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Recurrent syncope in the Andersen Tawil syndrome – Cardiac or neurological?

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ARTICLE INFO

Article history:
Available online 20 October 2015

Keywords:
Andersen-Tawil syndrome
Bidirectional ventricular tachycardia
Channelopathy
Syncope

Case presentation

An 8-year-old female patient was referred to a paediatrician for assessment of an episode of global muscle weakness after a 100 m sprint. There was no loss of consciousness. Proximal hip muscles and shoulder girdle weakness was noted and the possibility of a myopathy was raised. Muscle biopsy demonstrated "ultra-structurally normal muscle fibres". There was indolent progression of proximal muscle weakness over the years, with no diagnosis made.

At the age of 18 the patient experienced three episodes of transient loss of consciousness over a two-week period. A witness described sudden "unresponsiveness and generalised muscle twitching"; a period of confusion consistent with a post-ictal period was noted. There was no urinary incontinence or tongue biting. No trigger was identified. Inpatient EEG and MRI brain were normal. A further episode of transient loss of consciousness, documented in the hospital record as 'consistent with seizure activity' occurred; cardiac monitoring did not reveal an arrhythmia. A clinical diagnosis of epilepsy was made based on the description of the episodes and lack of a symptom rhythm correlation. The patient was commenced on sodium valproate, which prevented further episodes.

Surface electrocardiograms recorded during the admission documented asymptomatic, frequent polymorphic ectopy Fig. 1.

The QT_c was marginally prolonged at 465ms (Bazett's formula). Echocardiogram showed no evidence of structural heart disease. An outpatient Holter monitor confirmed the background rhythm was sinus, with episodes of non-sustained bidirectional ventricular tachycardia and frequent multimorphological ventricular ectopy with a 25% ectopic burden. Ectopy was suppressed completely during treadmill exercise testing. The effect of exercise on the QT interval was not recorded. Metoprolol, verapamil, sotalol and flecainide were sequentially tried, but were either ineffective or produced intolerable side effects.

At the age of 23 years the patient moved interstate and was referred for review. She had been seizure-free for 5 years. Medical background was unremarkable. Family history was incomplete (patient had no available history from the paternal side. No abnormalities were noted on the maternal side). Physical examination revealed short stature, mandibular hypoplasia, hypertelorism and a broad nasal root. Neurological assessment demonstrated a waddling gait, with inability to rise from a sitting position without assistance. No fasciculation or myotonia was evident. Marked proximal upper and lower limb girdle weakness, Medical Research

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Peer review under responsibility of Indian Heart Rhythm Society
http://dx.doi.org/10.1016/j.ipej.2015.10.006

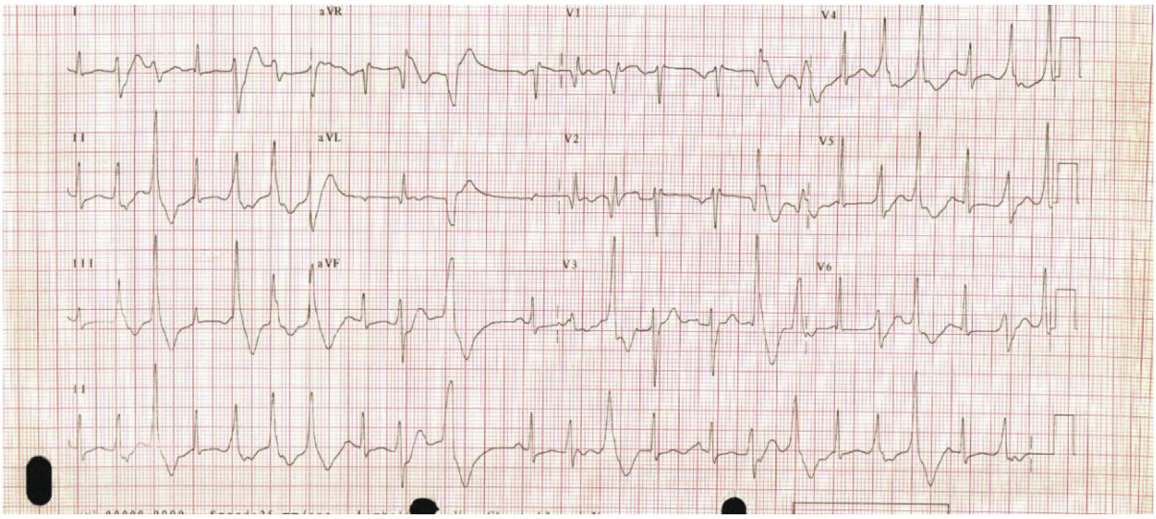

Fig. 1 – A 12 lead ECG recorded from the patient.

Council (MRC) 2–3/5, was found associated with hypotonia. Distal strength was largely preserved. Reflexes were symmetrically depressed. Cardiovascular examination found an irregular pulse. ECG showed frequent polymorphic ectopy as before.

A channelopathy for the cause of her frequent ventricular ectopy and syncope was postulated. Catecolaminergic polymorphic ventricular tachycardia (CPVT), was an obvious consideration, however the suppression of the ectopy during an exercise stress test, essentially excluded this diagnosis. Brugada syndrome and arrhythmogenic right ventricular cardiomyopathy were thought less likely as the ECG didn't show features typically associated with these disorders. The long QT syndrome although associated with polymorphic ventricular tachycardia, is not generally described with frequent ventricular extrasystoles at rest or bidirectional ventricular tachycardia. This patient not only had frequent multifocal ectopy, but had a documented episode of bidirectional ventricular tachycardia, a feature well described in the Andersen-Tawil syndrome. The baseline ECG didn't demonstrate the classic prominent U waves that have been documented in other ATS patients.

All the above channelopathies, besides ATS, are not traditionally reported with muscle weakness or facial dysmorphism and given the specific documented cardiac arrhythmias a clinical diagnosis of Andersen-Tawil syndrome was made.

In light of the lack of seizures for 5 years, the anti-epileptic medication was discontinued. Six months later, the patient experienced recurrent syncope, without convulsive activity. The patient described these episodes as different from those she had suffered at the age of 18. Holter monitoring, recorded peri-event, showed non-sustained runs of bidirectional ventricular tachycardia, as well as monomorphic ventricular tachycardia Fig. 2.

Due to accelerated symptomotology, positive ECG correlation and the clinical difference from previous syncope, an internal cardiac defibrillator (ICD) was advised. Immediately prior to implantation the patient became pregnant. She continued to suffer recurrent syncope and, at the beginning of the second trimester, an ICD was implanted. A pectoral muscle biopsy was sent for genetic analysis. This confirmed a mutation in c.652C > T of the *KCNJ2* gene, previously reported in the Andersen-Tawil syndrome [1].

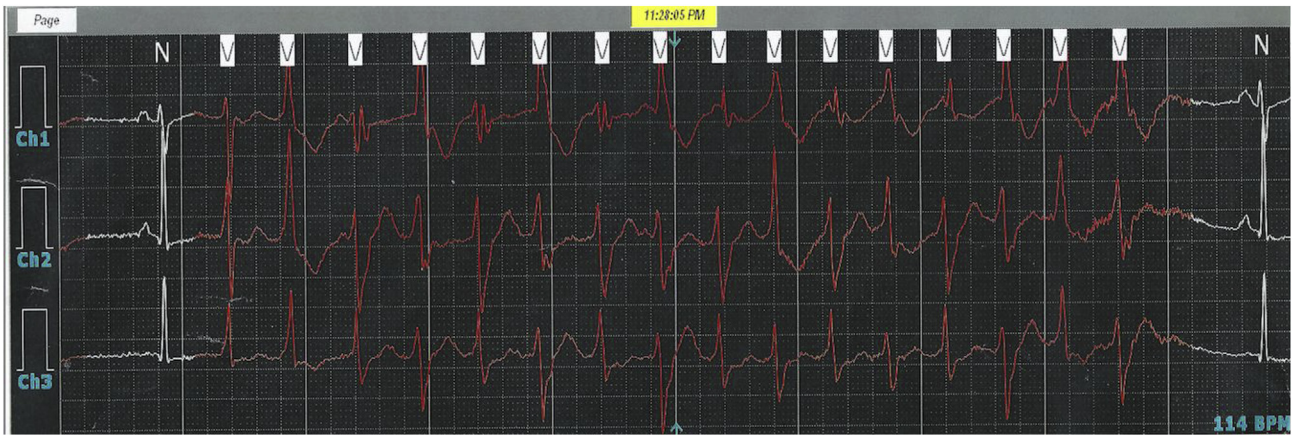

Fig. 2 – Holter monitor tracing demonstrating an episode of non-sustained bidirectional ventricular tachycardia.