Rectal perforation associated with sunitinib therapy

Key words: Sunitinib. Rectal perforation. Fistula. Antiangiogenic. Tyrosine kinase inhibitor.

Dear Editor,

We present a case report of a 70-year-old male with a history of left renal agenesis underwent a right-sided nephrectomy and ureterectomy in 2006 for a stage-III renal carcinoma, and has been on hemodialysis ever since.

Case report

In 2008 he was diagnosed with a rectal adenocarcinoma (pT3N0M0) and villous adenoma at 11 and 4 cm from the anal margin, respectively. Short-course radiotherapy (25 Gy in 5 Gy daily fractions) was administered and the patient underwent anterior rectal resection plus perianal adenoma resection. During follow-up a positron emission tomograph was performed (2011), which identified two nodules; one in the left suprarenal area and another in the nephrectomy surgical area, suggesting a locoregional recurrence of the renal carcinoma. In view of this finding treatment is initiated with sunitinib 50 mg/day for 4 weeks, with a two weeks rest between cycles. After 7 cycles of treatment the patient had a complete response as confirmed by an abdominopelvic scan.

Seven days after cycle thirteen the patient presents at the ER with pain, an anal growth and fever. A fluctuating abscess with crepitation is felt on palpation in the right gluteus, and digital rectal examination reveals a wide orifice, approximately 1 cm in diameter, at 5-6 cm from the anal margin on the left posterolateral rectal wall.

An abdominopelvic scan defines a communication between the rectal lumen and perirectal fat, as well as cellulitis in the gluteus maximus muscle. With a suspicion of rectal perforation associated with necrotizing fasciitis an urgent surgical procedure is decided upon. An incision is performed on the fluctuating area that lets fecaloid contents out. An abscess tract opens on the right posterior wall of the rectum. A counterincision is carried out and a drain is put in place.

A histopathologic examination of the orifice and its surroundings reveals inflammatory tissue with no evidence of malignancy.

Discussion

Sunitinib is a multitarget antiangiogenic agent that was licensed by the Food and Drug Administration for the treatment of gastrointestinal tumors (GISTs) resistant to imatinib in 2006, and of advanced renal cell carcinoma in 2008 (1). It inhibits the phosphorylation of receptors for vascular endothelial growth factor, platelet-derived growth factor, stem cell factor, and tyrosine kinase, among others (2).

Fatigue, diarrhea, mucositis/stomatitis, hematotoxicity, dermatotoxicity, etc., have been described during therapy (3). Intestinal perforation is an adverse effect with unknown incidence and pathophysiology, but three mechanisms have been suggested: a) decreased capillary density in the intestinal mucosa and decreased regenerability of the normal mucosa; b) tumor regression and necrosis in response to chemotherapy (4); and c) mesenteric ischemia from cholesterol embolism syndrome (5).

No potential risk factor for intestinal perforation may be ascertained given the limited number of cases, but some studies describe that preoperative short-course radiotherapy is not associated with a higher rate of intestinal perforation (6), hence sunitinib was deemed to be responsible for perforation in our patient.

Few gastrointestinal perforation cases associated with sunitinib therapy have been reported (7-9). Two perianal fistulas are found in the rectum, a vesicorectal one (10) and this, the first rectal perforation with a wide orifice described (Table I).
Rocío Santos-Rancaño, Jaime Zuloaga, Gonzalo Sanz-Ortega, Mario Ortega, Fernando Jiménez, Mauricio García-Alonso, Fernando Esteban, Rodrigo Sanz, Carlos Cerdán-Santacruz and Javier Cerdán-Miguel

Department of General and Digestive Surgery.
Hospital Clínico San Carlos. Madrid, Spain

References


