ECG and Holter Monitoring in Andersen-Tawil Syndrome

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1. Main clinical characteristics
2. 12-lead ECG features
3. Ventricular arrhythmias
PART I

MAIN CLINICAL CHARACTERISTICS
• ATS is type 7 of congenital LQTS and is caused by mutations in the gene KCNJ2 that encodes a protein that forms the rectifier potassium channel Kir2.1

• ATS is characterized by:
  - Periodic paralysis
  - Ventricular arrhythmias
  - Prolonged Q–U interval,
  - Mild facial or skeletal abnormalities

Initially ventricular arrhythmias were thought to be benign

Sudden cardiac death has been increasingly reported

The disease is rare, with an estimated prevalence of 1/1’000,000.

- 38 cases in Poland
- Prevalence in England 0.08/100,000.
- Zhang et al (2005) US 96 cases (12 countries)

SCD (Zhang, 2005): 96 ATS1 patients

The prevalence was higher in women

Hx of cardiac arrest 3/96 (<3%).

Family hx of SCD 4/33 (12%) kindreds

Zhang et al.(2005).

Affected gene is KCNJ2, which forms the inward rectifier potassium channel Kir2.1.

Mutation with a dominant negative effect: transversion (change of adenine for thymine) in nucleotide 440.

KCNJ2 mutations are detectable in only 60 % of patients with ATS

Until now no other mutations different from *KCNJ2* have been described.

Heart

- Arrhythmias
  - Ventricular extrasystoles
  - Ventricular tachycardia
  - NSVT
  - AV block
  - RBBB, LBBB,
  - Bifascicular block, etc

Skeletal muscle

- Flaccid paralysis
- Impaired skeletal development (extremities and facial area).

PART 11

• 12-LEAD ECG FEATURES OF ATS
12-LEAD ECG FEATURES OF ATS

REPOLARIZATION ABNORMALITIES

- Prominent U-waves
- Q-U interval prolongation

CONDUCTION DISTURBANCES

- AV block
- RBBB or LBBB
- Bifascicular block

The real QT interval is normal if the U wave is excluded from the analysis.

The corrected Q-U interval is significantly longer.

A manifest U-wave is present in 90% of ATS1.
Best seen in leads V2-V4 and in limb leads.

Prolonged Q-U interval (corrected)

[Síndrome de Andersen-Tawil: una revisión del diagnóstico genético y clínico con énfasis en sus manifestaciones cardíacas. Archivos de Cardiología de México, 84(4), 278–285]

PVCs monomorphic

\[\downarrow=U \text{ waves}\]

\[\text{QT } - \text{U (520 ms) at the expense of a U wave.}\]

\[\text{QU corrected (RR 720 ms) = 612}\]
• Prolonged terminal T-wave downslope with biphasic U waves in limb leads and enlarged U waves in V2 and V3
• QTc 440 ms;
• QUc 660 ms

Zhang et al.(2005).

- QTc = 410 ms; QUc = 611 ms.
- PR interval (200 ms) - indicates 1st-degree AV block for age (<175 ms).
- Wide T-U junction characterizes ATS1 and differentiates it from the bifid T waves of LQT2.
- In leads V2 and V3, the enlarged U wave is greater than half of the T-wave amplitude.
Frequent ventricular ectopy (arrow) and prominent U waves (arrowhead)

RBBB and prominent U waves seen across the precordial leads

- QTc 440 ms
- Q-Uc prolongation
- Prominent U waves in leads V3 and V4.

“U on P” phenomenon

U wave masquerading P wave during sinus tachycardia – 83%

“U on P” sign.

“U on P” sign (U-wave masquerading P-wave) the P-wave during sinus tachycardia is inscribed on the U-wave of the preceding beat

ABNORMAL T-U WAVES PATTERNS

Pseudo “Tee-Pee” sign

- A prolongation of the descending limb of the T+U wave during a PVC – 83%

ABNORMAL T-U WAVES PATTERNS

Post-extrasystolic T+U fusion

- Fusion of T and U waves in the sinus beat following a PVC – 83%
- Pseudo–LQTS pattern

- Compare the distinction between T and U waves in sinus beats previous to the PVC with the T+U fusion in the sinus beat following the PVC

Adrenaline test

- U-wave augmentation after adrenaline administration

- The ratio amplitude of U-wave / T-wave becomes > 1 after adrenaline when compared to baseline ratio < 1

Electrocardiogram in Andersen-Tawil Syndrome. New Electrocardiographic Criteria for Diagnosis of Type-1 Andersen-Tawil Syndrome. Current Cardiology Reviews, 222–228.

CONDUCTION ABNORMALITIES

OBSERVED IN 23% OF ATS1

AVB 1 – 31%
RBBB - 40%
LBBB - 9 %
Bifascicular block -9%

ABNORMAL T-U WAVE PATTERNS

- Prolonged terminal portion of T-wave downslope: 70%
- Wide T-U junction: 43%
- Biphasic U waves: 16%
- Enlarged U waves: 73%

**High predictive accuracy for ATS1 genotype prediction**
(Zhang, 2005):
- 94% Positive predictive value
- 91% Negative predictive value

Zhang et al.(2005).
PART III

VENTRICULAR ARRHYTHMIAS IN ATS
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Ventricular extrasystoles – 41%
  • Ventricular bigeminy – 59%

Ventricular tachycardia – 23%
  • Bidirectional tachycardia – 68%
  • Polymorphic tachycardia – 29%
  • Torsades de pointes – 3%

Zhang et al. (2005).
Frequent PVCs in bigeminy
NSVT=Bidirectional VT (most evident in lead II and V3).

Zhang et al. (2005).
Andersen-Tawil syndrome associated with aborted sudden cardiac death: atrial pacing was effective for ventricular arrhythmias. The American Journal of the Medical Sciences, 344(3), 248–50.
Holter monitor recording demonstrating bigeminy with nonsustained VT

BIGEMINY WITH NONSUSTAINED VT IN HOLTER

Control. EV, n = 16772. TVB, n = 284 episodios.
Flecainida 200 mg/día. EV, n = 351. TVB, n = 2 episodios.

BIGEMINY WITH NONSUSTAINED VT IN HOLTER

Holter monitor with monomorphic nonsustained VT
Loop recorder rhythm strip: Bigeminy followed by polymorphic VT, alternating with monomorphc VT, deteriorating into asystole.

Andersen-Tawil Syndrome

Figure 2. Intracardiac electrograms during spontaneous ventricular ectopy in a patient with Andersen-Tawil syndrome. Displayed are surface leads I, II, III, V1, and intracardiac electrograms recorded from the anterior left ventricle. The first sinus beat is followed by 2 successive ventricular ectopic beats, each with a different morphology. The arrows indicate Purkinje potentials preceding the local ventricular electrograms in sinus rhythm and the ectopic beats. The first ectopic beat is from an adjacent Purkinje site – hence the late Purkinje relative to the QRS. (Figure courtesy of Dr. Prashanthan Sanders, Dr. Frederic Sacher, and Dr. Michel Haissaguerre, Hôpital Cardiologique du Haut-Lévêque, Bordeaux, France)
Conclusions

- ATS has a characteristic ECG phenotype
  - Increased U waves are the hallmark of the disease
- Ventricular arrhythmias are frequent
  - PVCs in bigeminy are the most common finding
  - Ventricular tachyarrhythmias can also be present
- ATS is increasingly recognized as a cause of SCD