell count at 13300/mm^3 (with neutrophily at 91,3%) and C-reactive protein at 6,7 mg/l (normal value < 5 mg/l). Urine sediment and toxicology screen were normal.

Contrast enhanced abdominal computed tomography (MDCT) appeared rather normal except for some stercoral stasis in the distal ileum (not illustrated). The patient was kept in observation and his usual treatment was maintained.

Four days later, the clinical state of the patient worsened. The abdominal pain increased and general abdominal defense was now present at physical examination. The patient remained apyretic. Laboratory tests then revealed his white cell count was at 19800/mm^3 (with neutrophily at 85,4%) and C-reactive protein at 364 mg/l. Urine sediment, chest plain film, hemocultures and fecal culture were normal.

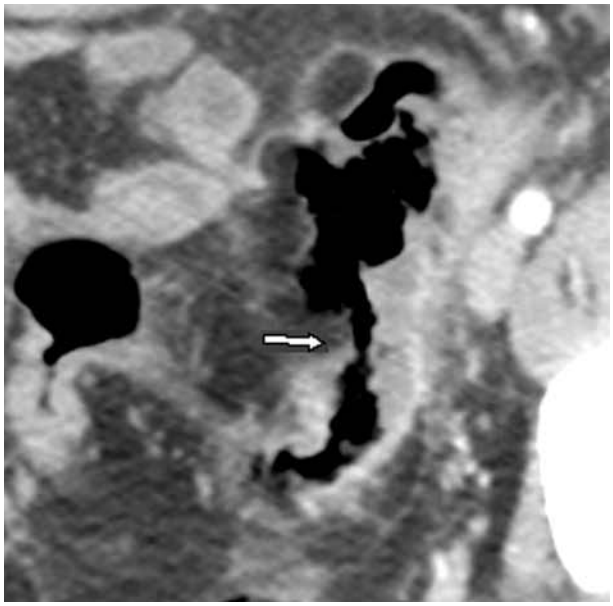

Fig. 1. — Axial CT views obtained just before laparotomy. The medium sigmoid wall has completely disappeared and colonic gas appears directly contiguous with the mesocolic fat and epiploic appendages. The limits of the completely necrotic segment appear extremely abrupt (white arrow).

Contrast enhanced abdominal computed tomography (MDCT) revealed a generalized left-sided colitis with pericolic fat stranding spreading out to the medium sigmoid. There was no diverticular disease, no pneumoperitoneum nor ascites.

A rectosigmoidoscopy was performed after the MDCT and showed deep and focal ulcers limited to the medio-sigmoid.

Correspondence to : Dr. Devresse, Department of Gastroenterology, Clinique St Luc, Rue St Luc 8, 5004 Bouge (Namur) Belgium.
E-mail: arnaud.devresse@proximus.be

Submission date : 30/04/2011
Acceptance date : 22/09/2011

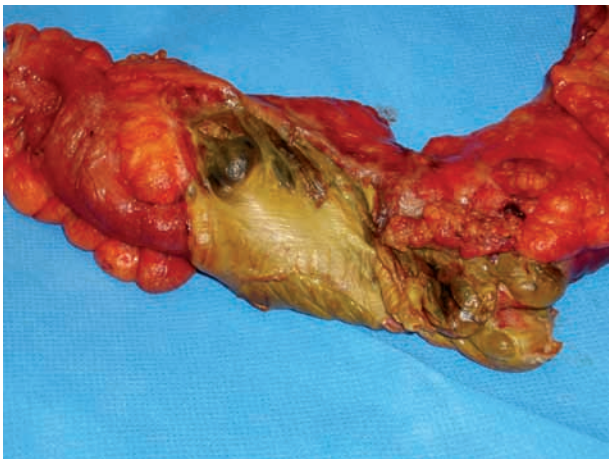

Fig. 2. — View of the large bowel section with a parietal necrosis after the surgical resection.

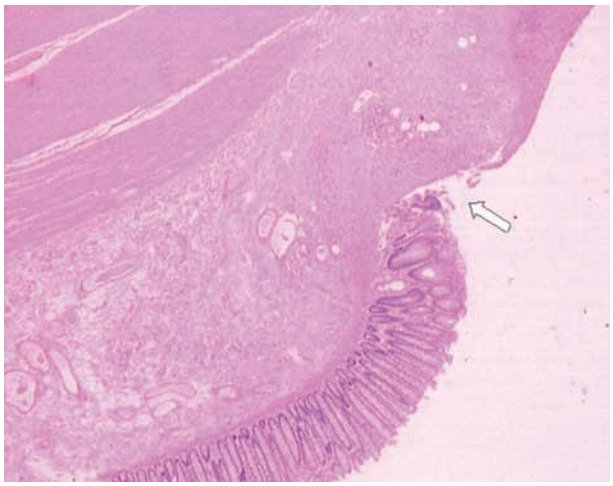

Fig. 3. — Histopathologic specimen (× 2.5) illustrating the junction of normal colonic and ulcerated mucosa (white arrow). Oedema of submucosa (star). No vessel occlusion is found.

A conservative treatment was attempted. Because of the deterioration of the clinical and the biological status, a new contrast enhanced abdominal computed tomography was made and revealed a complete necrosis of the medium sigmoid (Fig. 1).

The patient was transferred to the department of surgery for a partial colectomy. Macroscopic view (Fig. 2) and histology (Fig. 3) confirmed a necrotizing colitis without signs of either venous or arterial occlusion. After exclusion of classical causes of necrotizing colitis and a review of the literature, Clotiapine was considered as the etiological agent and the treatment was stopped.

At the follow-up of eight months later, the patient remained in good condition.

Discussion

Necrotizing enterocolitis after ingestion of atypical neuroleptics is a rare affection (1). In the year 2007, a French pharmacovigilance survey reported all cases of acute digestive complications after ingestion of antipsychotic drugs known to the pharmaceutical companies who sold those drugs around the world (2). Between 1997 and 2006, 70 cases were collected : 47 cases of intestinal necrosis, 6 cases of intestinal ischemic necrosis, 13 cases of ischemic colitis, 2 cases of ulcerative colitis, 1 case of hemorrhagic colitis and one case of colitis with intestinal perforation. Phenothiazine was involved in 65,7% of the cases.

These affections are mostly diagnosed in chronic treatments (on average 8 years) and rarely in short-term treatments (3).

The physiopathology appears multifactorial.

First of all, the peripheral anticholinergic effect of neuroleptics decreases the intestinal peristaltism and can lead to an intestinal distension rarely complicated by a perforation, as a consequence of an ischaemia due to mucosal capillary thrombosis. This phenomenon is increased by the simultaneous administration of anticholinergics (as observed in our patient considering the anticholinergic effect of Trazodone) (4,5).

The second mechanism is the antiserotoninergic effect which increases the slowing down of the intestinal peristalsis (6).

Finally, the anti-dopaminergic effect of neuroleptics may limit the intestinal perfusion by affecting the vasodilatory effect of the DA1 dopaminergic receptors (7).

Diagnosing necrotizing enterocolitis is complex. This diagnosis relies essentially on clinical analysis, biological analysis and imaging, and is confirmed by a pathological study , which shows a necrosis of the small intestine and/or colon with an intact mesentery and no signs of neither venous nor arterial occlusion (3).

The diagnosis of our patient was made by computed tomography and confirmed by surgery and pathology. The definitive etiology of this affection was established by systematic exclusion of other common causes of necrotizing enterocolitis. The patient had no recent history of cocaine abuse (confirmed by the negative toxicological analysis) and no history of thromboembolism. The hypothesis of venous or arterial occlusion was excluded by histological study. There were no clinical nor radiological signs of mechanical bowel obstruction and no history of previous abdominal surgery. Finally, pathogenic germs were not found in the fecal culture.

Conclusion

Necrotizing enterocolitis after ingestion of atypical neuroleptics is rare but potentially lethal. Common symptoms such as abdominal pain, constipation or even fecaloma can precede this complication and have to be taken very seriously in those patients, especially if their

clinical state is rapidly deteriorating. No article in the medical literature deals with the specific care required by this affection and no article describes the relevance of resuming a neuroleptics treatment after such adverse effects. Further investigations are necessary to answer, among other things, to that question. The particularity of our case is the very focal and transparietal attempt of the sigmoid, never described before to our knowledge, as well as the apparent acute toxicity due to an overdose of atypical neuroleptics, because this affection has mostly been linked with chronic toxicity.

References

1. AUSSEUR A., LEROY C., BAZIN B. *et al*. Acute necrotizing enterocolitis during a prolonged treatment with neuroleptics. *Presse Med*., 1995, **24** : 577-9.
2. PEYRIÈRE H., ROUX C., FERARD C. *et al*. Antipsychotics-induced ischaemic colitis and gastrointestinal necrosis : a review of the French phramacovigilance database. *Pharmacoepidemiol. Drug Saf*., 2009, **18** (10) : 948-55.
3. GNAMIEN S., BOUTILLIER I., REVILLION J.J., URBINA M.A. Acute necrotizing enterocolitis and neuroleptics. *Journal de Pharmacie Clinique*, 2001, **20** : 93-6.
4. LIEBERMAN J.A., SAFFERMAN A.Z., POLLACK S. *et al*. Clinical effects of clozapine in chronic schizophrenia : response to treatment and predictors of outcome. *Am. J. Psychiatry*, 1994, **151** : 1744-52.
5. HAYES G., GIBLER B. Clozapine-induced constipation. *Am. J. Psychiatry*, 1995, **152** : 298.
6. HIBBARD K.R., PROPST A., FRANK D.E., WYSE J. Fatalities associated with clozapine-related constipation and bowel obstruction : a literature review and two case reports. *Psychosomatics*, 2009, **50** : 416-9.
7. PEYRO SAINT PAUL L., MOSQUET B., HOURMAND-OLLIVIER I. *et al*. Ischemic colitis in psychiatry. *Gastroenterol. Clin. Biol*., 2008, **32** : 578-80.