Sunitinib Induced Immune Thrombocytopenia

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Abstract

Sunitinib is an oral tyrosine kinase inhibitor which prevents tumor growth and metastatic progression. It was approved for treatment of advanced renal cell cancer, gastrointestinal stromal tumor and advanced pancreatic neuroendocrine tumors. It has several adverse reactions on multi organ systems including hematologic system. Although the neutropenia and thrombocytopenia commonly happens as Grade 3 or 4 abnormalities following bone marrow suppression, in the rare cases, the immune mediated abnormality may drive the sunitinib-induced hematologic disorder. In this report, we present a case of immune-mediated thrombocytopenia induced by sunitinib. One month after first treatment cycle with sunitinib, leucopenia and thrombocytopenia were occurred. The patient had a normal bone marrow aspiration and biopsy, the thrombocytopenia was resistant to platelet transfusion which successfully was treated with prednisolone.

Keywords: Sunitinib; Carcinoma; Thrombocytopenia; Tyrosine kinase.

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Introduction

Sunitinib is an oral tyrosine kinase receptor inhibitor approved for advanced renal cell cancer, gastrointestinal stromal tumor and advanced pancreatic neuroendocrine tumors. Several receptors are inhibited with this drug which is included vascular endothelial growth factor receptors (VEGFR1, 2, 3), platelet-derived growth factor receptors (PDGFR), stem cell factor receptor (KIT), Fms-like tyrosine kinase-3 (FLT3), colony-stimulating factor receptor type 1 (CSF-1R), and the glial cell-line derived neurotrophic factor receptor (RET). Thus sunitinib prevents tumor growth and metastatic progression and was approved by US Food and Drug Administration (FDA) in 2006 for the treatment of metastatic renal cell carcinoma (mRCC) and gastrointestinal stromal tumor (GIST). Sunitinib has multiple adverse effects on body organ systems such as hematologic system. Neutropenia and thrombocytopenia commonly happened as Grade 3 or 4 abnormalities (1, 2).

In this report, we will present a rare case of sunitinib-induced thrombocytopenia that was related to immune system abnormality. To the best of our knowledge, a few case reports have been presented in the literature about sunitinib induced immune thrombocytopenia (3-5).

Case Presentation

A 64 years old woman with complains of general weakness and malaise, anemia (Hb:
and gender was normal (Figures 1 to 3). In addition to supportive therapy, because of prolongation of thrombocytopenia (less than 30,000/µl for 10 days) and observation of normal megakaryocyte, low dose prednisolone (15 mg daily) was started. Within 4 weeks of discontinuation of sunitinib, platelet count began to rise and eventually reached to 200,000/µl. Then Sorafenib was administered for two treatment cycles with no recurrent thrombocytopenia. Patient discontinued treatment due to financial problems and was treated with supportive therapy including analgesia, blood transfusion and TPN (total parenteral nutrition). She died one year later, while been on supportive therapy.

Discussion

Immune thrombocytopenia (ITP) is mediated by humoral and cellular immunity. It could be secondary to other diseases. For example infections, other autoimmune or immunodeficiency disorders, malignancy, liver and bone marrow disease, recent vaccination and transfusions and inherited thrombocytopenia syndromes (6). Drug induced immune thrombocytopenia (DITP) may occur with chemotherapy and immunosuppressive agents (7). According to previous medical literature, ITP has been occurred in a patient with RCC (8). So other causes of thrombocytopenia must be ruled out to verify the diagnosis of DITP. In our case, the patient did not use immunosuppressive medications and there is no sign of infection and other autoimmune and hepatic disease. We evaluate validity of this report by Naranjo nomogram that it acquired a score of 5 (probable
adverse reaction) (9). Although measuring the drug dependent antibodies (DDAb) is a more reliable method for evaluation of the causality relationship (7), it was not available for us. Despite of this limitation, considering the normal biopsy of bone marrow we believe that ITP can explain the cause of acute thrombocytopenia in our case. In addition, ITP appeared after the drug was administered and resolved after the suspected drug was withdrawn and the patient responded to treatment with corticosteroid.

Sunitinib has been documented causing myelosuppression resulting thrombocytopenia in literatures. Motzer et al. reported grade 3 of thrombocytopenia in 8 of 65 (12%) patients whom experience all grades (10). In other study, in 78 patients, 18 (23%) and 4 (5%) were faced with grade 3 and 4, respectively (11). Trinkaus et al. reported the first case of ITP secondary to sunitinib and their patient’s platelet count returned to normal after 2 weeks treatment with IVIG (1 g/kg over 2 days), intravenous tranexamic acid and withholding the sunitinib (3). The mentioned treatment was also used successfully by Mutahir et al. in the same duration (4). At last, Ansari and George normalized the patient’s platelet count by IVIG (0.4 gr/kg/day) and prednisolone (50 mg/day) after 3 weeks (5). Our case was treated by prednisolone (15 mg/day) only and platelet count improved within 4 weeks.

Conclusion

Sunitinib may induce thrombocytopenia by immune related mechanism. This type of thrombocytopenia is resistant to platelet infusion and could be managed with corticosteroids alone.

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