Case Report

Torsades de pointes during intravenous pentamidine isethionate therapy

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Postural hypotension, bradycardia and ventricular tachycardia are the only recognized cardiovascular side effects of pentamidine.[1,2] We report a case in which the Q–T interval became prolonged and torsades de pointes developed in a patient with acquired immune deficiency syndrome (AIDS) who was receiving intravenous pentamidine therapy for *Pneumocystis carinii* pneumonia.

Case report

A 29-year-old man who had AIDS presented with dry cough, dyspnea, fever, chills and malaise. The serum concentrations of sodium, potassium and creatinine were normal. The electrocardiogram (ECG) showed sinus tachycardia (heart rate 110 beats/min) and a corrected Q–T interval of 0.43 (normally 0.44 or fewer) seconds (Fig. 1A).[3] A brush specimen obtained by means of fibreoptic bronchoscopy showed *P. carinii*. Pentamidine isethionate, 4 mg/kg daily, was administered intravenously in 500 ml of 5% dextrose and water over 2 hours.

Over the next 2 days the patient became more dyspneic and remained febrile. Hydrocortisone, 250 mg intravenously, was given every 6 hours. The dyspnea improved but only temporarily, and mechanical ventilation was required 5 days later. ECGs at that time showed a normal sinus rhythm but a prolonged Q–T interval (0.55 seconds). The serum levels of magnesium and potassium were

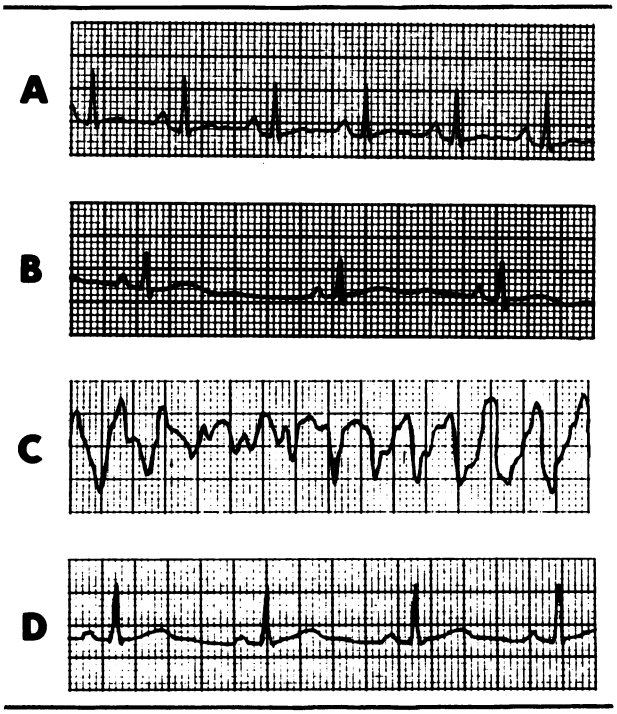

Fig. 1 — Lead II electrocardiogram (ECG). (A) ECG on admission to hospital of patient with acquired immune deficiency syndrome who presented with *Pneumocystis carinii* pneumonia. (B) Prolonged Q–T interval, prominent U waves and sinus bradycardia after 8 days of pentamidine isethionate therapy. (C) Torsades de pointes after 13 days of therapy. (D) ECG 1 year after therapy stopped.

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0.79 (normally 0.70 to 1.05) mmol/L and 3.1 (normally 3.2 to 4.5) mmol/L respectively. The serum potassium concentration increased to 4.8 mmol/L after intravenous potassium supplementation. However, an ECG showed persistent prolongation of the Q-T interval, prominent U waves and sinus bradycardia (heart rate 55 beats/min) (Fig. 1B).

Two days later the patient's condition improved, and mechanical ventilation was stopped. The dose of hydrocortisone was decreased to 100 mg intravenously every 6 hours. Three days later the patient had two episodes of syncope while lying down. The ECG showed a sinus rhythm of 60 beats/min, a prolonged Q-T interval of 0.60 seconds and intermittent polymorphic ventricular tachycardia in a torsades-de-pointes pattern (Fig. 1C). The serum potassium concentration was 2.8 mmol/L.

A lidocaine bolus and infusion therapy (2 mg/min) was started. A normal serum potassium level was reached within 4 hours with the use of supplements and was maintained for the rest of the patient's hospital stay. However, the bradycardia and the prolonged Q-T interval (0.45 seconds) persisted. There were two more transient episodes of torsades de pointes. The next day isoproterenol was infused at a rate of up to 8 mg/min to keep the heart rate above 90 beats/min. Magnesium sulfate, 1 g over 2 hours, was also infused. The patient refused the insertion of a pacemaker.

Despite this therapy, over the next 2 days the patient had three more episodes of torsades de pointes, which reverted to normal sinus rhythm after chest thumps. The pentamidine was replaced with trimethoprim-sulfamethoxazole, 15 mg/kg daily given intravenously. The isoproterenol and lidocaine therapies were gradually stopped over 24 hours. The resting heart rate remained greater than 90 beats/min, and there were no more episodes of ventricular dysrhythmia. The Q-T interval was 0.43 seconds before discharge, 22 days after admission.

One year later the patient was asymptomatic, and the Q-T interval was still 0.43 seconds (Fig. 1D).

Comments

This is the second report of torsades de pointes associated with pentamidine therapy in a patient with AIDS. The first described two patients, in whom the pentamidine therapy lasted 20 and 13 days respectively.[4] In the patient we have described, the Q-T interval was normal on admission but became prolonged during pentamidine therapy and was associated with bradycardia and repeated episodes of torsades de pointes. Prolongation of the Q-T interval after the start of pentamidine therapy also occurred in the cases described by Wharton, Demopulos and Goldschlager.[4] It is impossible to implicate pentamidine as the sole cause of torsades de pointes in a patient who was recovering from life-threatening pneumonia, had received other medications and had had abnormal electrolyte levels. However, the report of Wharton and colleagues confirms that pentamidine is probably a major cause of bradycardia and life-threatening polymorphous ventricular tachycardia. This association may explain previously reported cases of sudden death in patients receiving the drug.[5]

Pentamidine was found to cause severe bradycardia, hypotension and cardiac autonomic dysfunction in another patient.[2] Bradycardia may precipitate torsades de pointes by increasing the likelihood of a premature ventricular action potential during repolarization of the ventricle;[6] this together with the prolonged Q-T interval may have been an exacerbating cause in the patient we have described. Pentamidine is structurally similar to procainamide and prenylamine, both of which can induce torsades de pointes.[5]

The patient described here was also receiving intravenous hydrocortisone therapy for the *P. carinii* pneumonia.[7] Hydrocortisone has been found to cause severe hypokalemia, which has been implicated in the development of torsades de pointes.[8] However, hydrocortisone does not affect the Q-T interval and does not produce dysrhythmias in the absence of hypokalemia.

We believe that ECGs should be obtained regularly in patients receiving intravenous pentamidine therapy and that an alternative form of therapy should be considered if the Q-T interval becomes prolonged or bradycardia develops.

References

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