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ΑΡΧΕΙΑ ΕΛΛΗΝΙΚΗΣ ΙΑΤΡΙΚΗΣ 2021, 38(1):137–138

Surgery Quiz – Case 29

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An otherwise-healthy 71-year-old male patient with a known sizable recurrent left retroperitoneal malignant fibrous histiocytoma under pazopanib (*per os* 800 mg daily) with infiltration of the left ureter under double J stent and the descending colon causing incomplete large bowel obstruction, admitted to the emergency department with symptoms and signs of peritonitis. Abdominal computed tomography (CT) revealed the presence of: (a) a solid left retroperitoneal mass (approximate size 16×10×12 cm), (b) infiltration of the left ureter with the presence of a double J stent, and (c) infiltration and perforation of the descending colon along with a large quantity of free intraperitoneal air and paracolic fluid (fig. 1). Emergency laparotomy performed which revealed the presence of descending colon perforation and disseminated feculent peritonitis. The patient submitted to left hemicolectomy with end transverse colostomy and intraoperative saline peritoneal lavage. Postoperatively, pazopanib discontinued and tinzaparin (subcutaneously 4,500 anti-Xa IU daily), omeprazole (intravenously [IV] 40 mg per day) and imipenem (IV 1g q8h) were administered. Regarding surgical complications, postoperative period was uneventfull. On the 19th postoperative day, acute isolated severe thrombocytopenia (PLT $<10\times10^9$/L) and mild coagulopathy accompanied with hematuria occured. Abdominal CT revealed (fig. 2): (a) No superficial or deep surgical site infection, (b) no thrombotic and hemorrhagic complications, and (c) progressive disease according to the Response Evaluation Criteria in Solid Tumors (RECIST) 1.1 criteria with rapid and massive primary tumor growth measuring approximately 20×14×15 cm in size with a 2.5-fold increase in volume.

What was the cause of the massive primary tumor growth?
(a) Surgical trauma
(b) Discontinuation of vascular endothelial growth factor receptor (VEGFR) inhibitor
(c) Intratumoral hemorrhage
(d) Kasabach-Merritt syndrome

Comment

Surgical procedures such as biopsy and tumor resection are the gold standard for diagnosis and treatment of solid tumors. However, growing evidence suggests that even a minor surgical trauma can influence pathophysiological processes that might promote postoperative metastatic spread and tumor recurrence.

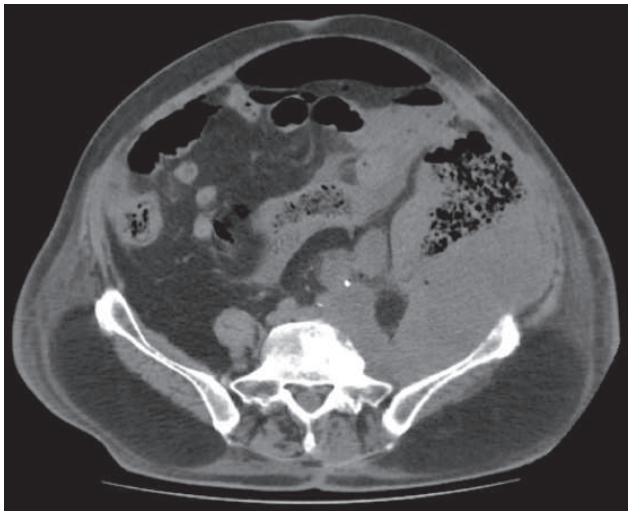

Figure 1

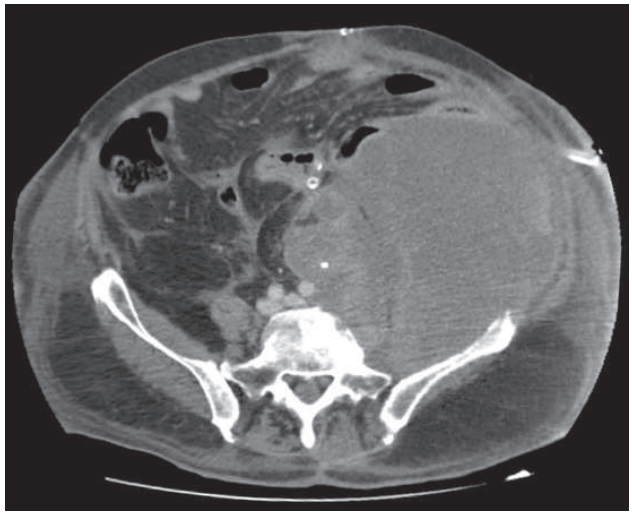

Figure 2

These pathophysiological processes encompass: (a) local effects including tumor seeding and wound healing response that can promote tumor cell migration, proliferation, differentiation, extracellular matrix remodeling, angiogenesis and extravasation, (b) local and systemic immunosuppression which impairs antitumor immunity and contributes to tumor cell survival, and (c) cancer cell release into circulation and tumor cell dissemination by surgical manipulation of the tumor.

The effects of antiangiogenic treatment on tumor growth are well documented. However less is known about the effects of antiangiogenic treatment discontinuation on tumor re-growth. Preclinical studies suggested rapid reversible re-growth of blood vessels, existence of a rebound phenomenon and tumor adaptation after antiangiogenic treatment discontinuation leading to accelerated tumor growth, increased local invasion and distant metastasis. Preclinical findings have raised questions about accelerated disease course in the clinical setting. Iacovelli et al in their retrospective study of 63 metastatic renal cell carcinoma who discontinued antiangiogenic treatment showed that tumor re-growth was related to the reason of discontinuation; re-growth was higher in patients who discontinued treatment because of disease progression or toxicity and lower in patients who discontinued treatment because of a sustained response; interestingly this study showed that the higher the growth rate, the shorter the survival. The authors concluded that discontinuation of antiangiogenic treatment may cause an increase in tumor growth rate which is related to patient survival. However, further clinical studies are needed to address the impact of antiangiogenic discontinuation on progression free survival and overall survival.

Kasabach-Merritt syndrome is a life-threatening thrombocytopenic coagulopathy due to platelet trapping and fibrinogen consumption within the abnormal vascular endothelial architecture of aggressive, highly vascularized and rapidly enlarging vascular tumors such as Kaposiform hemangioendothelioma and tufted angioma, and rarely solid tumors. The peak of Kasabach-Merritt syndrome activity is characterized by tumor growth in combination with profound thrombocytopenia and consumptive coagulopathy. In our patient's case, surgical trauma and VEGFR inhibitor discontinuation resulted in rapid and massive primary tumor growth with 2.5-fold volume increase on repeated CT. Subsequently, the massive primary tumor growth was the cause that resulted in Kasabach-Merritt syndrome with profound thrombocytopenia and mild coagulopathy suggestive of platelet trapping and fibrinogen consumption within the abnormal tumor vascular endothelial architecture.

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