CORRESPONDENCE

Rivaroxaban Induced Thrombocytosis: A Perplexing Clinical Challenge

Arijit Nag¹ · Maitreyee Bhattacharyya¹

Received: 27 December 2017 / Accepted: 24 February 2018 / Published online: 5 March 2018
© Indian Society of Hematology and Blood Transfusion 2018

Reactive thrombocytosis is a common clinical condition associated with certain infective and inflammatory conditions, acute hemorrhage, in post-operative states and in response to certain drugs. Rivaroxaban is an orally available Factor-Xa inhibitor approved for the prevention of Deep Venous Thrombosis in patients undergoing Hip/Knee Replacement Surgery. Potential hematological complications with the use of this drug include muco-cutaneous bleeding and thrombocytopenia [1]. We herein report a rarely reported occurrence of reactive thrombocytosis in response to Rivaroxaban.

A 36-year-old non-obese male patient had been switched to Rivaroxaban from initial therapeutic anticoagulation with Enoxaparin (for 4 weeks) after an episode of spontaneous sub-massive Pulmonary Embolism (PE). Patient had been diagnosed to be diabetic for 13 years (at the age of 23). He did require Insulin therapy to maintain glycemic state for the last 12 years and had been on basal-bolus Insulin regimen along with Metformin ever since. He has maintained euglycemic status on this regimen. He has no macrovascular or microvascular complications of diabetes mellitus and has been regularly and systematically evaluated for the same by the Department of Endocrinology. There was no history of spontaneous/provoked thrombosis in ant first degree relatives. The serial haemogram reports showed an isolated increase in the platelet counts from 2.1 lacs/ μ l before initiation of Rivaroxaban to 8.2 lacs/ μ l a week after initiation of therapy (Table 1). In view of the progressive increase in the platelet counts,

Rivaroxaban was stopped, and the patient was reinitiated on Enoxaparin. The platelet counts showed a steady decline after stoppage of Rivaroxaban and normalized after 10 days. The other etiologies of reactive thrombocytosis were systematically excluded as the patient had a no evidence of infective or inflammatory condition, iron-deficiency or recent blood loss. We also ruled out any possibility of clonal hematopoiesis/myeloproliferative neoplasm as the bone marrow aspiration/biopsy showed a normal hematopoiesis commensurate with age and negative clonal markers (JAK2, CALR, c-MPL mutations). We therefore provisionally related the thrombocytosis as ‘Rivaroxaban-induced’. As per the Naranjo scale for Adverse Drug Reaction (ADR), this would qualify as ‘possible’ ADR to Rivaroxaban.

Thrombocytosis is a rare side-effect occurring in adult patients undergoing hip or knee replacement surgery as per the summary of product-characteristic (CHMP). There has been only one formal case report in literature of Rivaroxaban-induced thrombocytosis and that had occurred after rivaroxaban was initiated following a major orthopedic procedure [2]. Thrombocytosis can often be a perplexing problem for the physician especially in patients with a past history of thrombosis. However, the possibility of it being a reaction to the anticoagulant (Rivaroxaban) should be borne in mind.

✉ Arijit Nag
coolwriju@gmail.com

¹ Institute of Hematology and Transfusion Medicine, Medical College and Hospital, Kolkata, Kolkata, India

Table 1 Laboratory parameters of the patient after starting Rivaroxaban and subsequently after switching to Enoxaparin

Date	21-09-2017 (Rivaroxaban initiation)	24-09	28-09 (Rivaroxaban stopped)	05-10	08-10
Hemoglobin (gm/dl)	13.2	13.0	13.2	13.4	13.4
Total leucocyte count ($\times 10^9/\mu\text{l}$)	8.4	8.25	8.2	8.3	8.24
Platelet count ($\times 10^9/\mu\text{l}$)	210	647	820	447	227
MCV (fl)	85	86	86	85	85
CRP	–	–	2	–	–
Serum ferritin (ng/ml)	–	–	58	–	–
Serum iron ($\mu\text{g/dl}$)	–	–	45	–	–
Transferrin saturation (%)	–	–	30	–	–

Funding The authors haven't received any external funding.

Compliance with Ethical Standards

Conflict of interest The authors both declare that they have no conflict of interest.

Informed Consent Informed consent was obtained from the patient.

References

1. CHMP Annex I Summary of Product Characteristics: Rivaroxaban. http://www.ema.europa.eu/docs/en_GB/document_library/EPAR_-_Product_Information/human/000944/WC500057108.pdf. Accessed 24 Nov 2017
2. Joyau C, Veyrac G, Piessard S, Delamarre-Damier F, Jolliet P (2014) P456: Rivaroxaban induced thrombocytosis: a not enough known adverse effect. Eur Geriatr Med 5:S225. [https://doi.org/10.1016/S1878-7649\(14\)70619-9](https://doi.org/10.1016/S1878-7649(14)70619-9)