Panhypopituitarism, hyponatremia and long QT interval syndrome: a case report

Mohammed F. Abdul-Mohsen, DM, MSc, MD
Ali I. Al-Sultan, MD FRCP

Abstract Acquired prolongation of QT interval in the conventional electrocardiogram has been reported in many medical problems including coronary artery disease, mitral valve prolapse, drug idiosyncracies especially antiarrhythmic and psychotropic drugs, electrolyte disturbances and endocrine abnormalities as in hypothyroidism. However, there is a body of evidence in the literature indicating that this problem is relatively uncommon in simple cases of hypothyroidism. We report a 60 year old Saudi patient who was transferred from the regular ward to the Coronary Care Unit (CCU) with severe hyponatremia, clinical manifestation of panhypopituitarism and prolonged QTc (730 ms). She developed a short paroxysm of Torsades-de-Pointes ventricular tachycardia early after the transfer to the CCU. Panhypopituitarism was documented through specific endocrinological investigations. The prolongation of QT interval and the hyponatremia were normalized shortly after the initiation of hormonal replacement therapy. We feel that adrenocortical insufficiency as a part of panhypopituitarism is a probable contributory factor in the development of this electrophysiological abnormality.

Saudi Medical Journal 1996; Vol. 17 (4): 531-535

KEYWORDS: Torsades-de-pointes ventricular tachycardia, adrenocortical insufficiency and panhypopituitarism.

The prolonged QT interval syndrome is a functional abnormality, probably associated with neurogenic influences, that may cause lethal ventricular arrhythmia.1 Two hereditary varieties have been reported: the Jarvel and Lange-Nielsen syndrome with autosomal recessive inheritance and associated with congenital deafness,2 and the Romano Ward syndrome in which hearing is normal but inherited as autosomal dominant.3 Some of these patients are susceptible to ventricular-arrhythmias, particularly the Torsades-de-Pointes form of ventricular tachycardia.

The acquired form of the long Q-T interval syndrome has been reported in coronary artery disease, mitral valve prolapse, electrolyte disturbance, endocrine abnormalities like hypothyroidism and adrenocortical insufficiency4 and as drug idiosyncracies, especially with some anti-arrhythmic and psychotropic drugs, antimony compounds and toxic doses of chloroquine. Acquired long Q-T syndrome usually carries a risk of serious arrhythmias and sudden cardiac death (SCD). In both acquired and hereditary forms, Torsades-de-Pointes ventricular tachycardia is usually the specific arrhythmia that triggers or degenerates into lethal ventricular fibrillation.

This report describes a case of acquired long Q-T interval syndrome, Torsades-de-Pointes ventricular tachycardia and life threatening hyponatremia related to panhypopituitarism.

Case Report A 60-year-old lady was transferred to the Coronary Care Unit (CCU) from the Female Medical Ward with severe dyspnea and acute confusion. The transfer diagnosis was unstable angina to rule out acute Non-Q-Wave myocardial infarction. She had presented to the Emergency Department two days prior to transfer to CCU with acute confusion noticed by the family one hour earlier. She was found to be hypoglycemic (venous plasma glucose 44 mg/dl) but became alert once the hypoglycemia was corrected. However, she continued to complain of excessive weakness and easy fatigability. There was no fever.

From the Department of Internal Medicine, King Faisal University, King Fahd Hospital of the University, Al Khobar, Saudi Arabia (Abdul-Mohsen, Al-Sultan).

Received January 1995. Accepted for publication in final form November 1995

Address correspondence and reprint request to: Dr. Mohammed Fakhry, P.O. Box 40032, Al Khobar 31952, Saudi Arabia.
or convulsions and no history of previous angina pectoris or use of anti-arrhythmic drugs. On examination, she was cachectic, pale, mildly cyanosed but not jaundiced. She was sweaty, confused, severely ill and in respiratory distress with a respiratory rate of 34/minute. Heart rate was 110/minute and supine blood pressure was 120/70. Her rectal temperature was 35.5°C, jugular venous pressure (JVP) was 11 cm. water. Precordial examination showed no signs of cardiomegaly, but there was a left ventricular third heart sound gallop and no murmurs. There were fine bilateral basal crepitations in both lung fields. The liver span was 13 cm. No pre-sacral or pedal edema. The ankle and knee jerks showed a delayed relaxation phase.

**Methods** Serum cortisol, thyroxine (T4), free thyroxine (free T4), total triiodothyronine (T3) and thyroid stimulating hormone (TSH) were measured by specific fluorometric polarization immunoassays (Imx). Prolactin (PRL), leutinizing hormone (LH), follicle stimulating hormone (FSH), estradiol and adrenocorticotropic hormone (ACTH) were measured in duplicate by specific RIAs. All samples were stored at -20°C until the time of assay.

**Results** Upon transfer to the CCU, random blood sugar was 132 mg/dl. Serum sodium was 114 mEq/L, chloride 95 mEq/L, potassium 5.1 mEq/L, calcium 8.6 mg/dl, magnesium 2.1 mEq/L, bicarbonate 18 mEq/L, total proteins 6.7 gm/dl, albumin 3.3 gm/dl and hepatic enzymes were normal. The measured serum osmolality was 246 mosm/kg and urine osmolality was 370 mosm/L. Spot urine before starting diuretic therapy showed a sodium of 43 mEq/L. Serum creatine phosphokinase (CPK) and lactic dehydrogenase (LDH) isoenzymes were normal. The initial 12-lead conventional electrocardiogram showed sinus rhythm at a rate of 70 beats/minute, diffuse T-wave inversion and prolongation of Q-T and QTc intervals, 670 and 730 ms respectively (Fig. 1). One hour later, she had an episode of Torsades-de-Points ventricular tachycardia lasting for about 7 seconds and terminated spontaneously (Fig. 2). The chest radiogram showed no cardiomegaly but radiological evidence of pulmonary edema.

![A twelve lead electrocardiogram showing diffuse and bizarre T-wave inversion, prolongation of QT and QTc. QTc = 730 ms.](image-url)
Echocardiography with color coded doppler studies showed trivial mitral regurgitation and aortic valve sclerosis with trivial aortic regurgitation. The left ventricular size and contractile function were normal. The patient was found to have hypothyroidism with total serum T4 of 4.1 ug/dl (Normal 4.5-12), serum free T4 of 0.62 ng/dl (normal 0.71-1.85), total serum T3 of 0.9 ng/dl (normal 0.81-2.0), serum TSH level of 3.9 mIU/ml (normal 0.4-5.0). She was also found to have central adenocortical insufficiency with morning cortisol level of 3.7 ug/dl (normal 8-28) and short ACTH stimulation test (cosyntropin, 250 ug intravenously) performed at 3:20 pm showed a baseline serum ACTH level of 13.2 pg/ml (normal 0-37), and cortisol level of 1.5 ug/dl, 4.9 ug/dl and 6 ug/dl at 0, 30 and 60 minutes respectively. Other hormonal profile revealed serum FSH level of 6.3 mIU/ml (normal 18-153), LH of 2.1 mIU/ml (normal 16-64), PRL of 10.8 ng/ml (normal 0.33-27.3) and estradiol of less than 2 pg/ml (normal 60-110). Magnetic resonance imaging (MRI) of the brain and pituitary gland revealed empty sella turcica.

**Follow-up** The pulmonary edema resolved in a few hours in response to small doses of furosemide (total of 40 mg intravenously). No vasodilator therapy was required. The replacement therapy in the form of L-thyroxine (50 ug initially then 100 ug daily) and hydrocortisone (100 mg Q6H initially then Q8H till correction of QT interval, with subsequent gradual reduction to maintenance dose and switching to prednisone) was initiated within 12 hours of patient’s transfer to the CCU. Severe hyponatremia was corrected within 24 hours and the prolongation of QTc interval was totally normalized within 4 days from the initiation of replacement therapy.

**Discussion** Our patient had central adenocortical insufficiency manifested by hypoglycemia, low serum cortisol, blunted cortisol response to ACTH stimulation and low basal plasma ACTH. Her serum gonadotropins levels were low for a menopausal woman. The diagnosis of central hypothyroidism during acute illness is at times difficult. Pure thyroid hormones binding abnormality and sick euthyroid are less likely in the presence of low free T4 and normal T3, respectively. Low free T4 and inappropriately normal TSH are highly suggestive of central hypothyroidism. The hypothyroid features found clinically confirm the diagnosis. Furthermore, the presence of a deficient hypothalamic, pituitary, adrenal, gonadal and thyroid axis is in keeping with hypopituitarism. The majority of patients with primary empty sella have normal pituitary reserve, but the association with hypopituitarism had been reported. The low serum osmolality, inappropriately high urinary sodium and osmolality suggest that the hyponatremia was antidiuretic hormone (ADH) mediated. The possible mechanism is decreased clearance of ADH due to hypothyroidism and increased release of ADH due to loss of cortisol inhibition.

This patient developed Torsades-de-Pointes ventricular tachycardia complicating prolonged QTc interval (730 ms). Significant QT prolongation and recurrent Torsades-de-Pointes ventricular tachycardia were described in a case of panhypopituitarism. It was attributed to hypothyroidism, whereas in another study of 14 biochemically hypothyroid patients they found that the mean (± SD) QTc interval measured 434 ± 33 ms and the QTc interval was more than 450 ms in only 3 patients. In a third retrospective study of 92 patients with hypothyroidism, the QTc interval was found to average 420 ms (range 330-600 ms).
but the prolongation of QTc interval was relatively uncommon. The mechanism of prolongation of QT interval is not fully understood. Hypothyroidism with or without hypothermia might trigger this disorder but adrenocortical insufficiency as a part of panhypopituitarism is a possible contributory factor in such cases.

In our patient, the pulmonary edema was likely to be due to fluid overload since the response to small doses of furosemide alone was dramatic. The QT interval prolongation was normalized within 4 days from the initiation of the replacement therapy. This observation proves to a great extent that the QTc prolongation in this case was related to the hormonal insufficiency (panhypopituitarism).

**Conclusion** Torsades-de-Pointes ventricular tachycardia is a serious cardiac arrhythmia that might occur in association with hypopituitarism. Prolonged QTc interval might be an early marker of this sinister cardiac arrhythmia.

**Acknowledgment** We would like to acknowledge Professor Gani O. A. Ladipo for reviewing the manuscript and Mrs. Wilhelmina Salalac for her secretarial services.

**References**

إن الاستطالة المكتسبة في زمن (QT) في تخطيط القلب الكهربيائي قد لوحظت في كثير من المشكلات الطبية مثل: مرض تصلب الشرايين التاجية، ومرض انزلاق الصمام الميتالي، وفي بعض التفاعلات الحادة لعدد من العقاقير الطبية مثل، مضادات اختلال نظم القلب وبعض أدوية الأمراض النفسية، وفي حالات عدم توازن كهربيائيات (الكتروليات) الدم، وكذلك في بعض أمراض الغدد الصماء مثل، تدني وظائف الغدة الدرقية. ومع هذا فإن حدوث الاستطالة في زمن (QT) ليست شائعة في مرضى تدني وظائف الغدة الدرقية وذلك استنتاجاً من الأبحاث المنشورة في هذا المجال.

ونحن هنا نستعرض حالة سيدة سعودية في الستين من عمرها تم نقلها إلى غرفة العناية الفائقة لمرضى القلب، بسبب وجود تدني خطير في مستوى الصوديوم في الدم، وكذلك علامات سريرية لتدني وظائف الغدة النخامية واستطالة في زمن (QT) (70، 7 من الثانية) ولقد أصيبت هذه المريضة بنوبة تسارع في نظام القلب من النوع البطيني المتأرجح حول خط الأساس. ولقد قمنا بإ.notifications حالة التدني في وظائف الغدة النخامية مختبرياً. وتم علاج حالة هذه المريضة بنجاح بجرد البدء في العلاج الاستعراضي لنقص الهرمونات.

وإذنا هنا لنشر وبدرجة كبيرة بأن التدني في إفرازات قشرة الغدة الكظرية النائج عن التدني في وظائف الغدة النخامية له دور في ميكانيكية حدوث هذا الحال في الوظائف الكهربيائية التي تحكم نظم القلب.