

Case report

Coronary artery spasm and acute myocardial infarction in naproxen-associated anaphylactic reaction

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We present the case of a 43-year-old man who suffered an acute myocardial infarction after oral administration of 250 mg of naproxen, prescribed as antiinflammatory-analgesic agent after tooth extraction. Both intradermal skin test and human basophil degranulation test were positive to naproxen. These findings suggest a naproxen-associated anaphylactic reaction with concomitant coronary artery spasm and posteroinferior infarction, a clinical event previously not reported with the use of this drug.

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Coronary artery spasm has been reported as a manifestation of anaphylactic reaction to inhaled cocaine (1), hydrocortisone therapy (2), and administration of iodinated contrast material (3). Acute myocardial infarction has been also observed after vespid sting (5). We describe a case of coronary artery spasm and acute myocardial infarction which occurred after oral administration of naproxen.

Case report

The patient, a 43-year-old non-atopic man, was a cigarette smoker of long standing and ingested about 30–40 g of ethyl alcohol a day. No history of allergy to drugs was present. He was attended by a dentist who extracted a tooth under local anesthesia (Ultracain®, carticaine 40 mg, epinephrine hydrochloride 0.012 mg/ml). Two hours later, he took one tablet of Naprosyn® (naproxen 250 mg) and one capsule of Precopén® (amoxicillin 500 mg). After half an hour, the patient complained of severe epigastric pain accompanied by sweating, dizziness, loss of consciousness, and incontinence. He was admitted to the emergency room in a state of cardiogenic shock.

The electrocardiogram showed a posteroinferior

subepicardial infarction with a maximum elevation of ST-segment of 5 mm in lead III (Fig. 1). The rhythm was irregular with a tendency towards bradycardia; P waves did not appear. The blood gas values were PaO₂ 43 mmHg, PaCO₂ 43.7 mmHg, and pH 7.25. The blood base excess was 6.6 mmol/l, and serum bicarbonate 21.1 mmol/l. After initiating treatment with dopamine and dobutamine, arterial blood pressure rose to 80/40 mmHg and consciousness was restored. Two hours later, the ECG demonstrated a sinus rhythm of 85 beats/min with no signs of ischemia (Fig. 1). Frequent ventricular premature systoles and supraventricular tachycardia were detected during continuous monitoring. These completely disappeared after a few hours. Peaks of serum enzyme activities were 336 U/l for creatine phosphokinase and 428 U/l for lactic dehydrogenase. Blood gas values, blood biochemistry, chest roentgenography, and Holter recordings during 10 days were normal. Ergometry was normal at 88% of the maximum theoretical heart frequency. The left ventricular ejection fraction by radionuclide ventriculogram was 46%. Coronary arteriography disclosed normal filling of the coronary arterial tree. No signs of atherosclerosis were observed.

The patient was discharged 10 days after admis-

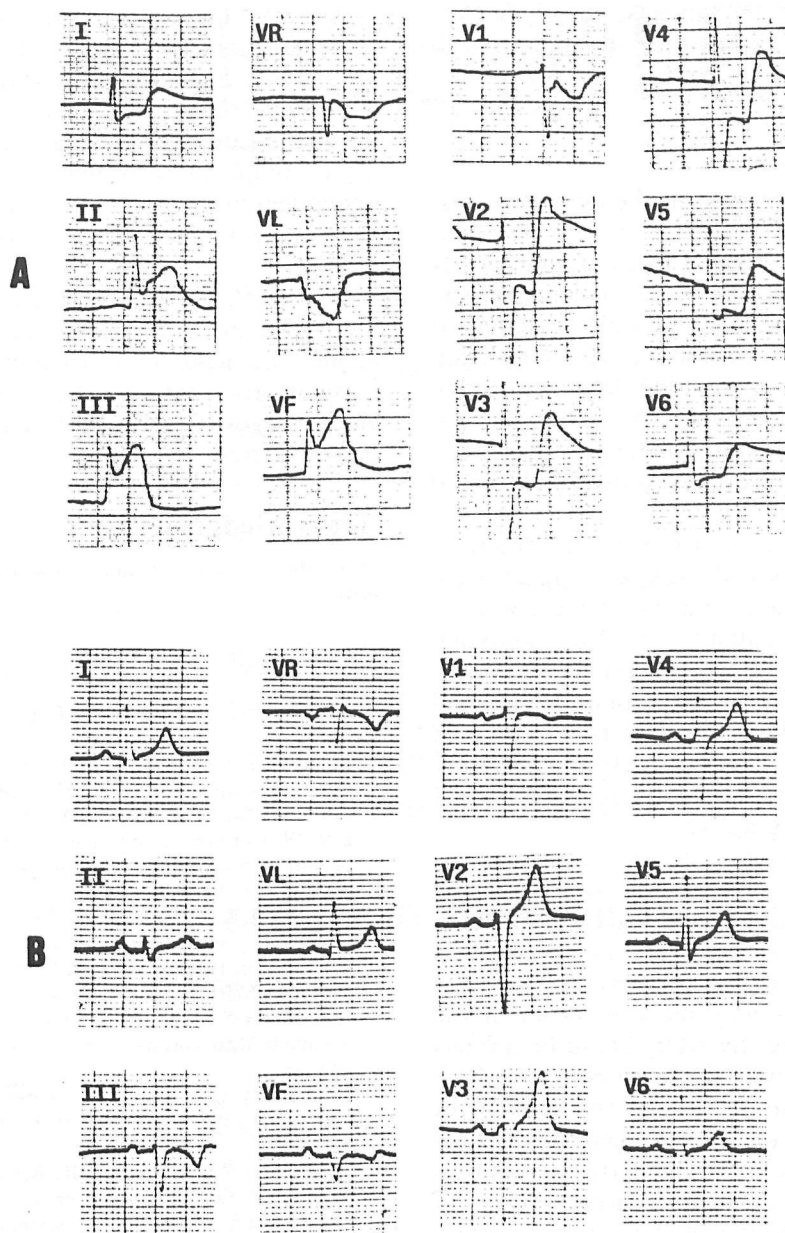


Fig. 1. Electrocardiogram on admission to the emergency room (A) showing a severe postero-inferior subepicardial infarction with a maximum elevation of ST-segment of 5 mm in lead III. Two hours later, the electrocardiogram showed resolution of the infarct pattern.

sion with the diagnosis of acute myocardial infarction in the course of an anaphylactic reaction. To determine the etiology of the anaphylactic reaction, he was remitted to the Allergy Unit.

In vivo tests including the skin prick test (SPT) performed with a standard allergen panel, intradermal tests and subcutaneous provocation with lidocaine, carticaine, and ampicillin gave negative results. The oral provocation test with amoxicillin was also negative. The SPT with naproxen was negative but the intradermal test with 100 µg/ml of naproxen elicited a positive wheal reaction (papule and erythema of 10 and 19 mm in diameter, respec-

tively). Twenty healthy subjects, taken as controls, gave no reaction at the same concentration. Oral provocation tests on different days to vehicle of Naprosyn were negative.

Serum IgE concentration was 156 IU/ml (normal value ≤ 110 IU/ml). There was no evidence of eosinophilia and serum complement was within normal limits. Lymphocyte transformation tests were negative for penicillin G, lidocaine, naproxen, diclofenac sodium, and indomethacin. Human basophil degranulation test (HBDT) was positive to naproxen with more than 50% degranulation. Ultracain and amoxicillin gave negative results with less than 15% de-

granulation. In 10 healthy subjects, less than 15% degranulation was observed after stimulation with naproxen.

Discussion

The negative results obtained in the cutaneous test with ampicillin and oral provocation with amoxicillin made it possible to discard these antimicrobials as the cause of the reaction in the patient. Hypersensitivity to local anesthetics was also discounted in view of the results of the cutaneous test. Naproxen was therefore considered to be the drug responsible for the anaphylactic reaction. The patient did not remember having received treatment with naproxen before, although he had received other nonsteroidal antiinflammatory drugs.

In patients without coronary artery obstruction, the mechanism which could explain an acute myocardial infarction includes spasms of the coronary arteries *in situ* (3). Our patient, apart from smoking, presented no other risk factor or previous symptoms of coronary disease. The consumption of alcohol was moderate. Nor did he consume drugs that could induce or exacerbate a coronary spasm. In addition, signs of coronary atherosclerosis were not observed in the coronary arteriography.

Histamine released during allergic reactions is capable of provoking vasoconstriction by H_1 -receptor stimulation. Histamine has been used as a provocative test to induce clinical coronary artery spasm in patients with variant angina pectoris (6). In these circumstances, spasms may have occurred in the coronary artery because the artery could be a focus of vascular hyperreactivity. Forman et al. (4) draw attention to the implication of vasoactive substances secreted by mast cells in the pathogenesis of coronary spasm. Some patients with atherosclerosis who suffer coronary spasms present a larger number of mast cells in the adventitia of the coronary artery affected (4). In our case, we could find no signs of atherosclerosis.

Although high levels of serum IgE were detected, atopy does not seem to be a risk factor in developing systemic reactions to drugs (7). Vasoactive substances secreted by mast cells can play a role in the pathogenesis of coronary artery spasm secondary to anaphylaxis, probably as a result of an IgE-dependent mechanism affecting the coronary artery, as was demonstrated by cutaneous tests and the HBDT.

It is concluded that coronary artery spasms can be the only symptom of drug allergy. In patients with angina and acute myocardial infarction with normal coronary arteriography, the possibility of having previously ingested some pharmacologic agent should be considered.

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