ECG in AVB

- Predicting Torsades de Pointes

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Case. Torsades de Pointes in CAVB

- F/78

- Underlying diseases
  - DM, HT, old CVA

- Spinal stenosis 수술 후 pneumonia 로 타원에서 supportive care 받던 분으로, dizziness 있어 본원 방문함.
내원시 심전도 (HR 44 bpm)

Sinus rhythm??
내원시 심전도 (HR 44 bpm)

Complete AV block
24hr Holter monitoring 중 syncope 발생
Temporary PM
Permanent PM implantation

No more dizziness / syncope
What is Torsades de Pointes (TdP)?

• A form of PMVT that occurs in the setting of QT interval prolongation.

• Terminologies to explain TdP
  • Long-short R-R cycle sequences
  • Transmural dispersion of repolarization
  • QT prolongation = prolongation of AP duration
  • Early afterdepolarization
  • PVC with R on T phenomenon
  • Twisting QRS complexes

_Braunwald’s heart disease. 10th ed. Vol. 1. pp782._
Relation btw Ventricular Action Potential and ECG

*RP: refractory period
*AP: action potential
Relation btw Ventricular Action Potential and ECG

P wave

Surface ECG

Ventricular AP waveform

Phase

0 1 2 3 4

QRS

T

Relative RP

QT prolongation = prolonged AP duration

Outward repolarizing K current

or

Inward depolarizing Na or Ca current
Transmural Dispersion of Repolarization

- AP duration difference between different myocardial layers
- Create a vulnerable window for development of reentry
Early Afterdepolarization $\rightarrow$ PVC $\rightarrow$ TdP

- Abnormal depolarization of Ca or Na $\rightarrow$ EAD $\rightarrow$ When reaching threshold potentials $\rightarrow$ generation of PVC (triggered beat) $\rightarrow$ initiation of TdP

PVC (R-on-T)

Perpetuation: mainly d/t reentry
PVC
Long pause
Longer QT interval

EAD $\rightarrow$ PVC (R on T) triggering $\rightarrow$ TdP

Long-short R-R sequence
Causes of TdP (QT prolongation)

1. Congenital long QT syndromes (see text for details)
   - Long QT syndrome type 1: Reduced repolarizing current \( i_{Ks} \) due to mutation in KCNQ1 gene
   - Long QT syndrome type 2: Reduced repolarizing current \( i_{Ks} \) due to mutation in KCNH2 gene
   - Long QT syndrome type 3: Delayed inactivation of the \( h_{Ma} \) due to mutations in SCN5A gene

   Others: Several other types of long QT syndromes have been described; long QT types 1, 2, and 3 account for 80–90% of cases

2. Acquired prolongation of QT interval
   - Electrolyte abnormalities
     - Hypokalemia
     - Hypomagnesemia
     - Hypocalcemia
   - Drugs
     - Antiarrhythmic drugs
       - Class IA: Quinidine, disopyramide, procainamide
       - Class III: Sotalol, amiodarone (QT prolongation common but torsade ventricular tachycardia is rare), ibutilide, dofetilide, almokalant
     - Antibiotics
       - Macrolides: Erythromycin, clarithromycin, azithromycin
       - Fluoroquinolones: Levofoxacin, moxifloxacin, gatifloxacin
       - Trimethoprim-sulfamethoxazole
     - Clindamycin
     - Pentamidine
     - Chloroquine
     - Antifungals: Ketoconazole, itraconazole
     - Antivirals: Amantadine
   - Antipsychotics
     - Haloperidol, phenothiazines, thioridazine, trifluoperazine, sertindole, zipralidene, ziprasidone
     - Tricyclic and tetracyclic antidepressants

   Antihistamines (histamine 1-receptor antagonists)
   - Terfenadine, astemizole, diphenhydramine, hydroxyzine

   Cholinergic antagonists: Cisapride, organophosphates
   - Citrate (massive blood transfusions)
   - Cocaine
   - Methadone
   - Fluoxetine (in conjunction with other drugs that prolong QT)

   Cardiac conditions
   - Myocardial ischemia and infarction
   - Myocarditis

   Marked bradycardia
   - Stress cardiomyopathy

   Endocrine disorders
   - Hypothyroidism
   - Hyperparathyroidism
   - Pheochromocytoma
   - Hyperaldosteronism

   Intracranial disorders
   - Subarachnoid hemorrhage
   - Thalamic hematoma
   - Cerebrovascular accident
   - Encephalitis
   - Head injury

   Nutritional disorders
   - Anorexia nervosa
   - Starvation
   - Liquid protein diets
   - Gastroparesis and ileojejunal bypass
   - Celiac disease

Harrison’s internal medicine. 19th ed. pp 1496.
ECG in AVB – factors predicting TdP

• Not everyone with AV block develops TdP.

Who are in a higher risk of TdP?
Clinical risk factors

• Older age
• Female gender
• HypoK, HypoCa, HypoMg
• Exposure to QT prolonging drugs
• Underlying disease
  • Heart failure
  • Left ventricular hypertrophy
  • Thyroid disease
  • Myocardial infarction
  • Obesity
• Polymorphisms or mutations in genes
• Various ECG findings
Bradycardia-Induced Abnormal QT Prolongation in Patients with Complete Atrioventricular Block with Torsades de Pointes

14 CAVB

6 TdP (+) 8 TdP (-)

HR (p=ns)

QRS (p=ns)

QT (p<0.01)

QTc (p<<0.005)

Am J Cardiol 1992;69:628-33
a. QT (QTc) prolongation

\[ \text{QTc} = \frac{\text{QT interval}}{\sqrt{\text{RR}}}. \]

Prevention of Torsade de Pointes in Hospital Settings
A Scientific Statement From the American Heart Association and the American College of Cardiology Foundation

*Upper limits of normal (99th percentile) for QTc
- 470ms (M), 480ms (F)

*QTc > 500ms
- Proarrhythmic marker
  Congenital (OR 2-3), acquired (OR 1.2)

Circulation 2010;121:1047-60.
b. QRS morphology change

Long QT Syndrome Complicating Atrioventricular Block
Arrhythmogenic Effects of Cardiac Memory

2:1 AVB (VR 36bpm)

CAVB (VR 38bpm)

Circ AE 2014;7:1129-35
Holter of our case patient
Long QT Syndrome Complicating Atrioventricular Block
Arrhythmogenic Effects of Cardiac Memory

- A change in QRS morphology at the time of AVB – in 1/3 patients
- T wave change, QT prolongation d/t cardiac memory → TdP risk

<table>
<thead>
<tr>
<th>Predictor of TdP</th>
<th>Odds Ratio (95% Confidence Intervals)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Model 1 (without QTC)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female sex</td>
<td>9.6 (1.5–59.9)</td>
<td>0.016</td>
</tr>
<tr>
<td>Complete AVB*</td>
<td>2.1 (0.1–23.1)</td>
<td>0.54</td>
</tr>
<tr>
<td>R-R during AVB (for 100-ms increase)</td>
<td>1.1 (0.9–1.3)</td>
<td>0.46</td>
</tr>
<tr>
<td>QRS width during AVB (for 10-ms increase)</td>
<td>0.9 (0.7–1.0)</td>
<td>0.06</td>
</tr>
<tr>
<td>Change in QRS morphology</td>
<td>5.4 (1.4–21.3)</td>
<td>0.016</td>
</tr>
<tr>
<td>Change in QRS axis</td>
<td>3.1 (0.7–13.5)</td>
<td>0.130</td>
</tr>
<tr>
<td>Change in QRS morphology and axis</td>
<td>10.7 (2.0–57.6)</td>
<td>0.006</td>
</tr>
</tbody>
</table>

*Complete AVB: ≥300 ms

Fragmented QRS is associated with torsades de pointes in patients with acquired long QT syndrome

- **Fragmented QRS** - Depolarization abnormality
  - Substrate for reentrant circuit after TdP initiation

Before TdP

After risk factor modification

*Heart rhythm* 2010;7:1808-14.
c. Transmural dispersion of repolarization

- An increase in QT interval does not necessarily lead to TdP.
- Comparison of TdP induction between class III AAD.
  - In a rabbit model of acute AV block
  - **sotalol** vs. **amiodarone**

*Dispersion (sotalol > AMD)*

*EAD, TdP (sotalol > AMD)*

c-1. Interventricular dispersion of repolarization

- Long-short sequence

Interventricular dispersion of repolarization (110ms) → TdP
d. T wave morphology

- Prolongation of AP duration
- Marked transmural dispersion of repolarization
- EAD triggering PVC, perpetuating TdP

Repolarization problem

QT interval prolongation

T wave morphologic change
d. T wave morphology

- T [peak] – T [end] interval
- Notched T wave (similar to LQT2)
- Complex (triphasic) T wave
- T wave alternans (macroscopic beat-to-beat alteration)
- Long QT with abnormal T-U wave
d-1. T [peak] – T [end] interval

• Comparison of Tpeak – Tend

• Pts with CAVB (TdP (-) vs (+))

![Graph showing Tpeak-Tend intervals for Control and TdP groups with median values of 65 ms and 244 ms, respectively.]

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Cutoff Value</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>PPV</th>
<th>NPV</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tpeak-Tend</td>
<td>117 ms</td>
<td>96.6%</td>
<td>98.2%</td>
<td>93.3%</td>
<td>99.1%</td>
</tr>
</tbody>
</table>
d-2. Notched T wave (similar to LQT2)

Phase 3: blocking delayed rectifier K current → QT prolongation

I\textsubscript{ks} (KCNQ1)

I\textsubscript{kr} (KCNH2)

LQT1

LQT2

Broad T

Bifid T
LQT2-like T wave morphology

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<th>Variable</th>
<th>TdP</th>
<th>Control</th>
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<tr>
<td></td>
<td>n = 30</td>
<td>n = 113</td>
<td></td>
</tr>
<tr>
<td>QT morphology</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LQT1-like</td>
<td>4 (13.8%)</td>
<td>10 (8.8%)</td>
<td>0.426</td>
</tr>
<tr>
<td>LQT2-like</td>
<td>16 (55.2%)</td>
<td>3 (2.7%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>LQT2 with T2&gt;T1</td>
<td>8 (27.6%)</td>
<td>0 (0%)</td>
<td>&lt;0.001</td>
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<tr>
<td>LQT3-like</td>
<td>2 (6.9%)</td>
<td>6 (5.3%)</td>
<td>0.741</td>
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<tr>
<td>“Bumps-ahead sign”</td>
<td>17 (58.6%)</td>
<td>20 (17.7%)</td>
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Torsades de pointes complicating atrioventricular block: Evidence for a genetic predisposition

**Tested gene**
: HERG, KCNQ1, KCNE1, KCNE2, SCN5A

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<th>29 with CAVB, QT&gt;600ms</th>
<th>vs.</th>
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<td>22 with CAVB, QT&lt;600ms</td>
<td>vs.</td>
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<td>100 healthy controls</td>
<td></td>
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</table>

CAVB with LQT was associated with **HERG mutation in 17%**!
d-3. Complex T wave

Causing acquired LQT

Blockade of combined K channels → complex T waves

d-3. Complex (Triphasic) T wave

Table 1
Clinical and Electrocardiographic Characteristics of Patients With Bradyarrhythmias With and Without Torsade de Pointes

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U wave? Sign of EAD?

Triphasic T : late positive component

d-4. Others

- T wave alternans (macroscopic beat-to-beat alteration)

- Long QT wave with abnormal T-U wave

Heart Rhythm 2015;12:498-505
A 2-Step Model for predicting TdP

The Morphology of the QT Interval Predicts Torsade de Pointes During Acquired Bradyarrhythmias

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</tr>
<tr>
<td>QTc interval</td>
<td>480 ms</td>
<td>96.6%</td>
<td>92.0%</td>
<td>75.7%</td>
<td>99.0%</td>
</tr>
<tr>
<td>QT interval</td>
<td>570 ms</td>
<td>90.0%</td>
<td>86.7%</td>
<td>64.3%</td>
<td>97.0%</td>
</tr>
</tbody>
</table>

Values derived from receiver-operating characteristic curves.
NPV = negative predictive value; PPV = positive predictive value; QTc = corrected QT interval.

- QT interval > 510ms
- LQT2-like T wave +
- T_{peak}-T_{end} > 85ms

Specificity 97.3%
PPV 84.2%

Specificity 99%
PPV 94%
Electrocardiographic predictors of bradycardia-induced torsades de pointes in patients with acquired atrioventricular block

- T wave alternans
  - 7 Yes
  - No 93
  - SN=35.0% SP=100%

- Reversed asymmetry
  - 3 Yes
  - No 90
  - SN=50% SP=100%

- Triphasic T wave
  - 4 Yes
  - No 86
  - SN=70.0% SP=98.6%

- T2 >> T1
  - 5 Yes
  - No 81
  - SN=85.0% SP=97.5%

Summary

• TdP is a polymorphic ventricular tachycardia caused by a long QT interval.

• Prolongation of AP (decrease in K⁺ or increase in Na⁺ or Ca++) → transmural dispersion of repolarization → EAD (reactivation of L-type Ca²⁺ or late I\textsubscript{Na} or Na-Ca exchanger) → PVC when EAD reaching threshold → initiation of TdP → perpetuation (transmural reentry)
Predictors for TdP risk from ECG

- **QT prolongation**
  → heterogeneous dispersion of repolarization

- PVC with long-short sequence, R-on-T

- Changes in **QRS** morphology and axis

- Changes in **T wave** morphology
  - T [peak] – T [end] interval
  - Notched T wave (similar to LQT2) – genetic component (+)
  - Complex (triphasic) T wave
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Thank you for your attention!