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CASE REPORT

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Familial Brugada syndrome uncovered by hyperkalaemic diabetic ketoacidosis

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We describe a case of diabetic ketoacidosis with concomitant hyperkalaemia that uncovered a typical Brugada syndrome electrocardiogram (EGC). Further provocation testing in the patient and his son confirmed familial Brugada syndrome. Diabetic ketoacidosis with hyperkalaemia may uncover an inheritable arrhythmia syndrome that may put the patient and his/her next of kin at risk for a sudden death, irrespective of diabetes mellitus.

A 59-year-old man was admitted because of nausea, vomiting, diarrhoea, polydipsia, polyuria, and abdominal as well as chest discomfort. His medical history included type-1 diabetes mellitus with retinopathy, nephropathy, and neuropathy. His respiratory rate was 30/min, his heart-rate was 100/min, and his body temperature was 37.8°C, while oxygen saturation and blood pressure were normal. Investigations revealed hyperglycaemia (46 mmol/L, ULN 5.6), hyperkalaemia (6.9 mmol/L, ULN 4.5), metabolic acidosis (pH 7.21, PaCO2 2.5 kPa, HCO3 7.3 mmol/L), and glucosuria/ketonuria. His electrocardiogram (ECG) showed convex ST segment elevations in right-pre-cordial leads (Figure 1) suspicious for acute myocardial infarction. He was treated with intravenous fluids and insulin, and coronary angiography was performed. However, angiography revealed no significant coronary disease and cardiac enzymes remained negative. His ECG returned to normal on normalization of his glucose and potassium (Figure 1). However, he subsequently developed severe pain in the right-lower abdomen. Abdominal ultrasound imaging was suggestive for appendicitis and a gangrenous appendix was surgically removed. Following this, he recovered quickly and could be discharged in good condition with the diagnosis of diabetic ketoacidosis due to appendicitis.

His peculiar ECG abnormalities, however, raised the suspicion of Brugada syndrome (BrS). Brugada syndrome is a familial sudden death syndrome with an increased risk of potential lethal ventricular tachyarrhythmias and is associated with particular right-pre-cordial ST-elevations known as the type-1 BrS-ECG. Its pathophysiological basis is debated but believed to include reduced cardiac excitability.1 Importantly, ECG abnormalities in BrS-patients may be latent, with the added presence of provoking factors such as drugs required to

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Figure 1 Electrocardiogram during ketoacidosis with concomitant hyperkalaemia (6.9 mmol/L), during normal conditions and during ajmaline provocation testing in the patient and his son. A type-1 Brugada syndrome-electrocardiogram ECG with coved-type segment elevations in the right pre-cordial electrocardiogram leads compatible with Brugada syndrome is seen during ketoacidosis and/or ajmaline provocation.
uncover the type-1 BrS-ECG. In these cases, drug-provocation testing with cardiac excitability-reducing drugs such as ajmaline (cardiac sodium channel blocker) may be used to uncover BrS. Accordingly, the patient, whose ECG had meanwhile returned to normal, underwent ajmaline testing. This reproduced the typical ECG changes seen on admission (Figure 1). Moreover, ajmaline testing in his 30-year-old son, who had no known medical condition, also evoked the type-1 BrS-ECG (Figure 1). This confirmed the diagnosis of familial BrS, although molecular genetic analysis of the SCN5A-gene (cardiac sodium channel encoding gene) revealed no mutations. In addition, cardiac imaging with echocardiography and magnetic resonance imaging (MRI) did not show gross structural abnormalities in the patient and his son. The family history was negative for epilepsy or sudden death but further family screening is currently undertaken.

Brugada syndrome is an autosomal-dominant inherited arrhythmia syndrome with an estimated prevalence of 1:2000.1 Because the ECG-derangements and tachyarrhythmias are often provoked by cardiac excitability-reducing drugs or fever, such drugs must be avoided,2 and fever/hyperthermia promptly treated. Interestingly, increased vagal tone also contributes. In high-risk patients, prophylactic implantation of a cardioverter/defibrillator is recommended. In our patient, it is likely that the infection (appendicitis), concomitant subfebrile temperature and increased vagal tone contributed to the type-1 BrS-ECG at admission. In addition, hyperkalaemia secondary to ketoacidosis will have contributed importantly, because hyperkalaemia and acidosis decrease sodium current magnitude by inactivating the cardiac sodium channel. Accordingly, BrS-like ECGs during hyperkalaemia were previously reported and the combination particularly carries a poor prognosis.3 It is important that hyperkalaemia is promptly treated in BrS patients, because these patients are exceptionally susceptible to the cardiac excitability-reducing effects of hyperkalaemia, possibly resulting in intractable ventricular tachyarrhythmias and/or asystole. In BrS patients such cardiac arrhythmias may be treated with cardiac excitability-enhancing drugs, e.g. isoproterenol.2

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**References**