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LETTER TO THE EDITOR

Olmesartan worsening known thrombocytopenia. A rare side effect of antihypertensive drugs

KEYWORDS
Drug-induced thrombocytopenia;
Olmesartan;
Myelodysplastic syndrome

Drug induced thrombocytopenia (DIT) is a relatively frequent condition with increasing diagnostic and clinical concerns requiring specific treatment. DIT disorders can be a consequence of decreased platelet production mainly due to bone marrow suppression or accelerated platelet immune-mediated destruction. Clinically, these patients present with moderate to severe thrombocytopenia (defined as a platelet count of less than 50×10^9/L), and spontaneous bleeding varying from simple ecchymoses, petechiae and mucosal bleeding to life-threatening spontaneous intracranial hemorrhage.[1]

A wide variety of medications including thiazide diuretics have proven to cause thrombocytopenia. Conversely, other common antihypertensive medications such as angiotensin receptor blockers (ARBs) are safe and well tolerated drugs with limited contraindications. Only few case reports have presented the development of thrombocytopenia in patients receiving ARBs however, robust data to support this statement are still lacking.[2,3] We present here one such case.

Case presentation

Patient is a 70-year-old male who presented at the emergency department complaining of headache and dizziness which started three days ago. The patient had a history of thrombocytopenia and had received therapy with corticosteroids. He was also receiving antihypertensive treatment with an ARB once a day (olmesartan medoxomil) that was been recently prescribed.

His blood count revealed severe thrombocytopenia (PLT: 16×10^9/L). Brain computed tomography (CT) revealed minor hemorrhage at the posterior cranial fossa. The patient was admitted to the Hematology department for further investigation.

During the same hospitalization his general condition remained stable without any neurological symptoms and signs of the cranial hemorrhage and his blood pressure ranged up to 160/80 mmHg. The rest of his physical examination was unremarkable and his lipid profile was normal. Based on the initial laboratory and imaging results the presumed diagnosis was refractory thrombocytopenia as part of a myelodysplastic syndrome (MDS). The diagnosis was confirmed by bone-marrow exam. Thus, the patient received therapy with γ-immunoglobulin, methylprednisolone, vinblastine and romiplostime.

Before discharged, a new brain CT scan was performed showing no change compared to the first one. His thrombocytopenia at that time remained stable (PLT: 20×10^9/L). He was also examined by a cardiologist who switched olmesartan to a different antihypertensive class medication (calcium channel blocker).

After six months the patient was re-evaluated as an outpatient and presented with a platelet count of 110×10^9/L (Figure 1).

Discussion

The current case report indicates worsening of a known thrombocytopenia, in a patient with a preexisting MDS, as possible side effect of olmesartan. It comes as supportive evidence of few previously published case reports describing ARB-induced thrombocytopenia mainly attributable to myelosuppression or to accelerated immune-mediated platelet destruction.[2] An alternative suggested

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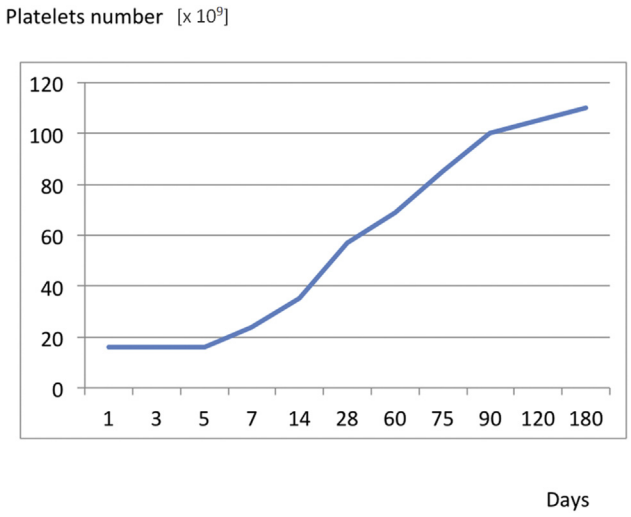

Figure 1 Platelets variation over time.

mechanism for this disorder might be the increased antithrombotic impact caused by the reduced activation of renin-angiotensin system (RAS).[1,2,4]

Hypertension is the most common cause that induces left ventricular diastolic dysfunction, associated with a poor cardiovascular prognosis[5] and a major risk factor for thrombotic events such as myocardial infarction and stroke,[6] reflecting a prothrombotic state that is present in hypertensive patients. RAS plays an important role in the pathogenesis of atherosclerotic complications. It can influence not only vascular tone but also disturb the balance of the hemostatic system with abnormalities in endothelial and platelet function, coagulation and fibrinolysis. The use of angiotensin-converting enzyme and ARBs protects against this prothrombotic state that is induced by the activated RAS which is more pronounced in hypertension.[4,7,8]

ARBs in general and olmesartan in particular are well tolerated demonstrating safety and high level of efficacy as observed in various studies and in a variety of patients, including the elderly, children, diabetics, obese patients and patients at high cardiovascular risk.

The most frequently reported adverse events of ARBs are gastrointestinal disorders (nausea/vomiting), nervous system disorders (dizziness/headache) and fatigue/malaise, whose incidence however is similar to that observed with placebo. When combined with hydrochlorothiazide, ARBs counteract the adverse metabolic effects of the diuretic, whereas they reduce ankle edema formation when combined with calcium blockers. ARBs are also safe and well tolerated in patients with nephropathy.

Concluding, our patient suffered from a refractory thrombocytopenia, as part of an MDS, possibly worsened by olmesartan prescription that was partly improved after olmesartan discontinuation, and MDS medication intensification. The effect of olmesartan and ARBs on the number and the function of platelets should be thoroughly investigated, especially in patients with preexisting hematologic disorders, before we could possibly attribute thrombocytopenia as a side effect of these agents.

Conflicts of interest

No conflicts of interest have been declared.

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