Myocardial infarction secondary to dipyridamole overdose

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SUMMARY

A case of myocardial infarction secondary to dipyridamole overdose is described in a 62-year-old woman with longstanding angina. Therapeutic doses of dipyridamole are associated with reversible myocardial ischaemia in a proportion of patients but serious adverse events are rare (Homma *et al.*, 1987). To our knowledge this is the first reported case of dipyridamole overdose in the literature.

INTRODUCTION

Dipyridamole, a pyrimidopyrimidine compound, was first marketed in 1959 as a coronary vasodilator (Kadatz, 1959). Subsequently its antiplatelet effect was recognized and currently dipyridamole is prescribed orally for patients with coronary artery disease, especially after coronary artery bypass surgery, following implantation of metal prosthetic heart valves, in peripheral vascular disease, neurological disease and intravenously for its coronary vasodilator effect during thallium myocardial imaging.

The effects of intentional overdose of oral dipyridamole in a patient with coronary artery disease, are described.

CASE REPORT

A 62-year-old woman with longstanding angina was admitted as an emergency to hospital having taken approximately 50 × 100 mg dipyridamole tablets 5 h earlier. One hour after ingestion she experienced severe chest pain of 30 min duration,

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but by the time of admission she was pain-free. Other than depression, which precipitated the overdose, there were no other symptoms, including vomiting. On examination she was well perfused with a heart rate of 92 beats min^{-1} and blood pressure of 140/90 mmHg. Remaining examination was unremarkable.

Full blood count and urea and electrolytes were normal. Her admission electrocardiogram showed sinus rhythm and left bundle branch block. She remained pain-free and haemodynamically stable and took her own discharge against medical advice several hours later.

Cardiac enzymes were compatible with myocardial infarction: on admission creatine kinase was 583 U^{-1} (NR $<175 \text{ U}^{-1}$), MB isoenzyme $>8\%$ (NR $<6-8\%$ CK), and 6 h later creatine kinase had risen further to 924 U^{-1} . There was no electrocardiographic change during her brief admission but the presence of left bundle branch block could obscure this.

DISCUSSION

Dipyridamole is prescribed orally for its inhibitory effects on platelet aggregation. Its mechanism of action has not been elucidated fully although it may interact with products of arachidonic acid metabolism, namely thromboxane and prostacyclin (Moncada *et al.*, 1979). Dipyridamole is also a potent vasodilator, increasing coronary blood flow by inhibiting cellular uptake of adenosine (Miura *et al.*, 1967). As a result it is a useful adjunct during thallium myocardial imaging, particularly in patients unable to perform a standard treadmill exercise test.

Reversible myocardial ischaemia secondary to dipyridamole is well recognized. Of 37 patients with coronary artery disease given 150 mg dipyridamole orally, six patients (16%) experienced angina and 13 patients (35%) had ischaemic electrocardiographic changes (Virtanen *et al.*, 1989). During thallium scanning with intravenous dipyridamole (0.56 mg kg^{-1}) in 293 patients chest pain occurred in 76 patients (26%) and ischaemic ST segment depression in 60 patients (20%; Homma *et al.*, 1987). Serious adverse events are rare: reports in the literature include one case of ventricular fibrillation during exercise dipyridamole thallium imaging (Bayliss *et al.*, 1983), two cases of myocardial infarction (Blumenthal *et al.*, 1988; Biddle *et al.*, 1989), one case of severe bronchospasm resulting in respiratory arrest and three coronary deaths (Lette *et al.*, 1989).

The mechanism whereby dipyridamole causes myocardial ischaemia is probably by coronary steal occurring in the setting of atheromatous coronary artery disease especially in the presence of intercoronary collateral vessels (Keltz *et al.*, 1987). Significant hypotension is unlikely to occur with therapeutic doses.

This patient took a substantial overdose and it is surprising that she was so stable haemodynamically. We cannot be certain of the precise number of tablets ingested and plasma dipyridamole levels were not measured. However the patient was not seen until 5 h after ingestion by which time her clinical status could have improved. The time of onset of chest pain coincides with the known pharmacokinetic profile of dipyridamole since peak plasma levels occur up to 150 min after oral

dosing (Rivey *et al.*, 1984). It is likely that myocardial infarction occurred as a result of coronary steal, perhaps exacerbated by hypotension which would be expected in this case and could have resolved by the time of presentation.

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