Sunitinib-induced thrombotic microangiopathy: a case report

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Abstract

Sunitinib-induced thrombotic microangiopathy (TMA) is a secondary TMA caused by Sunitinib.Despite the extensive use of the drug ,little is known about this complication of Sunitinib. In this study, we reported a 63 years old male with Sunitinib induced TMA treated for metastatic renal cell carcinoma.

Introduction:

Sunitinib is an oral antiangiogenic drug with anti-Vascular**endothelial growth factor** (VEGF) properties. It is used to treat renal cell carcinoma, pancreatic neuroendocrine tumours, and gastrointestinal stromal tumours (1)Treatment with anti-VEGF antibody medication improves the survival of patients with colorectal carcinoma (2, 3) and clear metastatic cell renal cell carcinoma (4).

Sunitinib-induced thrombotic microangiopathy (TMA) is a secondary TMA caused by sunitinib. Despite the extensive use of sunitinib in patients with renal cell carcinoma and other malignancies, little is known about this complication of sunitinib. No clinical trials of sunitinib have studied this complication in any group of patients.

TMA is characterised by microangiopathic hemolytic anemia (MAHA), thrombocytopenia, and various organ dysfunction (5). Multiple case reports of sunitinib-induced TMA have been published(6-11). In this study, we report another case of sunitinib induced TMA and discuss clinical and laboratory manifemanifestationis causes and pathogenesis of the disease.

CASE PRESENTATION

A 63-year-old man with metastatic renal cell carcinoma, diagnosed five years ago and treated with 50 mg of Sunitinib daily for about four months, presented to the emergency department of Imam Reza Hospital in Tabriz with altered mental status and petechia. The patient had been experiencing progressive symptoms of weakness and lethargy since last week. Gradually, petechiae and purpura appeared on the skin and the oral cavity. Physical examinations and imaging did not show any CNS lesion. Initial laboratory data showed a decrease in platelets(PLT: 14,000/mm3) and hemoglobin(Hb:10.5g/dL), white blood cell:10000 per microliter, elevated serum level of lactate dehydrogenase**,** and total bilirubin. High serum creatinine and granular cast in urine sedimentation suggested acute kidney injury. Initial and secondary urine analysis did not show evidence of proteinuria. Schistocytes were found in the peripheral blood smear.

Upon diagnosis of TMA, the patient underwent four plasmapheresis sessions for four consecutive days. Improvement in consciousness and renal function was observed after four days. The patient was discharged in good general condition after two weeks of ICU admission.

DISCUSSION

Renal cell carcinoma (RCC) is the most common kidney cancer, and it represents about 3% of the whole adult malignancies (12, 13). In addition, about Thirty percent of RCC patients present with metastatic disease (14). Anti-VEGF antibody therapy is increasingly used in renal cell carcinoma and metastatic colorectal cancer therapy (15-17). The two main treatments for metastatic RCC are immunotherapy and vascular endothelial growth factor (VEGF) tyrosine kinase inhibitors (TKIs) (18). The oral multi-targeted kinase inhibitors (MTKI) such as Sunitinib, Sorafenib, and Brivanib block the VEGF signalling pathway, while Bevacizumab blocks the action of circulating VEGF. Sunitinib is a multi-targeted tyrosine kinase that inhibits VEGF receptor 1 and 2 platelet-derived growth factor receptors (PDGFR) (19).

Although The most frequent side effects reported in these drugs are diarrhea, nausea, hypertension, fatigue, and skin lesions, After therapy with this agent, multiple studies have reported the development of proteinuria or acute renal failure. Recent studies described several patients treated with Sunitinib who developed a preeclampsia-like syndrome characterised by proteinuria, edema, and severe hypertension(7, 20, 21).

Studies showed that Genetic deletion or drugs that disrupted VEGF signalling lead to the loss of normal glomerular capillary endothelial cells, microvascular injury, and TMA (22,23).In the kidney, podocytes consistently express VEGF, and its receptors are expressed by glomerular endothelial cells(23). Anti-VEGF therapy by blocking VEGF receptors caused Endothelial injury is implicated in the pathogenesis of hypertension and arterial thrombosis and TMA (24). Daniel Roncone et al. (25) study shows the damage of glomerular capillary endothelial suggests thrombotic microangiopathy. Hohenstein et al. (26) demonstrate that following glomerular endothelium injury, platelets influx and after activation, they form microthrombi. This finding explains that VEFG has a crucial role in glomerular capillary integrity and the prevention of endothelial damage.

conclusion

This study reports a case of sunitinib-induced TMA diagnosed based on clinical presentation and response to treatment. Sunitinib-induced TMA is an uncommon adverse effect of sunitinib therapy, But it can be deadly. Due to the increasing use of this drug in cancer treatment, Oncologists should be aware of life-threatening thromboembolic events associated with sunitinib so that prompt and appropriate intervention can be undertaken.

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Conflicts of interest

The authors declare that they have no conflict of interest.

Ethics

This study was performed according to the principles outlined by the World Medical Association's Declaration of Helsinki on experimentation involving human subjects, as revised in 2000 and approved by the ethics committee of the Tabriz University of Medical Sciences.

Author Contributions:

Mohammadreza Ardalan: Had the idea and conception of the study.

Amirreza khalaji: Prepared a first draft of the manuscript and further revision.

Sepideh Zonuni Vahed: Drafting the article or revising it critically for important intellectual content.

Mohammadreza Moselmi: Prepared the manuscript and revised the article.

Alireza Mirghaffari: Drafting the article or revising it critically for important intellectual content.

Consent statement :

Written informed consent was obtained from the patient to publish this report and clinical images. Consent has been signed and collected by the journal s patient consent policy

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