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A Case of Torsade de Pointes Associated with Hypopituitarism due to Hemorrhagic Fever with Renal Syndrome

We describe a 51-yr-old man presenting with syncope due to torsade de pointes. The torsade de pointes was refractory to conventional medical therapy, including infusion of isoproterenol, $MgSO_4$, potassium, lidocaine, and amiodarone. His past history, physical findings, and hormone study confirmed that QT prolongation was caused by anterior hypopituitarism that developed as a sequela of hemorrhagic fever with renal syndrome. The long QT interval with deep inverted T wave was completely normalized 4 weeks after starting steroid and thyroid hormone replacement. Hormonal disorders should be considered as a cause of torsade de pointes, because this life-threatening arrhythmia can be treated by replacing the missing hormone.

Key Words : *Torsades de Pointes; Hypopituitarism; Hemorrhagic Fever with Renal Syndrome*

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INTRODUCTION

Hemorrhagic fever with renal syndrome (HFRS) is caused by Hantaan or Seoul virus (1). At autopsy, the anterior lobe of the hypophysis shows coagulative necrosis in 58 to 63% of patients in the hypotensive phase, and in almost all patients in the oliguric phase (2, 3). Nevertheless, clinically overt anterior hypopituitarism is rare, reportedly occurring in only about 2% of patients (4-6).

QT prolongation has various causes, including drug toxicity, electrolyte abnormality, myocarditis, cerebrovascular disease, chromosomal abnormalities of cardiac ion channels, and hormonal disorders, such as hypopituitarism, hypothyroidism, and adrenal insufficiency (7-11). It is well known that QT prolongation can be associated with polymorphic ventricular tachycardia (VT), which is usually resistant to antiarrhythmic drug therapy.

We experienced a case of torsade de pointes associated with anterior hypopituitarism that developed as a sequela of HFRS. We hypothesize that torsade de pointes may be caused by hypopituitarism and hypopituitarism by HFRS.

CASE REPORT

A 51-yr-old man presented with recurrent syncope associated with polymorphic ventricular tachycardia (VT) (Fig. 1). His past history was remarkable. Thirteen years earlier, he was treated for hemorrhagic fever with renal syndrome complicated with acute renal failure. Afterwards, his libido and axillary and pubic hair gradually decreased. He had no history of other medications.

VT developed repeatedly after DC cardioversion or spontaneous conversion in spite of antiarrhythmic drugs, including lidocaine and amiodarone, in addition to replenishing potassium and magnesium. Magnesium was given at 6 g/day after loading with 1 g for 1 day. During normal sinus rhythm, the rate was 65/min and QTc was 620 msec (Fig. 2).

To initially increase the heart rate, isoproterenol was continuously administered at a rate of 2-4 μg/min. Then, a temporary pacemaker was inserted in the right ventricle apex via the right subclavian vein. After initiating ventricular pacing at a rate of 80 bpm, no further VT developed. Two-dimensional echocardiography showed normal

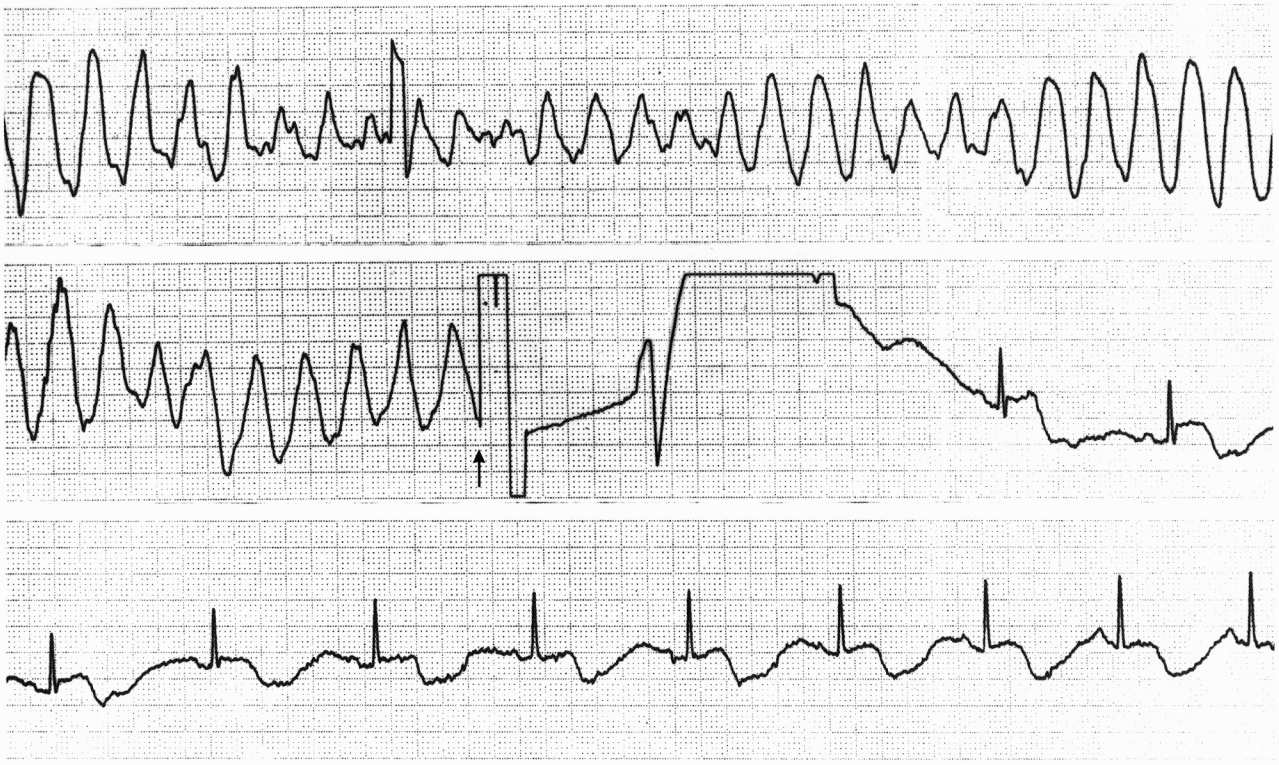

Fig. 1. Documented sustained polymorphic ventricular tachycardia with DC cardioversion (↑) in rhythm strip electrocardiogram.

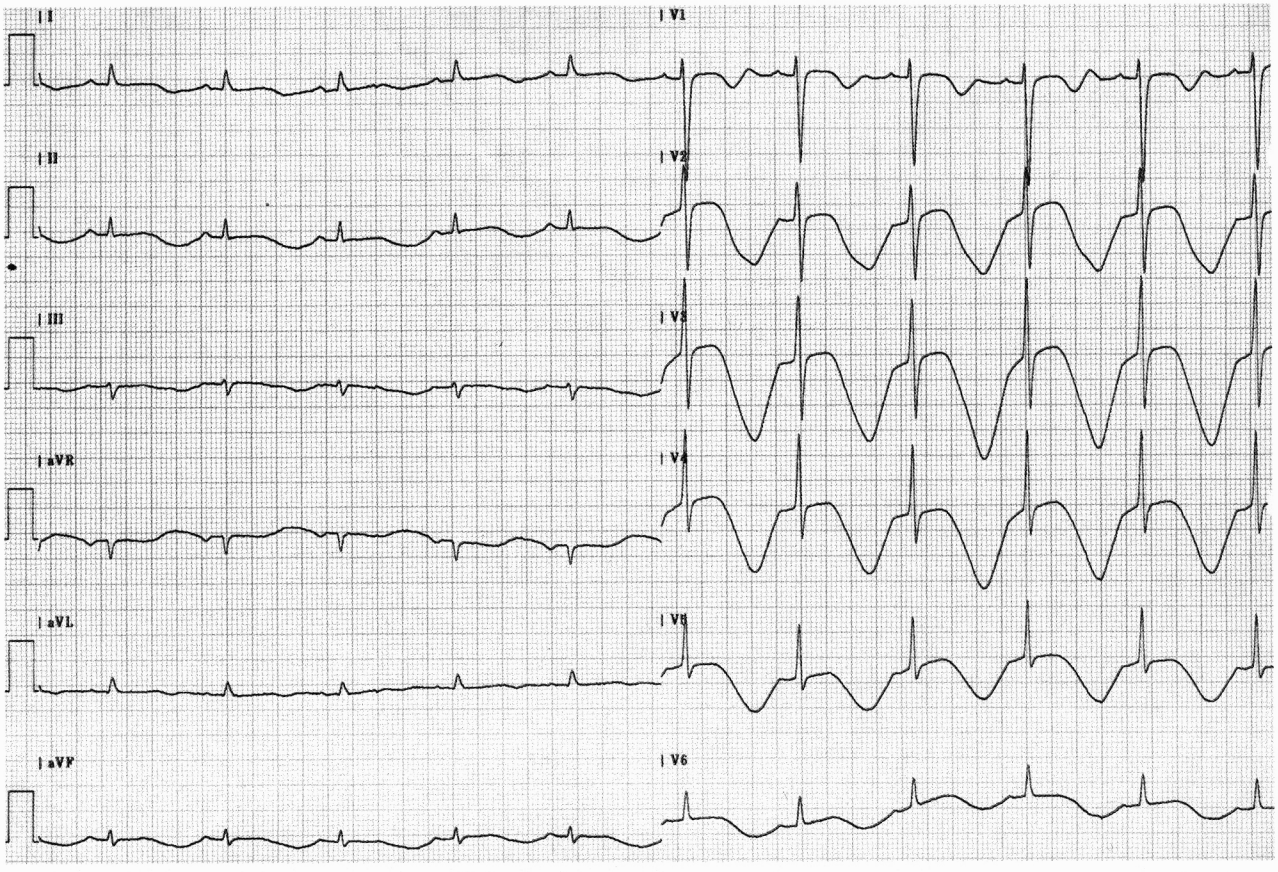

Fig. 2. Twelve-lead electrocardiogram on admission shows long QT intervals and deep inverted T waves.

cardiac chambers and ventricular wall motion. A treadmill test and coronary angiography were not performed. Laboratory examination revealed that the serum potassium was 4.1 mEq/L, magnesium 2.3 mEq/L, T4 3.8 μg/dL, free T4 0.22 μg/dL, T3 25 ng/dL, TSH 0.64 μU/mL, cortisol 4.1 μg/dL, ACTH 28.2 pg/mL, prolactin 1.0 ng/mL, LH 0.5 mIU/mL, FSH 1.7 mIU/mL, and GH 0.1 μg/L. The combined pituitary stimulation test using TRH 400 μg, LHRH 100 μg, and regular insulin 6 U suggested primary hypopituitarism (Table 1). Steroid (Deltacortef®, 7.5 mg) and thyroid hormone (Synthyroid®, 150 μg) replacement therapy was started 3 days after admission. Four weeks after steroid and thyroid hormone replacement therapy, T4 was 14.1 μg/dL, free T4 1.78 μg/dL, T3 74 ng/dL, TSH 0.16 μU/mL. After treatment, the QTc interval on the 12-lead electrocardiogram decreased gradually and was 396 msec 4 weeks later (Table 2, Fig. 3).

Table 1. Basal and combined pituitary stimulation test

	Basal	15 min	30 min	60 min
Blood sugar (mg/dL)	115	95	25	425
Adrenocorticotropic hormone (pg/mL)	28.2	21.0		24.6
Prolactin (ng/mL)	1.0	1.0		
Thyrotropin (μIU/mL)	0.64		0.86	
Lutropin (mIU/mL)	0.5		1.0	
Follitropin (mIU/mL)	1.7		2.0	
Cortisol (μg/dL)	4.1			3.4
Growth hormone (ng/mL)	0.1			0.1

Table 2. Sequential changes of QTc interval and value of thyroid hormone after synthyroid® 150 μg replacement

	On admission	1 weeks later	2 weeks later	3 weeks later	4 weeks later
T3 (ng/dL)	3.3	25	25	44	74
T4 (μg/dL)	3.9	3.8	4.7	7.5	14.1
FT4 (μg/dL)	0.22	0.22	0.31	0.48	1.78
TSH (μIU/mL)	1.12	0.85	1.05	1.06	0.16
QTc (msec)	620	480	470	480	396

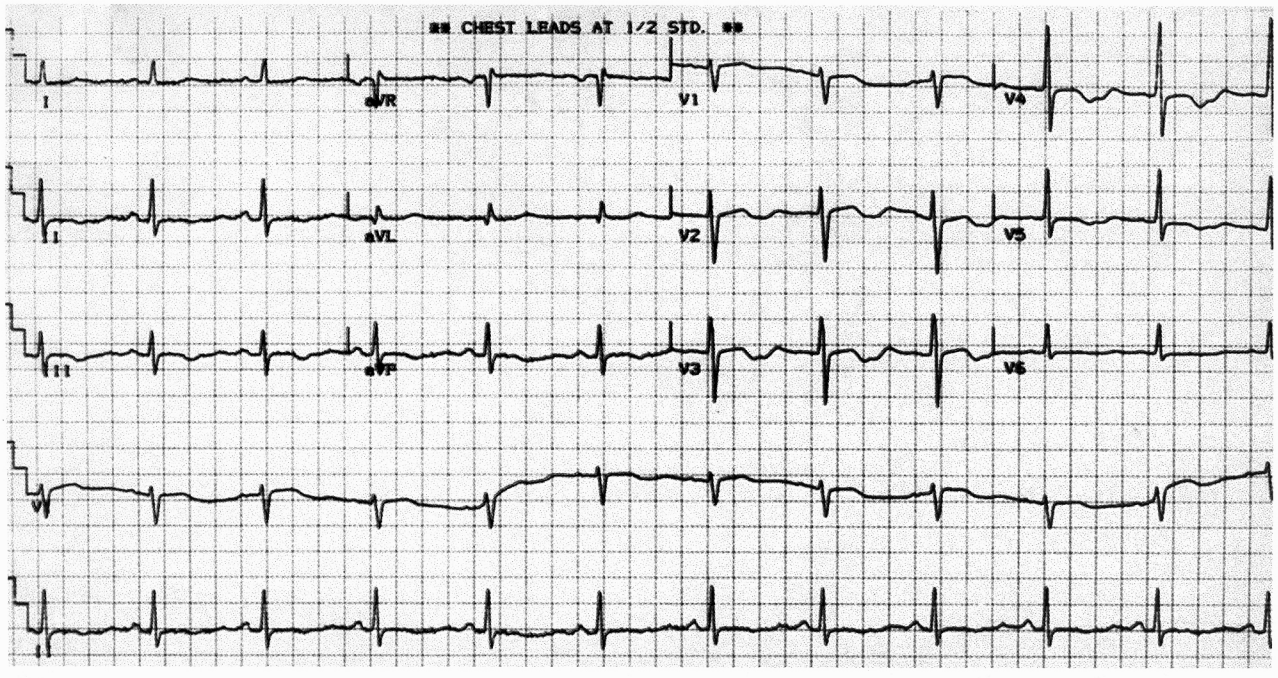

Fig. 3. Four weeks after starting steroid and thyroid replacement therapy, twelve-lead electrocardiogram demonstrates normal QT intervals.

DISCUSSION

We describe a case of torsade de pointes associated with anterior hypopituitarism that developed as a sequela of HFRS.

Torsade de pointes may occur as a consequence of congenital prolongation of the QT interval or may be associated with acquired QT prolongation, resulting from electrolyte disturbances, the use of various antiarrhythmic drugs, phenothiazines, or tricyclic antidepressants, liquid protein diets, intracranial events, bradyarrhythmias, and hormonal disorders.

To the best of our knowledge, this is the only report of an association between torsade de pointes and hypopituitarism that developed as a sequela of HFRS. Previous reports described cases of hypothyroidism with VT (7-9). Another report described a case of Sheehan's syndrome with hypomagnesemia and polymorphic VT (10).

Electrocardiographic abnormalities commonly associated with hypopituitarism are low QRS voltage, ST-segment depression, inverted T waves, and a prolonged QT interval (12, 13). Although the mechanism remains unclear, glucocorticoid deficiency, an intracellular-extracellular electrolyte imbalance of myocytes, and histopathological changes in the myocardium are thought to play a role in this disorder. Recently, it was reported that glucocorticoids up-regulate Kv 1.5 K^+ channel gene expression in the rat ventricle (14).

In our patient, QT interval prolongation and sinus bradycardia secondary to anterior hypopituitarism caused the proarrhythmic condition. After steroid and thyroid hormone replacement therapy, the QT interval was normalized and no further VT developed.

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