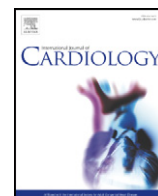




Contents lists available at SciVerse ScienceDirect

International Journal of Cardiology

journal homepage: www.elsevier.com/locate/ijcard

Letter to the Editor

Delayed eosinophilic gastroenteritis, a possible side effect of clopidogrel? ☆, ☆ ☆

Fangfang Wang, Jiangli Han *

Department of Cardiology and Key laboratory of Cardiovascular Molecular Biology and Regulatory peptides, Ministry of Health, Peking University Third Hospital, China

ARTICLE INFO

Article history:

Received 19 October 2012

Accepted 2 November 2012

Available online xxxx

Keywords:

Eosinophilic gastroenteritis

Side effect

Clopidogrel

Allergic reaction

Clopidogrel bisulfate, a widely used inhibitor of platelet aggregation, is generally well tolerated. Recent pilot study suggested that a second 600 mg loading dose of clopidogrel in elderly patients with high on-treatment platelet reactivity was still safe [1]. Allergic or hematologic adverse reactions to clopidogrel are well described and occur in about 1% of patients, of which 93% present with a maculopapular rash [2–4], but the eosinophil count was not mentioned. Mizuno et al. [5] reported one case of eosinophilic pneumonia caused by Clopidogrel. Until now, none of the published report has suggested eosinophilic gastroenteritis (EGE) as one of the adverse reactions of clopidogrel. A 76-year-old Chinese woman, underwent a successful percutaneous coronary intervention (PCI) in the left anterior descending artery (LAD) due to unstable angina pectoris in 2009, and then followed standard combined antiplatelet therapy with clopidogrel 75 mg/day and aspirin 100 mg/day. 15 months after stenting, she was hospitalized again due to an exercise-related upper abdominal pain. Her coronary angiogram (CAG) showed no thrombus and restenosis in the LAD stent. Blood routine test was normal. To avoid possible gastrointestinal irritation, aspirin was subsequently withdrawn and the patient kept on taking Clopidogrel 75 mg/day. After 29 months of administration with Clopidogrel, the patient developed persistent distension and pains in the upper-middle abdomen. Blood routine test in Outpatient Department showed that white blood cell (WBC) count was $15.27 \times 10^9/L$ and absolute eosinophil count (EC) was $8.22 \times 10^9/L$. Three days later, re-examination of blood routine test in Gastroenterology ward showed that WBC count was $14.04 \times 10^9/L$ and EC was $5.85 \times 10^9/L$.

Gastrointestinal endoscopy revealed multiple sites of eosinophilia infiltration distributed in duodenal submucosa, ileal and cecal mucosa (Fig. 1). Bone marrow smear showed increased eosinophilia (16%) without neoplastic cells; both gene test and autoimmune antibody test were negative. The diagnosis of eosinophilic gastroenteritis and hypereosinophilia was considered without known cause. The patient received symptomatic treatments with H_2 receptor antagonist but shown no significant improvement in symptoms. Clopidogrel was discontinued in view of the possible side effect, eosinophilic hyperplasia, suggested in the instructions after almost 36 months of administration. After clopidogrel was withdrawn, full recovery of the abdominal distension was observed within 3 days. Blood routine tests suggested that the proportion and absolute value of eosinophilia recovered gradually.

The etiology and pathogenesis of EGE are still not well understood, but this disease may result from the interaction of a genetic predisposition with environmental factors such as intolerance or allergy to certain foods [6,7]. As to the above mentioned patient who exhibited manifestations of blood eosinophilia and EGE after 29 months of administration with clopidogrel, a possible cause of the disease may be delayed drug allergies. The deduction of clopidogrel-induced EGE was supported by the rapid symptom remission upon drug cessation supports. Based on our experience, when unaccountable gastrointestinal symptoms are observed in patients receiving clopidogrel after

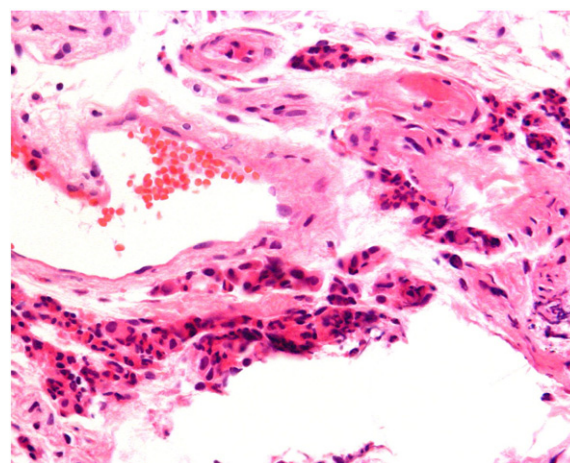


Fig. 1. Endoscopic biopsies from duodenum. Histologic sections from duodenal mucosa demonstrated aggregates of numerous eosinophils within the submucosa (hematoxylin and eosin stain, original magnification $\times 400$).

☆ These authors take responsibility for all aspects of the reliability and freedom from bias of the data presented and their discussed interpretation.

☆☆ Acknowledgement of grant support: No grant support.

* Corresponding author. Tel.: +86 13910801907.

E-mail address: jianglihan2011@gmail.com (J. Han).

PCI, clopidogrel-induced EGE might be included in the differential diagnosis and routine blood counts should be performed promptly.

The authors of this manuscript have certified that they comply with the Principles of Ethical Publishing in the International Journal of Cardiology [8].

Acknowledgments

We thank Dr Hejun Zhang (Department of Gastroenterology) who provided the figure.

References

- [1] Laine M, Paganelli F, George FD, Camoin-Jau L, Bonello L. Biological efficacy and clinical safety of a second 600mg loading dose of clopidogrel in elderly patients with high on-treatment platelet reactivity: a pilot study. *Int J Cardiol* in press, <http://dx.doi.org/10.1016/j.ijcard.2012.08.019>.
- [2] Lokhandwala J, Best PJ, Henry Y, Berger PB. Allergic reactions to clopidogrel and cross-reactivity to other agents. *Curr Allergy Asthma Rep* 2011;11:52–7.
- [3] Lokhandwala JO, Best PJ, Butterfield JH, et al. Frequency of allergic or hematologic adverse reactions to ticlopidine among patients with allergic or hematologic adverse reactions to clopidogrel. *Circ Cardiovasc Interv* 2009;2:348–51.
- [4] Raccah BH, Shalit M, Danenberg HD. Allergic reaction to prasugrel and cross-reactivity with clopidogrel. *Int J Cardiol* 2012;157:e48–9.
- [5] Mizuno Y, Shimizu H, Yamashita M, Horie Y, Mizo A. A case of clopidogrel-induced eosinophilic pneumonia. *Nihon Kokyuki Gakkai Zasshi* 2011;49:838–42.
- [6] Suzuki S, Homma T, Kurokawa M, et al. Eosinophilic gastroenteritis due to cow's milk allergy presenting with acute pancreatitis. *Int Arch Allergy Immunol* 2012;158(Suppl. 1):75–82.
- [7] Temiz T, Yaylaci S, Demir MV, Kahyaoglu Z, Tamer A, Uslan MI. Eosinophilic gastroenteritis: a rare case report. *North Am J Med Sci* 2012;4:367–8.
- [8] Coats AJ, Shewan LG. Statement on authorship and publishing ethics in the International Journal of Cardiology. *Int J Cardiol* 2011;153:239–40.