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Cabozantinib Adverse Reactions In Patients With Renal Cell Carcinoma

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Abstract

The most recent first-line therapy for Metastatic Renal Cell Carcinoma (mRCC) is Cabozantinib (CAB), a Tyrosine Kinase Inhibitor (TKI). Skin responses in a patient with RCC are among the reports of adverse CAB reactions. Other TKI (Sunitinib) reported cases of acute interstitial nephritis caused by medication. To demonstrate this, we present a case of CAB-induced adverse effects in a patient with RCC that occurred after one month of treatment and led to stomach ulceration with bleeding, acute interstitial nephritis, and acute renal failure. Following a biopsy-based differential diagnosis, the offending medicine was immediately discontinued and corticosteroid therapy started. Renal function improvement was noted, and CAB use was later restarted at a modest dose of 20 mg per day.The goal of the study is to give patients with advanced renal cell carcinoma the right guidance to minimise the impact of adverse events and to maximise the efficacy of CAB.

Introduction

Prior to being approved by the US-FDA in 2012, cabotinib (CAB) was used as a second-line treatment for medullary thyroid cancer and renal-cell carcinoma (RCC). By blocking AXL and RET, it is a small molecule inhibitor of tyrosine kinase, cMET, and VEGFR2. New European Association of Urology RCC treatment recommendations recommend nonspecific TKI as the initial treatment for RCC [1]. Due to its recent usage in mRCC, there are no prior reports of this medication's negative side effects, with the exception of one case of cutaneous response secondary to CAB [2]. Recently, it has been the first line of treatment for mRCC patients with intermediate or poor prognosis who benefit from a high rate of progression-free survival and moderate to high levels of G3-4 toxicity [3]. Patients in the phase III trial greatly benefited from immunotherapy when combined with it.

Acute interstitial nephritis brought on by drugs impairs renal function, although early identification and drug discontinuation could restore it to normal. A shorter hospital stay and faster recovery are benefits of steroidal therapy [6, 7]. The current case report describes the negative effects of CAB in a patient with RCC.

Case Presentation

The main complaints of the 72-year-old male patient, who has had T2DM and hypertension for the past 15 years and is receiving regular treatment, were blood in the urine twice, chills, rigours on and off for the previous two days, decreased urine output, and constipation. He has been receiving treatment with T. Cabozantinib 60 mg P.O. daily for a month after receiving a recent diagnosis of Papillary Renal Cell Carcinoma. The anal canal and mucosal regions were normal according to the colonoscopy, but the upper G1 endoscopy revealed bleeding and erosion of the antrum and pylorus, which indicated serious gastric ulcerations. His laboratory tests revealed a hyponatremia-induced anaemia and severe renal failure. The estimated glomerular filtration rate was 35 ml/min/1.73 sq BSA, the level of C-reactive protein was 47.8 mg/L, the time between points was 12 sec (control) and 21.5 sec (test), and the INR was 1.79.

Each of the following tests came out negative: anti-nuclear antibody, rheumatoid factor, anti-mycloperoxidase, anti-proteinase 3, and peripheral and cytoplasmic anti-neutrophilic antibodies. The patient's renal biopsy revealed a grey-brown hemorrhagic tumour measuring 6.5 cm by 6 cm by 4 cm and occupying the lower pole and part of the midpole. There was a pelvicalyceal system involved. Polygonal cells with somewhat eosinophilic cytoplasm and hyperchromatic nuclei with evident nucleoli lined the papillary structure of the malignant tumour. Lesions with tumour infiltration were found. Additionally, there was a significant eosinophilic and edematous interstitial inflammation. In comparison to the medulla, the cortex was more inflamed.

Eosinophilic tubulitis and lymphocyte foci were seen. With Naranjo's score and WHO-UMC causality showing "likely" for cabozantinib, acute interstitial nephritis leading to tubular damage was predicted as a negative drug reaction (Score 7).

He was receiving corticosteroid treatment, hemodialysis, and a temporary withdrawal from CAB medication. His renal function tests and stomach ulcerations significantly improved after just two weeks of medication. There were no additional causes for the adverse reaction, and patients' health quickly improved after the medicine was stopped.

Discussion

For one month, the patient received CAB therapy. Acute interstitial nephritis with gastrointestinal bleeding caused by CAB was discovered as a result of the chief complaints, laboratory tests, renal biopsies, and

endoscopy. Changes in renal functioning and acute renal failure are also important adverse effects of TKI, and intestinal bleeding is a black-box warning of CAB. Uncertainty surrounds the pathophysiology of the CAB implicated in this reaction [8,9]. Immunologic reaction or type I hypersensitivity, delayed tubule destruction, and direct nephrotoxicity are all factors in drug-induced interstitial nephritis [10,11].

Hemolyticuremic syndrome is another differential diagnosis that could apply in this situation. The only way to diagnose drug-induced interstitial nephritis in a tumour is through biopsy. Acute renal failure was clearly indicated by significant deviations in renal function.The following tyrosine kinase receptors are part of CAB: colony stimulating factor-1, IMS-like tyrosine kinase-3, platelet-derived growth factor receptor, and stem cell factor receptor C-kit [12,13].

Acute interstitial nephritis and drug-induced stomach ulcers are treated with corticosteroid treatment and prompt discontinuation of the offending substance. It is advisable to start CAB at a lesser dose after the conditions have improved [14,15]. The side effects and unfavourable responses that may be experienced again after re-administration should be fully understood by both the doctor and the patient.

This is the first instance of acute interstitial nephritis with bleeding stomach ulcers caused by CAB. On ADR of CAB, attention might be paid and more research done in the future.

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