

## QT prolongation after ampicillin anaphylaxis

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**SUMMARY** Tall T waves and pronounced prolongation of the QT interval developed 24 hours after an apparently complete recovery from an acute anaphylactic reaction to oral ampicillin in a previously healthy woman of 29. These electrocardiographic abnormalities gradually subsided over five days. The prolongation of the QT interval has not previously been reported after anaphylaxis.

Acute anaphylactic reactions are sudden, frightening, and potentially lethal responses to various allergens. Very often they are provoked by drugs, most commonly penicillin or agents used for radiological investigations. Electrocardiographic changes occurring in association with anaphylaxis have been reported by several observers. These took the form of ST segment depression or elevation, T wave changes, arrhythmias, or conduction disturbances. The fact that such changes occur is not generally appreciated, and there are only a few published reports. We describe a case of severe anaphylaxis after oral ampicillin in which there were tall T waves and pronounced prolongation of QT interval—electrocardiographic findings that have not previously been reported in association with anaphylaxis.

### Case report

A 29 year old previously healthy senior house officer collapsed 30 minutes after taking a first dose of 250 mg of oral ampicillin for an upper respiratory tract infection. She was pale and clammy with an unrecordable blood pressure and had a bowel evacuation during the episode. She quickly recovered after immediate resuscitative measures, including intravenous hydrocortisone 200 mg and adrenaline 1 ml 1:1000, and oxygen inhalation. Fifteen minutes later she again became hypotensive (systolic blood pressure 40 mm Hg) and drowsy but she responded to hydrocortisone and adrenaline. Physical examination was unremarkable and two 12 lead electrocardiograms taken that day were normal.

Twenty four hours later, however, when she had apparently completely recovered, her electrocardiogram showed generalised tall peaked T waves and pronounced prolongation of the QT interval by 41% (QT<sub>c</sub> 0.58 s, upper limit of normal for age and sex 0.41 s (Figure)). Serum sodium, potassium, and calcium and renal function tests were all normal. There was no evidence of myocardial necrosis from cardiac enzyme estimations, and an echocardiogram and a ventilation perfusion lung scan were also normal. Paired serum samples were taken immediately after the episode and two weeks later and showed no evidence of recent viral infection. The electrocardiographic changes lasted five days and gradually subsided. She was treated with prednisolone 30 mg per day and discharged on the eighth day with no clinical or electrocardiographic abnormalities. Further inquiries showed that she had collapsed one year before after taking a single dose of ampicillin for urinary symptoms. She had recovered spontaneously and no specific diagnosis had been made at that time.

### Discussion

Anaphylactic reactions may occur after parenteral administration of drugs and they have also been reported after oral intake.<sup>1</sup> There are two main clinical presentations of anaphylaxis: (a) respiratory with bronchospasm or laryngeal oedema or both; and (b) cardiovascular with collapse and shock. Diffuse urticaria may be associated with both, and both presentations can be rapidly fatal.

The incidence of electrocardiographic changes after anaphylaxis is not known exactly, but such changes seem to be more common in patients presenting with cardiovascular collapse.<sup>2</sup> Bernreiter first reported an elderly patient who developed tran-

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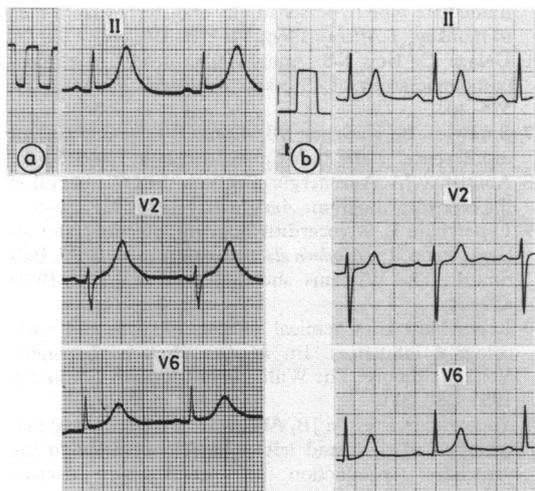


Figure Electrocardiograms (a) 24 h after anaphylaxis ( $QT_c = 0.58$  s) and (b) 10 days after anaphylaxis ( $QT_c = 0.41$  s).

sient atrial fibrillation, intraventricular conduction disturbances, and T wave changes after acute anaphylaxis.<sup>3</sup> Fourteen cases of anaphylaxis were reviewed by Booth and Patterson, and electrocardiographic changes were seen in six.<sup>4</sup> These were variable and included ST segment elevation and depression, nodal rhythm, and atrial fibrillation. The prolonged QT interval seen in our patient who survived severe anaphylaxis has not been described before.

The pathological basis of these electrocardiographic changes is uncertain. Electrocardiographic changes developed in eight out of nine monkeys in which anaphylaxis had been experimentally induced.<sup>5</sup> Again there was no characteristic pattern. Distinct myocardial necrosis was seen in these animals at necropsy. No evidence of such lesions was found by Delage and Irely in a review of necropsies of patients who died of anaphylaxis.<sup>6</sup> Booth and Patterson postulate the following mechanisms as being responsible for the electrocardiographic changes—a direct antigen-antibody myocardial reaction, effect of anaphylactic mediators or sympathomimetics administered as treatment, anoxia, pre-existing heart disease, or a combination of these factors.<sup>4</sup>

There was no other obvious cause other than anaphylaxis to account for the electrocardiographic changes in our patient. Prolonged QT intervals have been associated with myocardial ischaemia, electrolyte disturbances, drugs, and at times have been congenital or idiopathic. Serial measurements of cardiac enzymes in plasma samples did not suggest any myo-

cardial necrosis in the present case and there were no biochemical disturbances, such as hypocalcaemia, that are known to prolong the QT.<sup>7</sup> Neither ampicillin nor hydrocortisone are known to affect electrocardiograms. Adrenaline altered QT intervals in experiments in dogs. Abildskov reported that rapid intravenous injection of adrenaline led to transient QT prolongation (for 12 seconds) followed by reduction in QT interval (2 minutes).<sup>8</sup> The persistent change was a shortened QT interval which was also seen with slow infusion of adrenaline. Thus it is unlikely that the prolonged QT interval seen in our patient was caused by the adrenaline used for resuscitation.

The aetiological factors responsible for these changes are debatable. QRS prolongation and other changes have been described in animals in experimental anaphylactic shock.<sup>9</sup> The QRS prolongation was partly attributed to vagal action, because it was less intense after vagotomy, although QRS was prolonged to some extent in heart and lung preparations. We saw no change in QRS in our patient. Histamine released during allergic reactions can produce electrocardiographic changes in human subjects. Intravenous injection of 4–22  $\mu\text{g}/\text{min}$  of histamine caused tachycardia, depression or inversion of T waves, and an increase in QT duration in some experimental subjects.<sup>10</sup> These changes were thought to be due to the sympathetic response to histamine-induced hypotension because they could be prevented by previous administration of phenylephrine hydrochloride. The influence of sympathetic activity on the QT interval has been demonstrated by studies of stellate ganglion stimulation. Yanowitz *et al* showed that left stellate stimulation in open chest dogs increased T wave amplitude and prolonged QT interval.<sup>11</sup> In the same study it was shown that right stellectomy produced similar electrocardiographic changes and the authors suggested that these neurogenic electrocardiographic abnormalities were the result of an imbalance between right and left sympathetic tone. Neurogenic factors may be responsible for the QT prolongation and T wave changes seen with cerebrovascular accidents.<sup>12</sup> The period of syncope in our patient, however, was not immediately accompanied by electrocardiographic changes, which came later. Thus the electrocardiographic changes demonstrated in this patient may have been secondary to histamine release during the anaphylaxis or due to a pronounced increase in sympathetic activity as a result of hypotension.

A prolonged QT interval suggests an alteration in myocardial repolarisation and has been associated with serious rhythm disturbances and sudden death in various conditions. No arrhythmias were recorded

in our patient who was closely monitored, but it is possible that a proportion of sudden deaths in anaphylaxis without respiratory manifestations could be due to serious rhythm disturbances related to QT prolongation. Routine electrocardiographic monitoring of the patients surviving immediate anaphylaxis would help in identifying electrocardiographic and rhythm disturbances.

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## Notice

### British Cardiac Society

The Annual General Meeting for 1986 will take place in York on 2 and 3 April 1986, and the closing date for receipt of abstracts was 2 January 1986.

The Autumn Meeting will be held at the Wembley Conference Centre, London, on 25 to 27 November 1986, and the closing date for receipt of abstracts will be 1 August 1986.

## Correction

Asynchronous left ventricular wall motion early after coronary thrombosis *D Gibson, H Mehmel, F Schwarz, K Li, W Kübler* — We apologise to Dr Helmuth Mehmel for the misspelling of his name in our January issue (page 4).