EKG finding suggesting genetic cardiac disease

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Case 1

- 19 y/o male comes in with syncope
- PMHx: denies
- PSHx: denies
- FHx: brother died @24; paternal uncles died @17 and 23 y/o
- Social: Neg x 3
- Meds: None
- Allergies: NKDA
- Physical exam: unremarkable except for hyperkeratotic lesions on palms and soles
Case 1
Case 1
Arrhythmogenic Right Ventricular Cardiomyopathy (Dysplasia)

- primary heart muscle disease characterized by progressive degeneration and fibrous-fatty replacement of right ventricular myocardium
- associated with arrhythmia
- ventricular tachycardia/fibrillation with left bundle branch block
- major cause of sudden cardiac death in young people and athletes
  - prevalence 0.4% to 0.8% (in Italy and Greece)
  - in US 1: 5000 (0.02-0.1%)
Arrhythmogenic Right Ventricular Cardiomyopathy (Dysplasia)

- disease of the desmosome
- autosomal dominant
  - rarely autosomal recessive (Naxos disease)
  - woolly hair, palmoplantar keratoderma
Figure Legend:

Endomyocardial biopsy from the right ventricle from patients of Figures 2 and 4, showing an active lymphocytic myocarditis (arrows) (HE 250x) with areas of interstitial and replacement fibrosis (F).
Figure Legend:

Right ventricular endomyocardial biopsy from patient of Figures 1 and 3, showing a severe fibrofatty infiltration of the myocardium, suggesting an arrhythmogenic right ventricular dysplasia (hematoxylin eosin 100×).
• EKG features
  • T-wave inversions in leads V1 through V3
  • QRS duration >110msec in leads V1 through V3
  • presence of an epsilon wave (small upright electric potential after end of QRS)
  • left bundle branch type ventricular tachycardia
  • frequent extrasystole
From: Histologic findings in patients with clinical and instrumental diagnosis of sporadic arrhythmogenic right ventricular dysplasia


Figure Legend:
12-lead electrocardiogram from a 27-year-old man with palpitations, showing a sustained ventricular tachycardia with left bundle branch block morphology.
Case 2

- 52 y/o male with syncope
- PMH: HTN
- PSHx: Denies
- FHx: Brother died @ 25y/o
- Social: neg x 3
- VSS, Physical exam benign
Case 2 EKG
Hypertrophic Cardiomyopathy

- Primary disorder of the myocardium associated with increased cardiac muscle mass
- Usually asymmetric
- 1:500 persons affected (700,000 American estimated)
- Global disease affecting various races and both sexes equally
Hypertrophic Cardiomyopathy

- Estimated prevalence is higher than seen in cardiovascular practice.
- Most affected individuals are not diagnosed clinically.
- Clinicians assess only a small fraction of the HCM populations (tip of the iceberg).
  - Fortuitous diagnosis during routine clinical evaluation or family screening.
  - Increased screening due to unexpected EKG findings or imaging studies.
- 1-2% mortality.
Hypertrophic Cardiomyopathy

- heterogeneous disease with 11 or more (upto 21) gene mutations associated with sarcomere protein

- > 70% patients have mutations in 2 genes
  - beta-myosin heavy cain (40%)
  - myosin-binding protein C
Hypertrophic Cardiomyopathy

- autosomal dominant

- genetic testing is available commercially
  - however reliance on determining malignant versus benign types is unreliable in determining overall prognosis
  - therefore genetic testing does not influence treatment strategies

- family screening of HCM identified individuals first and second degree relatives is recommended with echocardiogram (or CMR)
  - screening of children with echocardiogram can start as early as 12 years and repeat echo every 12-18 months until age 18-20 years

Circulation. 2011; 124: e783-e831
Hypertrophic Cardiomyopathy

• wall thickness >30mm with various pattern of distribution
  
  • most common pattern is asymmetric septal hypertrophy (75%)
  
  • concentric pattern (20%)
  
  • apical hypertrophy (10%)

FIGURE 1 Cardiovascular Magnetic Resonance Images Demonstrate Diversity of the Hypertrophic Cardiomyopathy Phenotype

(A) Asymmetric hypertrophy of ventricular septum (VS), sparing the left ventricular (LV) free wall. (B) Focal hypertrophy sharply confined to basal anterior septum (arrows). (C) Thin-walled apical aneurysm (arrowheads) with muscular mid-ventricular apposition of hypertrophied septum and LV wall (asterisks), and distinct proximal (P) and distal (D) chambers. Adapted with permission from Maron et al. (19). (D) Extensive, transmural late gadolinium enhancement involving ventricular septum (arrows). (E) Massive thickening (i.e., 33 mm) confined largely to anterolateral LV wall, greatly underestimated by echocardiography (arrowheads). Adapted with permission from Maron et al (9). (F) Genotype positive-phenotype negative HCM family member with 3 myocardial crypts penetrating thickness of basal inferior wall (arrows).
Hypertrophic Cardiomyopathy

- **EKG features**

- Left ventricular hypertrophy in precordial leads and non-specific ST segment and T-wave changes

- Asymmetric septal hypertrophy
  - deep, narrow, dagger like Q waves in lateral (V5-6, I and aVL) and inferior (II, III, aVF)
  - Q waves <40msec
Hypertrophic Cardiomyopathy

- Apical HC
- Large precordial voltages
- Giant T wave inversions in the precordial leads
- Inverted T waves are also seen in the inferior and lateral leads.
Risk of sudden death is usually related to ventricular tachycardia and ventricular fibrillation.

ICD therapy recommended in high risk individuals.

- **Secondary prevention** for all patients with a history of aborted cardiac arrest.
- **Primary prevention** advised if patients have 2 or more major risk factor.

*Hypertrophic Cardiomyopathy*

![Pyramid Profile of Risk Stratification Model](image-url)

**Major and minor risk markers appear in boxes at the left.** At right are the results of ICD therapy in 730 children, adolescents, and adults assembled from 2 registry studies (28,29). *Extensive LGE is a novel primary risk marker that can also be used as an arbitrator when conventional risk assessment is ambiguous.***SD events are uncommon after 60 years of age, even with conventional risk factors (38). BP = blood pressure; CAD = coronary artery disease; EF = ejection fraction; ICD = implantable cardioverter-defibrillator; LV = left ventricular; LGE = late gadolinium enhancement; LVH = left ventricular hypertrophy; NSVT = nonsustained ventricular tachycardia; SD = sudden death; VT/VF = ventricular tachycardia/ventricular fibrillation; y = years.*
Hypertrophic Cardiomyopathy

- most common cause of sudden death in young athletes
- currently screening is usually history and physical
- ACC does not recommend routine EKG in all athletes due to insufficient data
- AED are recommended in all places where there is competitive athletics occur
Case 3

- 20 y/o male with syncope
- PMHx: None
- PSHx: T&A
- Social: neg x 3
- FHx: denies; no h/o sudden cardiac death
- Physical exam benign
- Labs within normal limits
Case 3 EKG
Long QT Syndrome

- can be congenital or acquired
  - Acquired long QT
    - myocardial ischemia
    - cardiomyopathy
    - hypokalemia
    - hypocalcemia
    - hypomagnesemia
    - autonomic influence
    - drugs
    - hypothermia
Long QT Syndrome

• Congenital long QT
  • genetic channelopathy with variable penetrance
  • 300 different mutations in 5 genes identified so far
  • associated with syncope, polymorphic ventricular tachycardia, and sudden cardiac death
Long QT Syndrome

- Diagnosis mainly relies on EKG and clinical history
  - Long QTc with syncope
  - There is a score system if diagnosis not clear
  - Score of > 4 is highly probable of Long QT syndrome

<table>
<thead>
<tr>
<th>Finding</th>
<th>Score</th>
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<tbody>
<tr>
<td>Electrocardiographic†</td>
<td></td>
</tr>
<tr>
<td>Corrected QT interval, ms</td>
<td></td>
</tr>
<tr>
<td>≥480</td>
<td>3</td>
</tr>
<tr>
<td>460–470</td>
<td>2</td>
</tr>
<tr>
<td>450 (in males)</td>
<td>1</td>
</tr>
<tr>
<td>Torsades de pointes‡</td>
<td>2</td>
</tr>
<tr>
<td>T-wave alternans</td>
<td>1</td>
</tr>
<tr>
<td>Notched T-wave in 3 leads</td>
<td>1</td>
</tr>
<tr>
<td>Low heart rate for age§</td>
<td>0.5</td>
</tr>
<tr>
<td>Clinical history</td>
<td></td>
</tr>
<tr>
<td>Syncope‡</td>
<td></td>
</tr>
<tr>
<td>With stress</td>
<td>2</td>
</tr>
<tr>
<td>Without stress</td>
<td>1</td>
</tr>
<tr>
<td>Congenital deafness</td>
<td>0.5</td>
</tr>
<tr>
<td>Family history</td>
<td></td>
</tr>
<tr>
<td>Family members with definite LQTS</td>
<td>1</td>
</tr>
<tr>
<td>Unexplained SCD in immediate family members &lt;30 yrs old</td>
<td>0.5</td>
</tr>
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Scoring: ≤1 point, low probability of long QT syndrome (LQTS); 2 to 3 points, intermediate probability of LQTS; and ≥4 points, high probability of LQTS. †Findings in the absence of
Long QT Syndrome

• QT should be determined as mean value derived from 3-5 cycles
• beginning of QRS to end of T wave
• measurements made in leads II, V5 and V6
• correct for heart rate using Bazett formula

Table 1

<table>
<thead>
<tr>
<th>Rating</th>
<th>1–15 yrs</th>
<th>Adult Male</th>
<th>Adult Female</th>
</tr>
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<tbody>
<tr>
<td>Normal</td>
<td>&lt;440</td>
<td>&lt;430</td>
<td>&lt;450</td>
</tr>
<tr>
<td>Borderline</td>
<td>440–460</td>
<td>430–450</td>
<td>450–470</td>
</tr>
<tr>
<td>Prolonged</td>
<td>&gt;460</td>
<td>&gt;450</td>
<td>&gt;470</td>
</tr>
</tbody>
</table>
Long QT Syndrome

3 main genotypes identified

• LQTS1
  • cardiac death associated with physical activities
  • associated with swimming

• LQTS2
  • arrhythmic events associated with loud noise (ie ringing of alarm clock)

• LQTS3
  • events occur in sleep
Long QT Syndrome

Figure 1  Distinctive T-Wave Patterns in the 3 Major LQTS Genotypes

T-wave morphology by LQTS genotype: LQT1: typical broad-based T-wave pattern (corrected QT [QTc] 570 ms); LQT2: typical bifid T-wave (QTc 583 ms); and LQT3: typical late-onset peaked/biphasic T-wave (QTc 573 ms). Reprinted, with permission, from Moss et al. (17).
Long QT Syndrome

• Treatment

• Beta-blockers is first line therapy for anyone who’s considered intermediate to high risk

• ICD therapy should be considered in high risk individuals

Figure 4 Suggested Risk-Stratification Scheme for ACA or SCD in LQTS Patients

Risk stratification categories for LQTS patients based on published event rates; more specific risk subsets by age group are detailed in Table 3. Kaplan-Meier (KM) estimates are based on a cohort of 869 LQTS patients (52). CPR = cardiopulmonary resuscitation; TDP = torsades de pointes; other abbreviations as in Figure 2.
Case 4

- 32 y/o male presents with syncope, viral illness with fever of 102 F
- PMHx: denies
- PSHx: denies
- Social Hx: Neg x 3; adopted from Vietnam at age 2
- FHx: unknown
- Physical exam: benign
- Labs: within normal limits
CASE 4: EKG in ED
CASE 4: EKG next day
Brugada Syndrome

• first described in 1992
• autosomal dominant disorder
• mutations in the cardiac sodium channel gene
• known to cause sudden cardiac death and syncope in young, healthy individuals with structurally normal healthy hearts
Brugada Syndrome

- Diagnosis based on symptoms and EKG findings

- Typically manifest in adulthood
  - mean age of sudden death 41 +/- 15 years

- EKG finding can be dynamic or concealed

- Prevalence 5/10,000 in western literature
  - prevalence in Japan reported at 12/10,000

- Prevalence lower in Europe and United States
  - highest among Southeast Asian immigrants
Brugada Syndrome

Diagnostic criteria:

- EKG finding along with clinical findings of:
  - documented VT/VF
  - family history of sudden cardiac death <45 years old
  - coved-type EKGs in family members
  - inducibility of VT on EP studies
  - syncope
  - nocturnal agonal respiration

Brugada Syndrome

- **Type 1**
  - Coved ST segment >2mm with negative T wave in V1-V3
  - Can be unmasked with sodium channel blocking agents or febrile state

- **Type 2**
  - >2mm saddleback shape ST segment in V1-V3
  - T wave either positive or negative

- **Type 3**
  - Either saddleback or coved appearance with ST segment elevation <1mm

*Figure 3. ECG abnormality diagnostic or suspected of Brugada syndrome. Type 1 ECG (coved-type ST-segment elevation) is the only diagnostic ECG in Brugada syndrome and is defined as a J-wave amplitude or an ST-segment elevation of ≥2 mm or 0.2 mV at its peak (followed by a negative T wave with little or no isoelectric separation). Type 2 ECG (saddle-back-type ST-segment elevation), defined as a J-wave amplitude of ≥2 mm, gives rise to a gradually descending ST-segment elevation (remaining ≥1 mm above the baseline) followed by a positive or biphasic T wave that results in a saddle-back configuration. Type 3 ECG is a right precordial ST-segment elevation (saddle-back type, coved type, or both) without meeting the aforementioned criteria.*
Brugada Syndrome

- EKG changes can be dynamic.

- Provocative testing with Procainamide and elicit Type 1 Brugada
Brugada Syndrome

Treatment

- Patients should be considered for ICD therapy
Conclusion

- Arrhythmogenic right ventricular cardiomyopathy (ARVC) is myocardial disease characterised by fatty or fibrofatty replacement of the right ventricle. Associated arrhythmias (VT/VF) is major cause of death in young patients. Episilon wave is an unique feature seen on EKG of patients with ARVC.

- Hypertrophic cardiomyopathy is an autosomal dominant disorder which is a leading cause of death in young athletes.

- Congenital Long QT syndrome is channelopathy that can be screened for on routine EKG.

- Brugada syndrome has a distinctive EKG pattern. However the dynamic EKG changes can make this diagnosis challenging.