

## Letter to the Editor

### Serum sickness-like reaction associated with clopidogrel

Clopidogrel (Plavix<sup>®</sup>) is a selective inhibitor of platelet aggregation used preventively in the setting of myocardial infarction, coronary stent implantation and stroke [1]. Clopidogrel structurally resembles another thienopyridine antiplatelet drug ticlopidine (Ticlid<sup>®</sup>) differing only by the presence of a carboxymethyl side group on clopidogrel. The drugs differ in their toxicity profile, with ticlopidine being more significantly associated with haematological adverse events such as agranulocytosis [2]. Recent reports have described a syndrome of arthritis and rash or pruritus associated with both clopidogrel and ticlopidine [3, 4]. We describe a case of serum sickness-like reaction (SSLR) associated with clopidogrel that along with the earlier reports, highlights that SSLR may be an uncommon but potentially underreported adverse event associated with the thienopyridine antiplatelet drugs.

A 51-year-old man presented with an acute coronary syndrome. Longstanding medications included atorvastatin, metoprolol and enteric coated aspirin 325 mg daily.

Subsequent cardiac catheterization revealed an angioplastable lesion. Following the insertion of a coronary artery stent, he was started on clopidogrel 75 mg once daily. Ten days later he developed fever followed by arthralgias and skin rash. Physical examination revealed an exanthematous rash over the chest and back and stress pain of the shoulder and knee joints bilaterally. Complete blood count, liver function tests, creatinine and urine microscopy were normal. Symptoms resolved over a week with discontinuation of clopidogrel and a tapering dose of prednisone. He remains on atorvastatin, aspirin and metoprolol.

The constellation of fever, arthritis, and rash occurring 10 days following initiation of a new drug support the diagnosis of clopidogrel-associated SSLR. Other recent reports suggest that SSLR may be associated with both clopidogrel and ticlopidine [3, 4]. Dakik *et al.* reported a 65-year-old woman who developed an urticarial rash and arthritis 12 days after starting ticlopidine 250 mg twice daily after coronary artery stent placement [3]. The authors labelled this as 'hypersensitivity vasculitis'; however, the time sequence, arthritis, urticarial rash and lack of internal organ involvement are most consistent with SSLR. Garg *et al.* described two cases of 'arthritis' associated with clopidogrel. One was a 76-year-old woman who developed pruritus and symmetrical polyarthritis 2 weeks after starting clopidogrel following coronary

stent insertion [4]. The second case was a monoarthritis occurring 3 weeks after initiation of clopidogrel and may have been unrelated to drug [4]. In all cases the symptoms were self-limited with no recurrence after discontinuation of ticlopidine and clopidogrel, respectively [3, 4]. Although cutaneous reactions and arthritis have been associated with both clopidogrel and ticlopidine in post-marketing reports, no specific cases of SSLR have been reported. The structural similarity between clopidogrel and ticlopidine would suggest the potential generation of similar, although as yet unidentified, reactive metabolites. These metabolites along with immunological and host factors are thought to be important for the pathophysiological basis of SSLR [5]. Interestingly, bupropion (Zyban<sup>®</sup>), an antidepressant which has also been associated with SSLR, shares some structural features with clopidogrel and ticlopidine, although the putative reactive metabolite is unknown [6].

Although none of the cases, including ours, was rechallenged with the drug in question, these cases should increase awareness of a potential association between ticlopidine and clopidogrel and SSLR.

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