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Case Report
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First Reported Case of Upper Gastrointestinal Bleeding due to Dieulafoy Lesion in a Patient Undergoing Cabozantinib Treatment for Renal Cell Carcinoma: A Case Report

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Abstract

Cabozantinib, a multi-kinase inhibitor widely used in the treatment of renal cell carcinoma (RCC), is associated with a spectrum of adverse effects, among which gastrointestinal (GI) toxicity remains noteworthy. However, the occurrence of upper gastrointestinal bleeding (UGIB) induced by cabozantinib is sparsely documented. Herein, we discuss the case of a 62-year-old male patient with RCC on cabozantinib therapy who developed melena secondary to a Dieulafoy lesion. Although he was hemodynamically stable at presentation, laboratory assessments revealed substantial blood loss.

Esophagogastroduodenoscopy (EGD) identified the Dieulafoy lesion as the bleeding source, and hemostasis was achieved using adrenaline injections paired with hemoclips placement. This case underscores the potential association between cabozantinib therapy and UGIB, highlighting the necessity for vigilant monitoring in this patient population.

Introduction

Cabozantinib is a tyrosine kinase inhibitor (TKI) that targets multiple proteins, including MET, AXL, and VEGFR2, and has been established as an effective treatment for advanced RCC, hepatocellular carcinoma, and medullary thyroid carcinoma [1-3]. While its clinical efficacy is well supported, cabozantinib is also associated with notable adverse effects, such as hypertension, diarrhea, fatigue, and hepatotoxicity [4,5]. Gastrointestinal complications—although less common—have included perforations, fistulas, and bleeding events. This report presents a rare instance of UGIB in the context of ongoing cabozantinib therapy, wherein the underlying etiology was identified as a Dieulafoy lesion. This uncommon source of significant GI hemorrhage warrants attention given its implications for clinical management.

Case Presentation

A 62-year-old male with a history of metastatic RCC had been receiving cabozantinib at a dosage of 60 mg/day for six months. He presented to the emergency department with symptoms of fatigue, dizziness, and black tarry stools. On examination, his vital signs were notable for

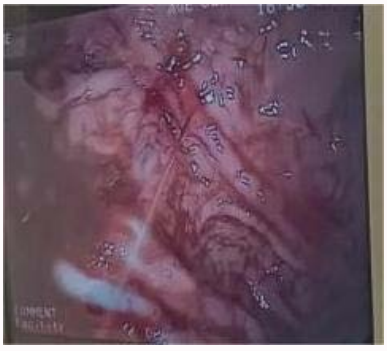

Figure 1: Gastric fundus.

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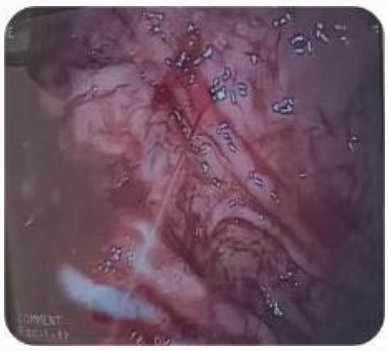

Figure 2: Dieulafoy lesion.

hypotension (blood pressure 100/60 mmHg) and tachycardia (heart rate 118 bpm), although his respiratory rate was normal at 16 breaths per minute with an oxygen saturation of 98% on ambient air. He was alert and cooperative during assessment. Physical examination was unremarkable except for a digital rectal examination that confirmed the presence of melena. Esophagogastroduodenoscopy revealed an actively bleeding Dieulafoy lesion located in the gastric fundus (Figures 1,2). Hemostasis was effectively achieved through adrenaline injection and placement of hemoclips. The patient was closely monitored post-procedure and remained clinically stable with no recurrence of bleeding episodes. Cabozantinib therapy was temporarily discontinued, and he was initiated on proton pump inhibitor (PPI) therapy. Upon stabilization, the patient was discharged with instructions for follow-up evaluations to reassess the feasibility of resuming cabozantinib treatment.

Discussion

Dieulafoy lesions are an uncommon but clinically significant cause of UGIB, accounting for approximately 1% to 2% of non-variceal upper GI hemorrhages [2]. These lesions result from a dilated submucosal artery that erodes through the overlying mucosa, leading to acute bleeding [4]. While GI bleeding is recognized as an adverse event associated with cabozantinib therapy, its incidence remains relatively low. Cabozantinib, as a VEGFR inhibitor, disrupts angiogenesis and compromises endothelial integrity, potentially enhancing susceptibility to epithelial damage and bleeding. Moreover, inhibition of the MET and AXL signaling pathways exacerbates vascular fragility, further increasing the risk of hemorrhage. The temporal relationship between URIB onset and initiation of cabozantinib therapy in this case suggests a plausible causal association, although direct causation cannot be definitively established. Clinical trial data from the METEOR study-a phase III trial evaluating cabozantinib in RCC-reported GI bleeding events in 6% of patients, with severe bleeding episodes documented in approximately 2% [3]. While the overall risk of GI bleeding with cabozantinib appears to be lower when compared to other TKIs such as sorafenib or sunitinib, it remains a noteworthy concern. Risk factors for GI bleeding in patients undergoing TKI therapy include pre-existing GI pathology, concurrent use of anticoagulants, and tumor-associated vascular invasion. In this patient, aside from cabozantinib use, no additional predisposing factors were identified. Management of Dieulafoy lesions involves endoscopic methods such as adrenaline injection, thermal coagulation, or mechanical interventions like hemoclip application or band ligation [1]. When endoscopic therapies prove insufficient, angiographic embolization or surgical resection.

Conclusion

In summary, this case highlights the critical need to consider upper gastrointestinal bleeding (UGIB) as a potential adverse event associated with cabozantinib therapy. Although Dieulafoy lesions represent an uncommon etiology of gastrointestinal hemorrhage, their occurrence in individuals undergoing treatment with vascular endothelial growth factor receptor (VEGFR) inhibitors points to a possible pathogenic connection. Clinicians should maintain a heightened awareness of gastrointestinal bleeding in patients treated with cabozantinib, particularly in those presenting with symptoms such as anemia, melena, or hemodynamic instability. Endoscopic intervention remains the primary modality for management, while decisions regarding drug continuation or dosage adjustments should be tailored to each patient's clinical scenario. Future research is necessary to clarify the mechanisms underlying tyrosine kinase inhibitor (TKI)-induced gastrointestinal bleeding and to develop evidence-based protocols for its management.

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