

CLOPIDOGREL-INDUCED LEUKOCYTOCLASTIC VASCULITISNAVIN PATIL¹, BALAJI O¹, KARTHIK RAO^{2*}, TALHA A³, CHAITAN³¹Department of Pharmacology, Kasturba Medical College, Manipal, Udipi, Karnataka, India. ²Department of Internal Medicine, Kasturba Medical College, Manipal, Udupi, Karnataka, India. ³Intern, Kasturba Medical College, Manipal. Email: karthikrao85@gmail.com*Received: 24 March 2017, Revised and Accepted: 22 April 2017***ABSTRACT**

Cutaneous adverse drug reactions are very common in a hospital setting while treating patients. Drug-induced vasculitis is a very common form of vasculitis affecting all age groups, and many drugs have been implicated in causing vasculitis. Clopidogrel is an antiplatelet drug used in the management as well as prevention of coronary artery disease. It is known to cause various side effects ranging from bleeding, gastrointestinal disturbances, to skin rashes. Leukocytoclastic vasculitis is a form of hypersensitivity vasculitis and is very rarely seen with clopidogrel. Hence, we report a case of clopidogrel-induced leukocytoclastic vasculitis in an old male patient after coronary stenting.

Keywords: Clopidogrel, Vasculitis, Angioplasty, Adverse drug reaction.

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INTRODUCTION

Drug-induced vasculitis is one of the most common forms of vasculitis causing inflammation of the blood vessels by use of various pharmacological agents. It usually resembles idiopathic vasculitis, but stopping of the offending agent along with histopathological analysis usually helps in identifying the condition. Various drugs associated with vasculitis include antibiotics, antipsychotic agents, anti-tumor necrosis factor alpha agents, and other agents such as lithium and allopurinol [1]. Hence, we report a case of clopidogrel induced leukocytoclastic vasculitis in a 65-year-old male patient post-percutaneous transluminal coronary angioplasty in a tertiary care hospital in Southern India.

CASE REPORT

Informed consent was taken from the patient. A 65-year-old male patient came with complaints of profuse sweating with giddiness on April 6, 2016. His vitals were stable with heart rate of 75 beats/minutes and blood pressure of 140/80 mmHg. Cardiovascular examination revealed normal S1 and S2, and respiratory system examination revealed respiratory breath sounds to be normal. Chest X-ray was normal with no cardiomegaly and normal pulmonary vasculature was seen. Electrocardiography revealed evolved inferior wall myocardial infarction. Echocardiography revealed no regional wall motion abnormality and normal left ventricle resting systolic function. Hence, the patient was treated with intravenous nitroglycerin, heparin, antiplatelet, diuretics, beta-blockers, and statins and was stabilized. Hence, diagnosis of ischemic heart disease with evolved inferior wall myocardial infarction and was referred to tertiary medical center on April 9, 2015. Coronary angiography revealed coronary artery disease with proximal left anterior descending artery 80% lesion, proximal right coronary artery total occlusion, and left circumflex artery to be normal. Then, after confirming the lesion, patient underwent percutaneous transluminal coronary angioplasty with stenting to left anterior descending artery and right coronary artery and was put on sustained release nitroglycerine 30 mg, aspirin 150 mg, clopidogrel 300 mg loading dose followed by 75 mg, nicorandil 10 mg, amlodipine 5 mg, rosuvastatin 40 mg, and pantoprazole 40 mg. Beta-blockers were not advised in view of complete heart blockade post-intervention. The patient was discharged on April 11, 2015. Two months later, the patient complained of burning sensation in legs with maculopapular rash along with palpable purpura on the right forearm (Fig. 1). A diagnosis of leukocytoclastic vasculitis was made. Clopidogrel was suspected as the

cause after ruling out other conditions, and dose was reduced to 50 mg once daily. In 2 weeks, the lesions subsided and the patient condition improved.

DISCUSSION

Leukocytoclastic vasculitis, also called the hypersensitivity vasculitis, affects predominantly the small vessels with no gender predilection with an incidence of 30 million cases/year globally [2]. Most common affected organ is the skin with more predilections for lower extremities, but one-third of cases affect the trunk as well as the upper extremities. It usually presents as painful burning rash, palpable purpura, sometimes also presents as maculopapular rash, bullae, plaques and ulcer [2]. Various etiological factors known to cause this condition include infections, drugs, collagen vascular disorder, autoimmune conditions, foods, and malignancies. The differential diagnosis includes Henoch-Schonlein purpura, drug-related eosinophilia and systemic symptoms, amyloidosis, meningococemia, immune thrombocytopenic purpura, and antiphospholipid antibody syndrome. Circulating immune complex is involved, but the pathogenesis is still unclear [2].

Clopidogrel is a thienopyridine derivative, used in the treatment as well as the prevention of coronary vascular disease. It acts by irreversibly inhibiting the P2Y₁₂ receptors on the platelet surface and thereby inhibits the ADP and fibrinogen induced platelet aggregation [3]. Along with aspirin, it is used to prevent ischemic episodes in coronary artery disease patients and to check the restenosis of stented coronaries and is found to have synergistic activity [4]. It is usually associated with various side effects ranging from diarrhea, epigastric pain, bleeding, neutropenia, thrombocytopenia, to bone marrow toxicity. Hypersensitivity reactions range from rashes, urticarial, to even life-threatening angioedema. Cutaneous adverse effects include mucocutaneous exanthemas, lichenoid eruptions, acute generalized exanthematous pustulosis, and fixed drug eruptions [3]. There are only a few cases of leukocytoclastic vasculitis due to clopidogrel been reported so far, and to the best of our knowledge, this is the second case to be reported [3]. The diagnostic criteria for leukocytoclastic vasculitis include age >16 years, proven temporal association of drug palpable purpura, maculopapular rash, biopsy of the skin showing neutrophils around an arteriole or venule [3]. In our case, the reaction started after 2 months of clopidogrel therapy and patient developed palpable purpura. Patient was 65 years old and biopsy of the lesion revealed neutrophil



Fig. 1: Maculopapular rash/palpable purpura after clopidogrel

and eosinophil accumulation around the arteriole. Our case was similar to the first case reported and the reaction occurred after starting clopidogrel therapy and subsided after the dose was reduced compared to one observed in the literature where the offending agent was stopped. Other etiological factors were ruled out. Causality assessment was done as per the Naranjo's *et al.* scale [5], and a probable causal relationship was ascribed. The adverse reaction was found to be of mild severity and

not preventable as per the Hartwig's *et al.* severity [6] and Schumock and Thornton's preventability scale [7], respectively.

CONCLUSION

Clopidogrel, essential drug used in prevention and treatment of coronary vascular disease, is used for long periods of time, so proper monitoring of adverse drug reactions is warranted. Furthermore, further studies can be done to find out the incidence of leukocytoclastic vasculitis associated with clopidogrel.

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