

## Acute myocardial infarction and cerebrovascular accident in a young girl after a viper bite

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**SUMMARY** A 17-year-old girl developed an acute myocardial infarction immediately after being bitten by a viper and four days later she had a cerebrovascular accident. The close clinical and laboratory follow-up of this case suggested that myocardial damage could be attributed to a direct cardiotoxic effect of the venom, while the brain injury that subsequently appeared was probably the result of a disseminated intravascular coagulopathy, possibly in conjunction with vasculitis.

Acute myocardial infarction and/or ischaemia caused by snakebite has been reported a few times.<sup>1,2</sup> This injury was attributed to arterial thrombosis resulting from severe hypotension,<sup>1</sup> or to direct toxic effect of the venom on the myocardium.<sup>2</sup> In addition, emphasis was given to disseminated intravascular coagulation in cases of snakebite by the *Vipera echis carinatus*,<sup>3</sup> but toxic vasculitis was thought to be the main cause of haemorrhagic complications.<sup>4</sup> Neurological manifestations that constitute the predominant features in cobra bites were found in one-third of the cases with viper bites where bleeding and nephrotoxicity were encountered at higher rates.<sup>4</sup> Necropsy findings of subarachnoid and leptomeningeal haemorrhage as well as blood clot formation in the cerebral hemispheres have also been reported.<sup>5</sup>

The case of a 17-year-old girl who sustained successive injuries to heart and brain after a viper bite is presented, the sequence of these events suggesting that different mechanisms were involved.

### Case report

On 23 July 1979, at about 6 00 am while working in a tobacco field in central Greece, a previously healthy 17-year-old girl was bitten on the inner aspect of the left big toe by a snake. The only poisonous snakes in this area are *Viperidae*, *Vipera berus* (adder), *Vipera ammodytes*, and *Vipera lepetina*, as is the case in the rest of the country.

Shortly after the bite the patient experienced severe substernal pain, nausea, and collapse. The local physician who saw the patient about half an hour later administered an antihistaminic compound intramuscularly, high doses of corticosteroids intravenously,

and Pasteur antivenom subcutaneously. Four hours later the patient was admitted to the local hospital where the electrocardiogram showed paroxysmal atrial tachycardia at a rate of 180/min and pronounced ST elevation in leads II, III, aVF, as well as in leads V4 to V6 (Fig. 1A). Conversion of paroxysmal atrial tachycardia to regular sinus rhythm ensued after the intravenous administration of 5 mg verapamil. Frequent multifocal ventricular extrasystoles were interrupting the regular sinus rhythm, at times bursting into salvos. Atropine, given subcutaneously, increased the sinus rhythm and diminished the ventricular extrasystoles. The ST changes remained, however. At that stage the patient was transferred by helicopter to Athens and admitted to the coronary care unit of "Evangelismos" Hospital late in the afternoon of the same day.

On admission the patient was alert and coherent. Two fang marks were present at the inner aspect of the left big toe and the whole limb was swollen, cyanotic, and painful. On auscultation, tachycardia at a rate of 120/min and gallop were heard. The blood pressure was 120/70 mmHg. The electrocardiogram confirmed the previous findings but its monitoring showed no ventricular extrasystoles throughout the hospital course. As the ST became isoelectric, on the second day, Q waves appeared in leads II, III, aVF, along with T wave inversion in leads V3 to V6 (Fig. 1B). On the fourth hospital day the patient presented with right-sided hemiparesis and aphasia.

During the first six days in hospital she was given an intravenous drip of xylocaine 1 g in 1000 ml dextrose 5% in water, prednisolone 5 mg tid, heparin 5000 units every six hours intravenously, and thereafter dipyridamole 75 mg tid.

The laboratory follow-up (Table) showed a gradual

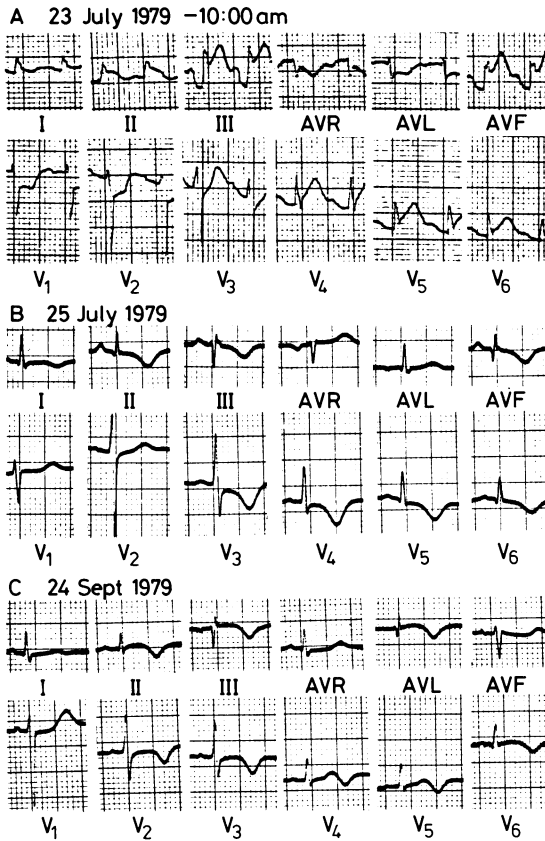


Fig. 1 Electrocardiograms (A) four hours after the episode; (B) on the third hospital day; (C) two months after the episode.

reduction in haematocrit from 42% on admission to 31% on the fifth day in hospital. The haemoglobin changes were similar. The platelet count from a low rate on admission returned to normal levels on the eleventh hospital day. White blood cell count showed an increase (14 500 per  $\text{mm}^3$ ) only on the third day, with 75% polymorphonucleocytes. Serum enzymes were raised on admission and they decreased to normal values on the sixth day except for lactic dehydrogenase which did so one day later. Serum bilirubin, total, direct, and indirect, showed a slight rise on admission and returned to normal levels after the third day. The sedimentation rate was within normal limits on admission and was moderately increased after the sixth day. More detailed haematological studies on the fourth day showed 3.7% reticulocytes, serum iron 14.7  $\text{mmol/l}$ . Coombs test was negative. Prothrombin time (Quick's method) increased to 21 s (control 12.9 s), thrombin time to 17.1 s (control 12.1 s), Lee-White's test under heparin administration was prolonged to 28 s, partial thromboplastic time 69.8 s (control 63.3 s), and fibrinogen 5.16 g/l. Urinalyses showed albuminuria throughout the hospital stay and haemoglobinuria between the sixth and the ninth day. Liver function tests, blood sugar, blood urea nitrogen, electrolytes, serum protein electrophoresis, immunoglobulins, and haptoglobulins were within normal limits. Chest x-ray film and fundoscopic examination were normal.

During the 19 days in hospital the patient showed slight improvement in her neurological functions and satisfactory progress of her heart condition.

Two months later she was readmitted for additional evaluation. Hemiparesis had subsided, and aphasia

Table Haematological and biochemical data presenting changes

Date (1979)	24 July	25 July	27 July	28 July	4 August	9 August
Haematocrit (%)	42	36	31	31	32	34
Haemoglobin (g/100 ml)	14.3	11.1	10.1	10.1	10.8	11.5
Platelets ( $\text{mm}^3$ )	60 000	60 000	67 000	—	200 000	—
Reticulocytes (%)	—	2.4	3.7	—	—	—
White blood cells (per $\text{mm}^3$ )	9 000	14 500	8 350	7800	7 500	8000
Sedimentation rate (1st hour)	4	—	—	35	50	15
Lee-White's time (s)	28*	26*	—	—	—	—
Prothrombin time (s)	—	17 (12.1)	21 (12.9)	—	12.9 (12.8)	—
Thrombin time (s)	—	—	17.1 (12.1)	—	12.3 (12.2)	—
Partial thromboplastic time (s)	—	—	69.8 (63.3)	—	63.0 (63.2)	—
Fibrinogen (g/l)	—	—	5.16	—	—	—
Serum bilirubin (%)	1.0	—	0.9	0.8	0.4	—
Direct	0.4	—	0.4	0.3	0.2	—
Indirect	0.6	—	0.5	0.5	0.2	—
Serum enzymes (units)						
AST	122	132	40	20	10	—
AAT	47	68	62	28	27	—
LDH	630	—	920	200	—	—
CK	402	—	49	—	—	—

\*Heparin 5000 units intravenously every six hours, —, no data available. Numbers in parentheses denote control values.

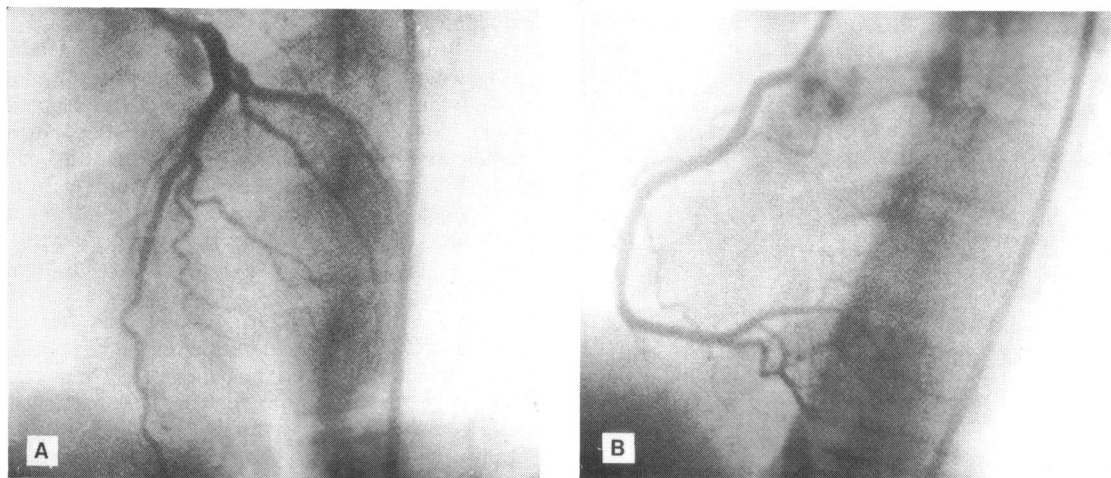


Fig. 2 Coronary arteriogram. (A) left coronary artery; (B) right coronary artery.

showed improvement. The electrocardiogram showed the picture of an old inferior wall myocardial infarction (Fig. 1C). A treadmill exercise test was performed at various levels and showed no abnormalities. The patient underwent cardiac catheterisation and coronary angiography. Catheterisation disclosed normal pressures, and coronary arteriography showed both coronary arteries and their branches to be patent throughout (Fig. 2A, B). The left ventriculogram showed decreased contractility of the posterior and inferior wall.

### Discussion

As to the mechanism responsible for the myocardial infarction and the cerebrovascular damage in this patient one should consider the following factors: (a) direct toxic effect of the venom,<sup>2</sup> (b) shock,<sup>1</sup> (c) arterial obstruction occurring from ensuing thrombosis<sup>3</sup> or haemorrhage.<sup>4</sup>

The course of events in the myocardial incident suggests a direct toxic effect of the venom on myocardial tissue. Chest pain preceded the shock while the electrocardiographic evidence of acute myocardial ischaemia and ventricular irritability persisted long after recovery from shock. Specifically, shock might have been the result of the venom's cardiotoxic effect which, besides damaging the myocardium, seems to have triggered the initially observed paroxysmal atrial tachycardia. A direct toxic effect of cobra venom on the cat's myocardial tissue has been described by Kellaway and Trethewie<sup>6</sup> and a similar effect of viper venom has been suggested by Sarangi *et al.*<sup>4</sup>

Alternatively, it seems reasonable to suppose that prolonged hypotension along with haemolysis and a high fibrinogen could have contributed to the

development of myocardial infarction. The absence of major arterial occlusion on coronary angiography performed about two months after the episode does not rule out the possibility of major thrombosis that might have cleared by that time, nor that multiple small vessel occlusions might have been present.

On the other hand, the brain damage observed almost four days after the viper bite was unlikely to be the result of the venom, nor could it be related to shock which was present in the very early stages only. It is, however, possible that despite intermittent heparin administration the stroke could have been the result of an embolism from thrombus forming upon the endocardial surface of the infarcted myocardium.

But the gradual disturbance of the patient's haematological picture suggests that this relatively late complication might also have been the result of a thrombotic process. There is some doubt as to the effects of viper venom. Bhargava *et al.*<sup>3</sup> proposed that deficiency of multiple coagulation factors as well as the extent of such a deficiency is highly presumptive of disseminated intravascular coagulation in cases of snakebite by the viper *Echis carinatus*. According to Sarangi *et al.*,<sup>4</sup> however, haemorrhagic manifestations in viper bite cannot be solely a result of consumptive coagulopathy, but could be attributed to toxic vasculitis caused by a non-enzymatic fraction of the viper venom that produces endothelial damage.

On the whole, the time sequence of the clinical and laboratory findings in this case are strongly suggestive of an immediate toxic effect of the venom upon the patient's heart and of a subsequent damage to the brain by disseminated intravascular coagulation of its vascular bed. A final possibility is that the brain damage was the result of haemorrhage. The laboratory findings would not suggest that heparin was in any

way responsible, but the necropsy findings by the authors previously quoted<sup>5</sup> indicate that the possibility of intra- or extracerebral haemorrhage directly resulting from constituents of the venom cannot be discounted.

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