A witnessed VF/arrest in a previously healthy 40-year old man

Ronald Kanter, MD

Nicklaus Children's Hospital

Professor emeritus, Duke University

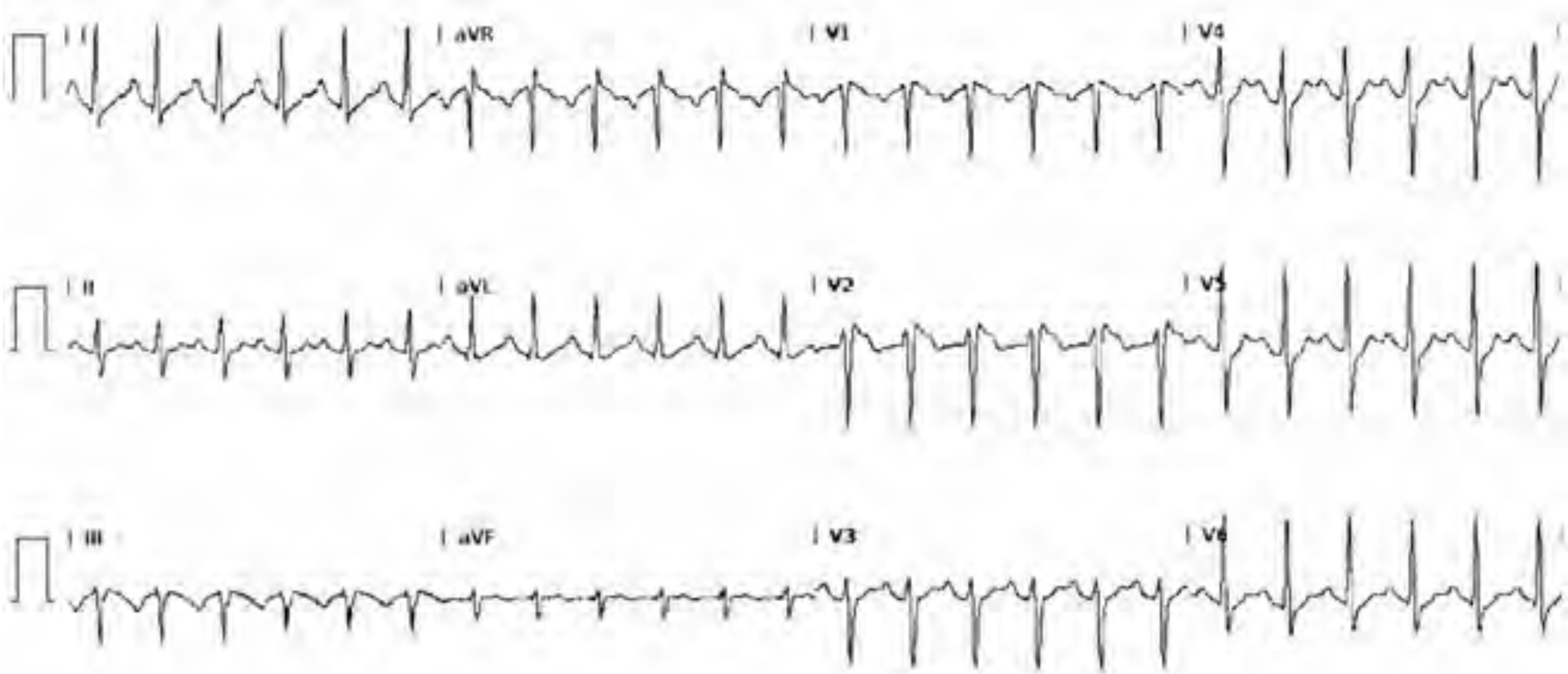
I was asked to see the children of a 40 year old male who experienced witnessed sudden cardiac arrest while performing on-stage during a piano concert. They are 2(m), 5(f), and 7(m) yrs old. Their histories are negative and ECGs normal.

Returning to proband, CPR was initiated immediately by an audience member, followed a few minutes later by AED application and confirmation of VF. ROSC was established after 3rd shock.

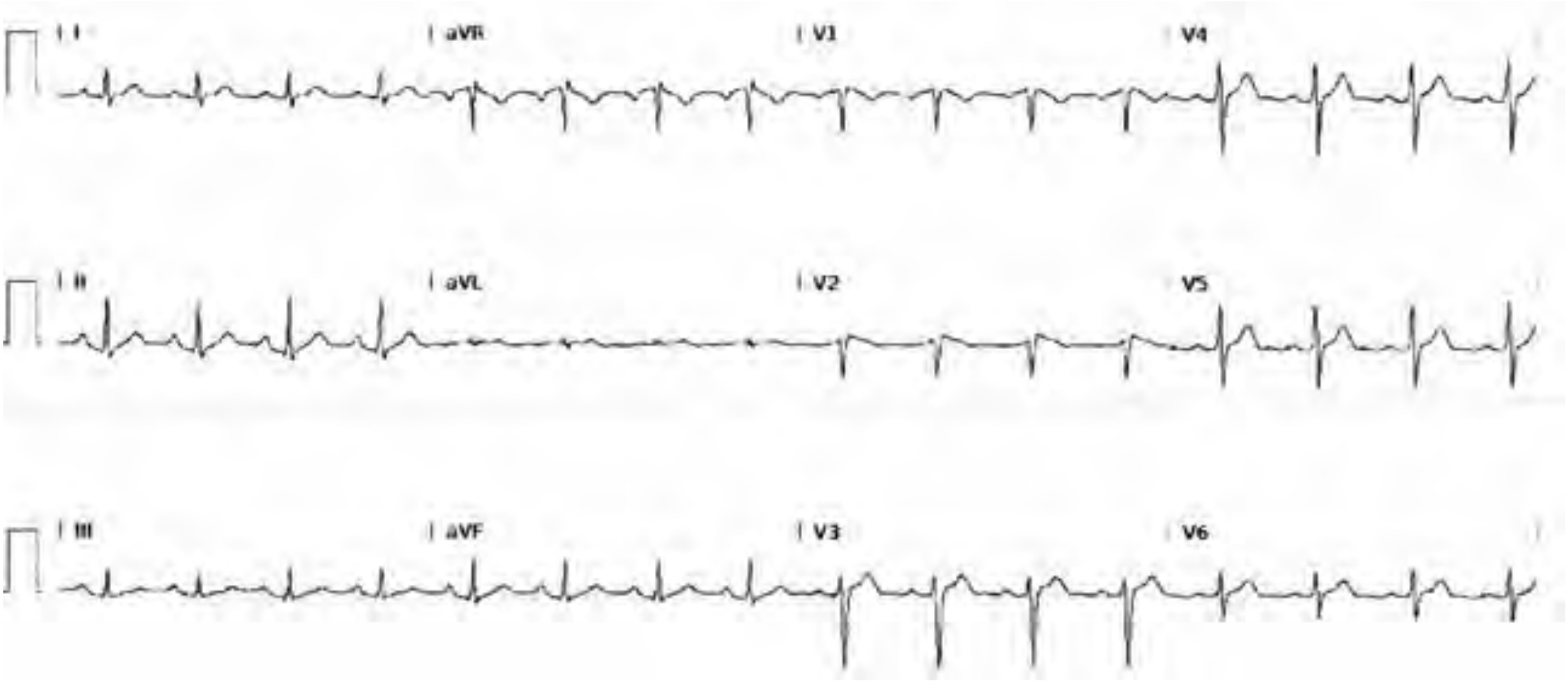
He had low-grade fever in ambulance, and he was later found to be COVID(+). The following 12-lead ECG (standard lead placement) was obtained:

In ambulance, 90” post-event. Rate=143 bpm. Medications given:

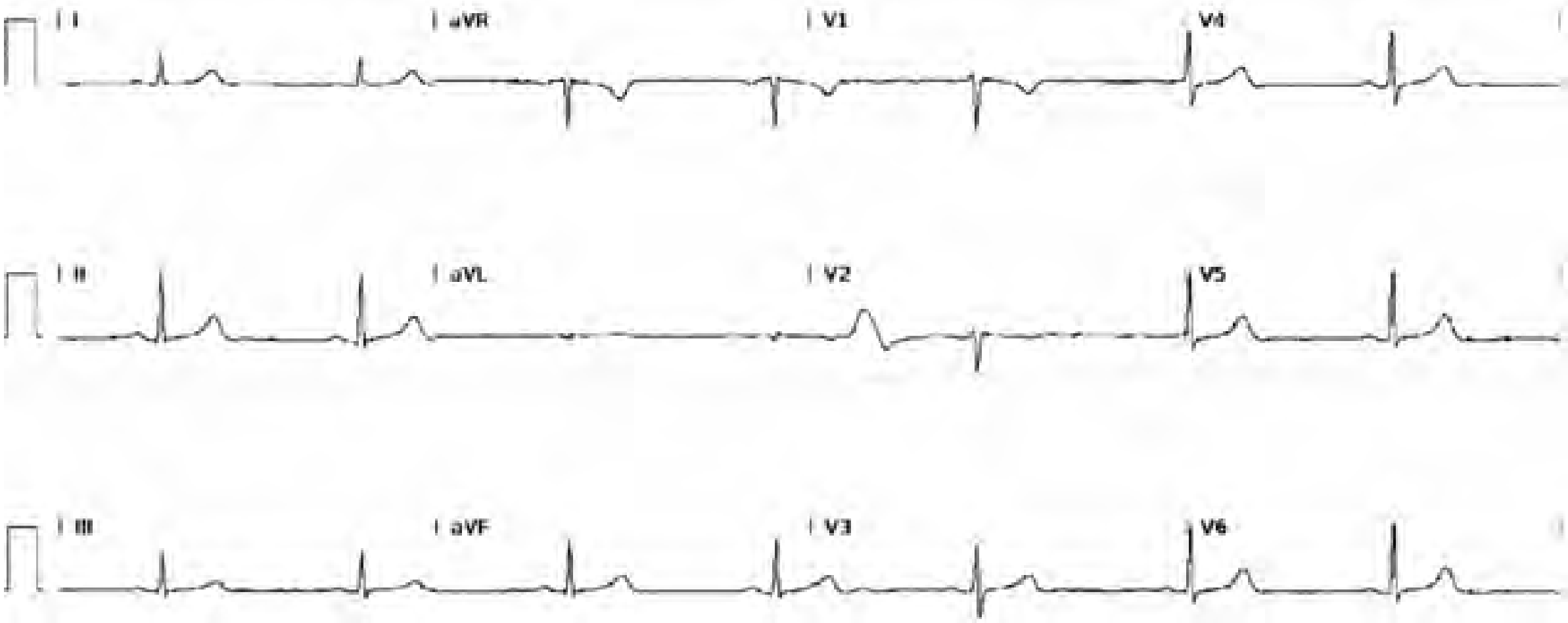
Amiodarone, ketamine, fentanyl, midazolam, norepinephrine, propofol, rocuronium, cisatracurium, atropine, etomidate, furosemide, heparin, aspirin, normal saline, KCl



2 days after VF/arrest. Rate 95 bpm (afebrile)



5 days after VF/arrest. Rate 44 bpm



-Coronary arteriography showed no pathology, and after recovery from cardiogenic shock, cardiac structure and function were normal. cMRI was normal. ICD was implanted on day 9, post-event.

-Father's past medical and family histories are completely non-contributory.

-Genetic test (Invitae: "Arrhythmia and Cardiomyopathy Comprehensive Panel") results:

Heterozygous variant in SCN5A: c.1282G>A (p.Glu28Lys), adjudicated as VUS

- Amino acid change acidic and polar -> basic and polar
- Variant has been observed in individuals with AF, BrS, and/or LQTS
- Present in population databases (gnomeAD 0.01%)
- PolyPhen-2 in silico predicts variant to be tolerated
- Experimental studies have shown SCN5A function to be altered by this variant

-The diagnosis of Brugada syndrome was made. The 2- and 5-year old children have the same variant.

Question 1

If you agree with the diagnosis of Brugada syndrome, which of the above features is most compelling for this diagnosis:

1. The history (VF/arrest while performing a piano concert)
2. The ECG in the ambulance during low-grade fever
3. The genetic test results
4. Normal cardiac structure/function

Additional Patient History

During routine remote monitoring from ICD, a “VT” episode was recorded, corresponding exactly to a piano concert in Israel. It showed sinus tachycardia at 180 bpm when patient was completely asymptomatic.

Responses from SADS Advisory Board

- “Fever-induced ST elevation is not a rare phenomenon, and could be ‘red herring’.”(*Heart Rhythm* 2013;10:1375)
- SCN5A variant characterized as not being LOF; may be slightly GOF (*Sci Rep* 2018;8:3129); or even wildtype (Glazer, Roden)
- *(After formal consultation with family):* This variant has been cited 76 times out of 800,000 individuals sequenced at nucleotide 1282 per gnomeAD, or 1 per 10,615 individuals. With a population prevalence of 1:40,000 having SCN5A-mediated BrS (ie, BrS having prevalence of 1:10,000, and 25% of those caused by SCN5A variant), this means that our patient’s variant is **4x more common than all SCN5A causative BrS patients combined.**

Having established that the diagnosis of Brugada syndrome in the father is now in doubt, what would be the appropriate next step:

1. Perform a sprint treadmill test on the father.
2. Perform an ajmaline test on the father.
3. Repeat ECGs on the children, including high V1 and V2 leads.
4. Ensure that an AED is always present for the children.

HINT: It's your call. Nothing, in fact, as been done yet!

Syncope in a 17-year-old during Sports

SADS Foundation Symposium: Challenging Cases in Genetic Heart Conditions
April 24, 2025, San Diego, CA

Anthony C. McCanta, M.D., FHRS

Children's Hospital of Orange County

CHOC Children's Specialists

Associate Clinical Professor of Pediatrics

University of California Irvine

Pediatric and Congenital Electrophysiology

No relevant financial disclosures

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Rady Children's Health

GOOOOAAALLLLL!!!!!
- WHAT? Oh No!?

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Syncope in a 17-year-old girl during a high school soccer game

- During celebration- immediately after goal

- Patient ran to celebrate with team, raised hands in air, and prior to hugging teammate, collapsed in teammate's arms
- Teammate lowered patient to the ground
- Parents and bystanders did not initially recognize that anything was wrong
- Teammates assessed patient, found her to be breathing and called for help, 911 called
- Patient recovered consciousness after ~ 30 seconds prior to assessment by coach and trainer
- Trainer's assessment: patient conscious and breathing with irregular and thready pulse, no active resuscitation performed
- Patient disoriented when EMS arrived

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Rady Children's Health

Syncope in a 17-year-old girl during a high school soccer game

- Past Medical History: negative, no medications. No hospitalization
- Social History: No illicit drug use, no EtOH. Junior in High School. ***Competitive Soccer Player → already accepted a Division I scholarship***
- Family History: No sudden cardiac or unexplained deaths. However, father with history of multiple syncopal events with raising hands above head
- ROS: No head injuries. No fevers, no illness. Prior viral respiratory illness 1 month prior (not tested for COVID-19 or influenza). Occasional palpitations for 5-10 seconds at rest. Prior syncope x 1 while hugging father. No prior syncope during exercise

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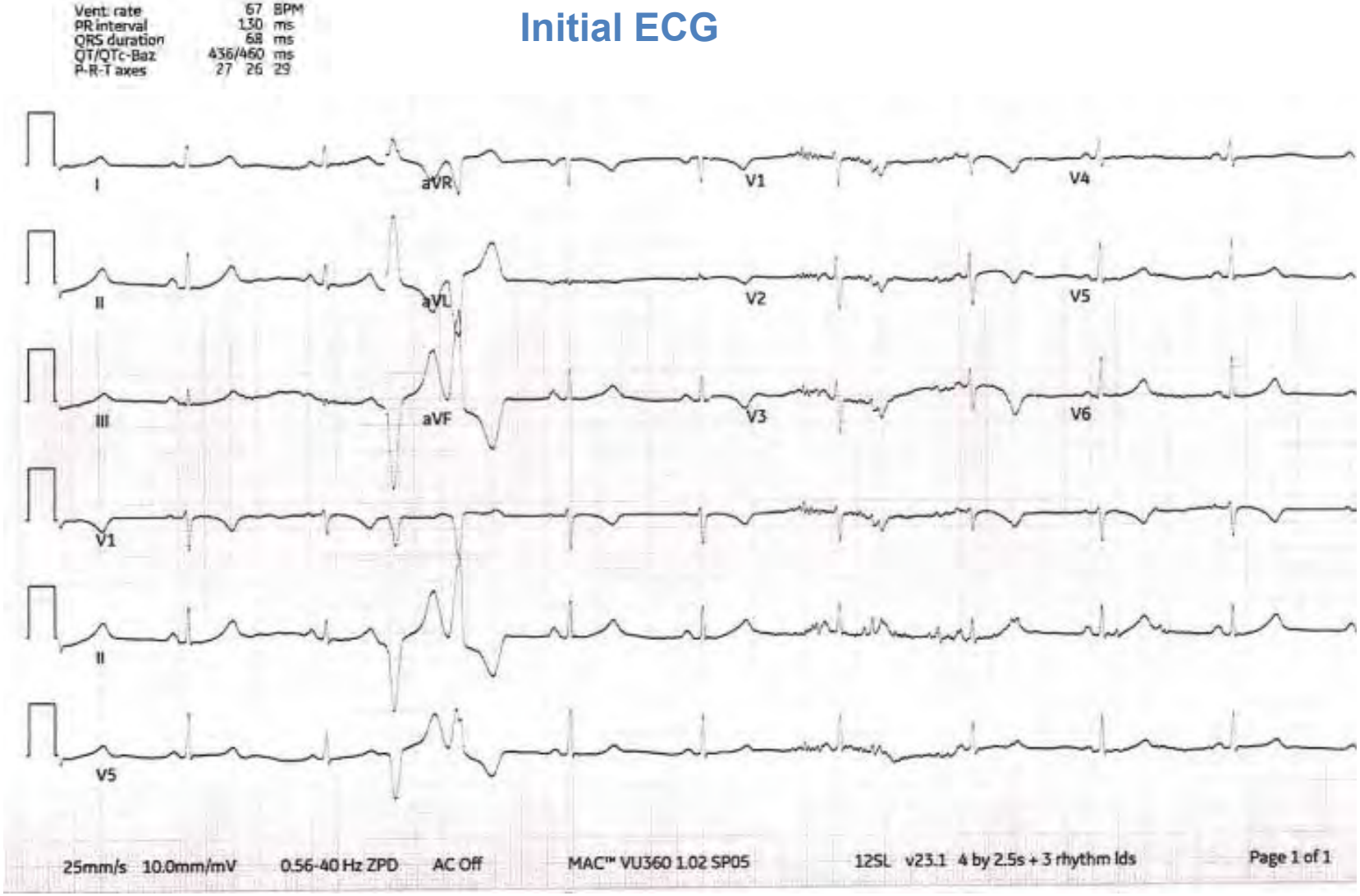
Initial ECG



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Transport and Emergency Workup at Outside Hospital

- Hypotensive during transport BP 80/40 mm Hg
- Pulse 50-60 bpm with frequent extrasystoles (PVCs on transport monitor)
- Normal mental status, no post-ictal state

- Initial Labs
- Normal Glucose 96 mg/dL
- Normal electrolytes (Na 137 mmol/L; K 4.9 mmol/L)
- Normal Hgb 14.8 g/dL
- Normal BNP 37 pg/mL (nl < 100 pg/mL)

- Elevated troponin 856 ng/L (nl <45 ng/dL)
- Mildly elevated D-Dimer 0.57 ug/mL (nl <0.5)

Differential Diagnosis:

- VasoVagal? Hands up
- Seizure?
- Benign PVCs?
- Cardiomyopathy
  - Arrhythmogenic CM
  - Dilated CM?
- Channelopathy
  - CPVT?
  - LQT?
  - Brugada?
- Myocarditis?
- Coronary anomaly?

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Syncope in a 17-year-old girl during a high school soccer game

- Echocardiogram:

1. Mildly dilated right atrium.
2. Borderline dilated right ventricle.
3. Mildly diminished right ventricular systolic function.
4. Dysynchronous left ventricular systolic contraction.

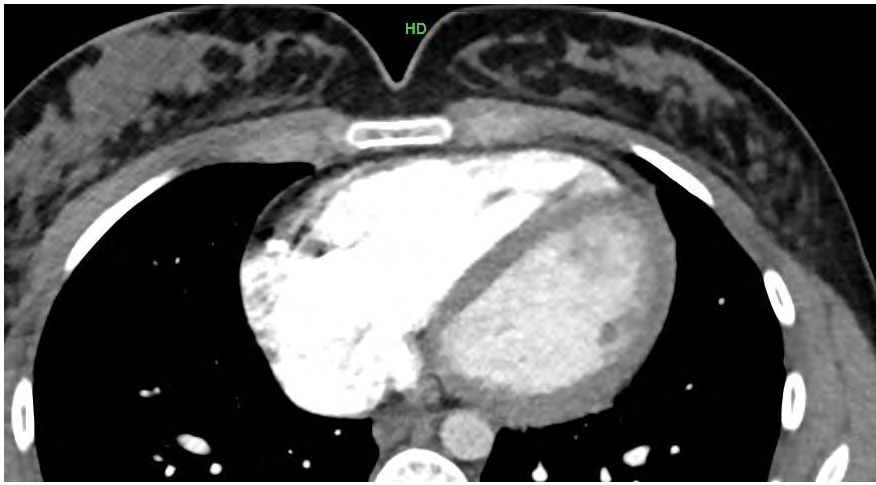
Normal take off and proximal courses of the left main, the left anterior descending, the left circumflex, and the right main coronary arteries by 2D imaging

CTA Evaluating for pulmonary embolism

1. No evidence of acute pulmonary embolism.

2. Dilated right ventricle with trabeculated appearance and fat attenuation in the right ventricular wall.

(Coronaries not evaluated)



NEXT STEPS?

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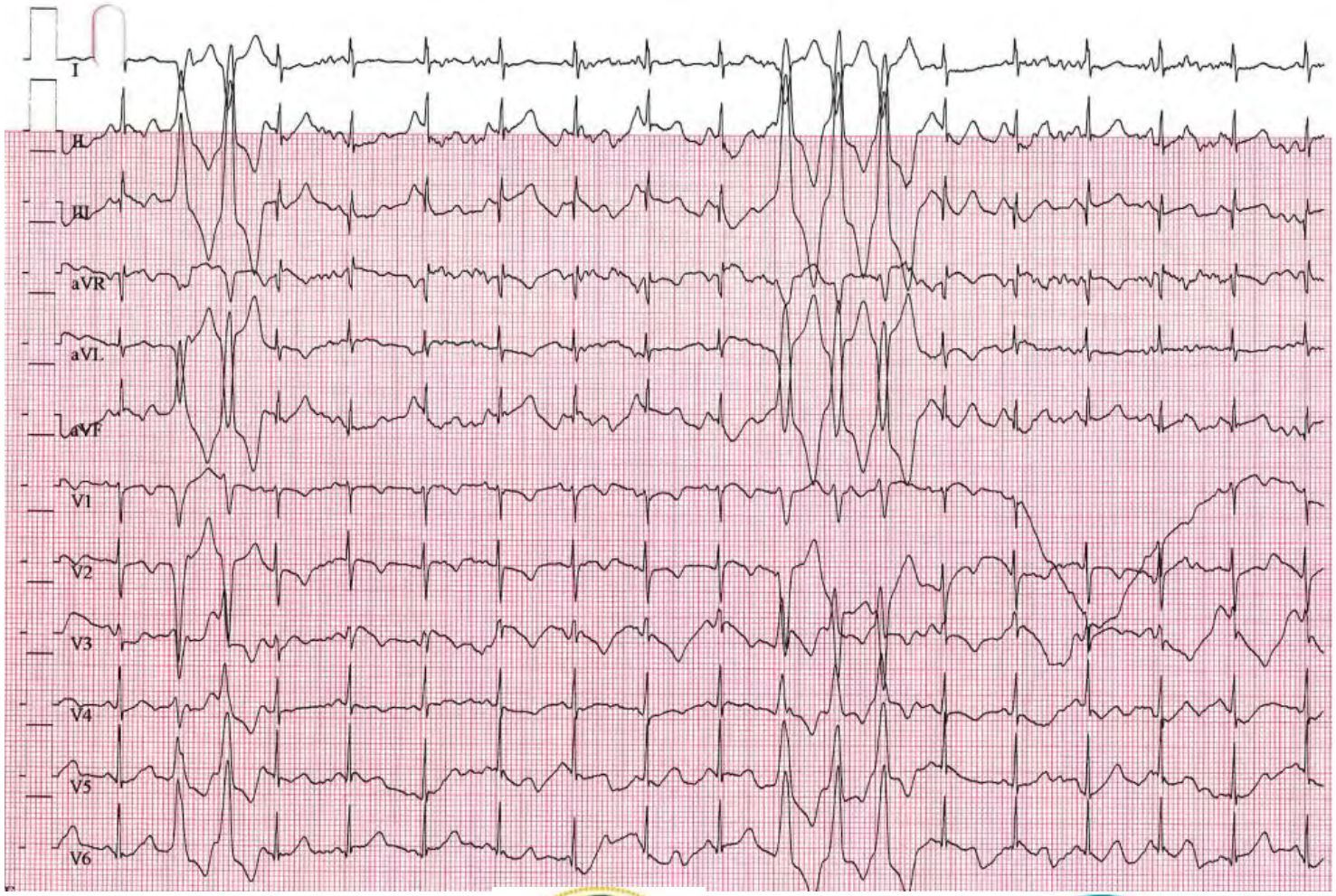
Initial Treadmill Stress Test
Baseline and Stage 1



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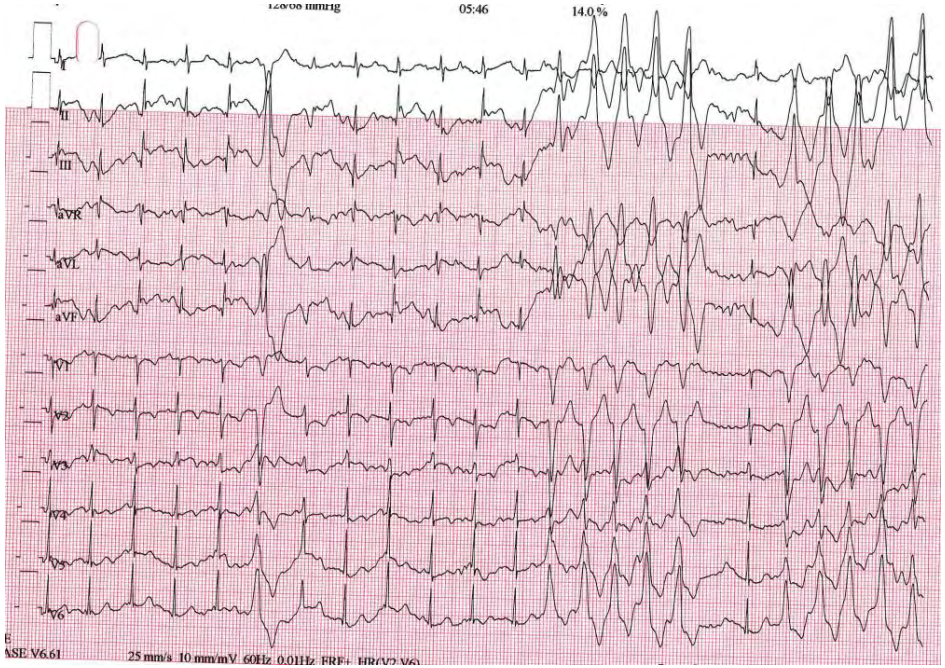
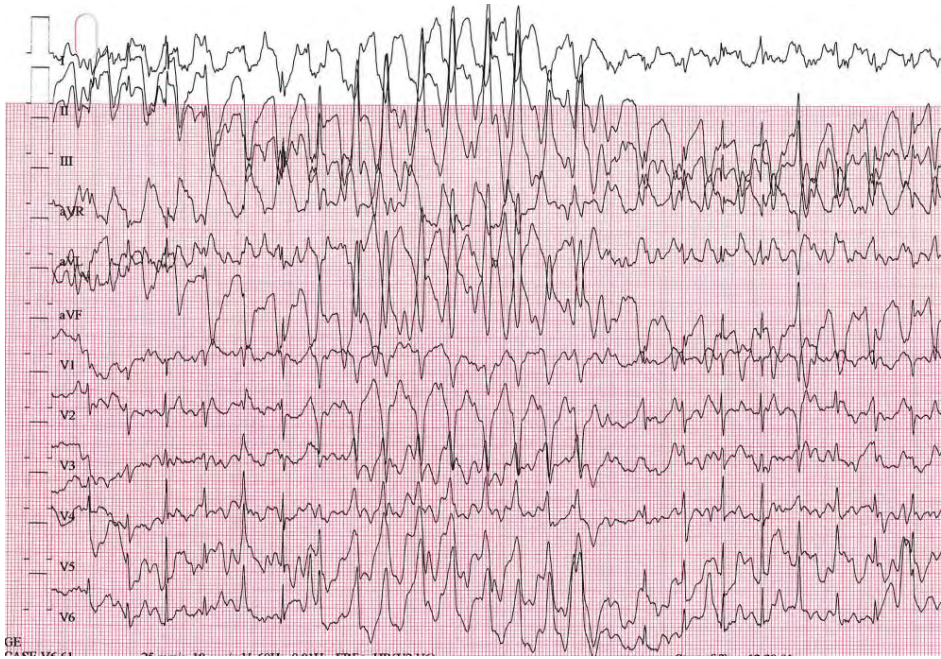
Initial Treadmill Stress Test

Stage 2



Stage 3



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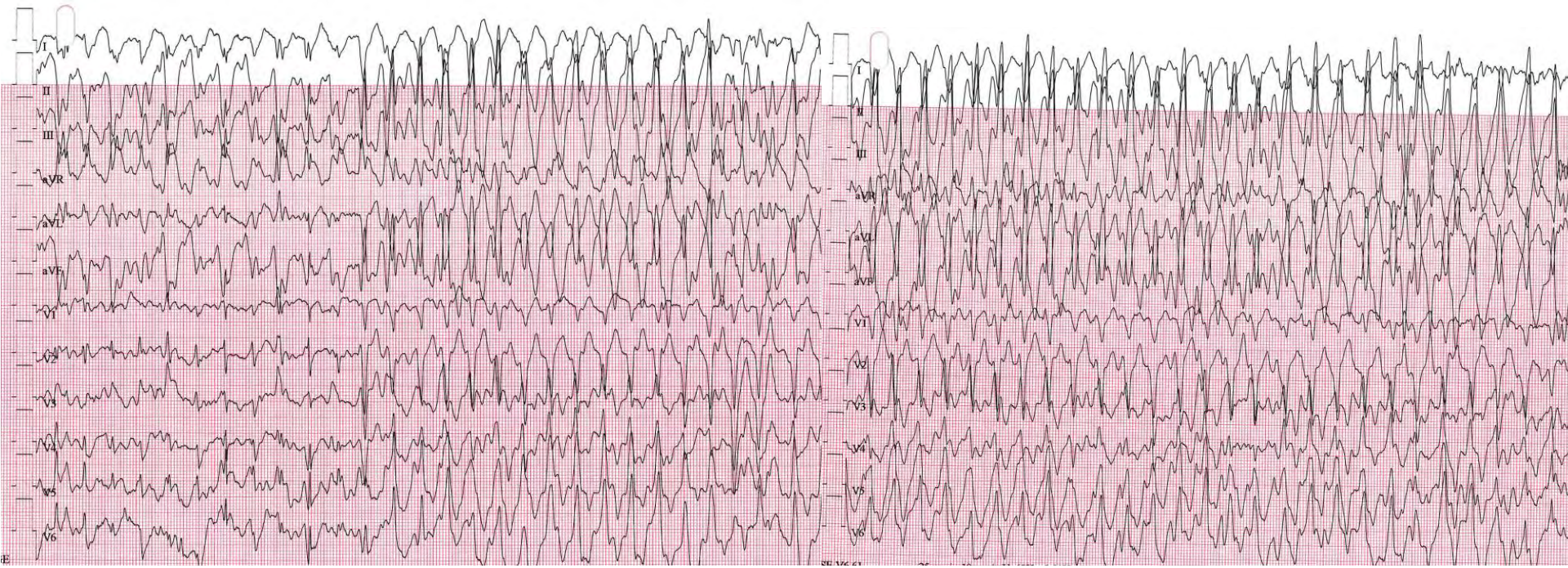
Initial Treadmill Stress Test

Stage 4

Stage 5



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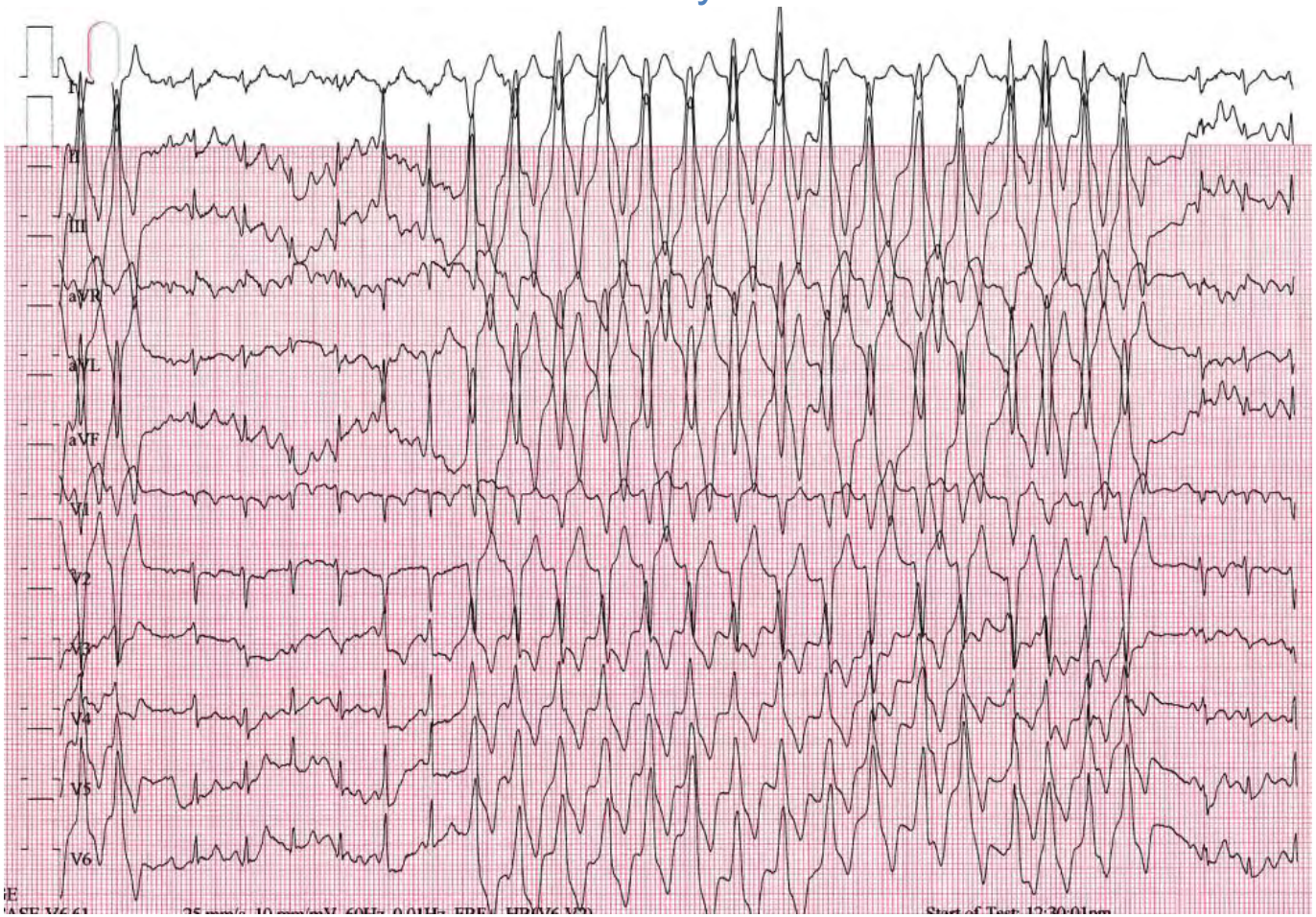
Initial Treadmill Stress Test

Recovery



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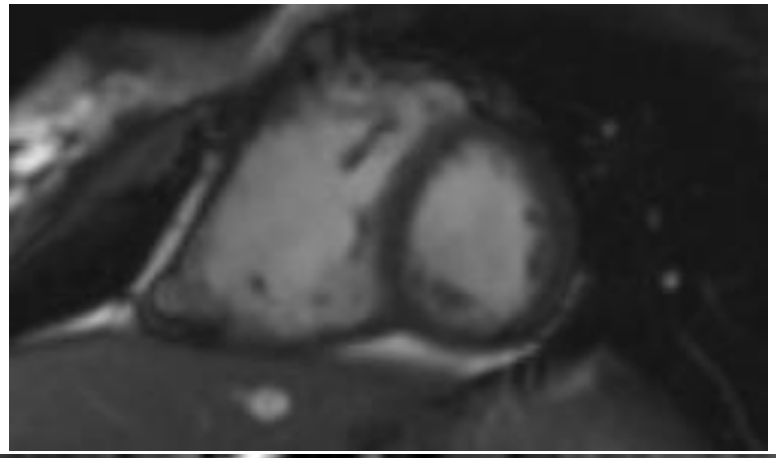
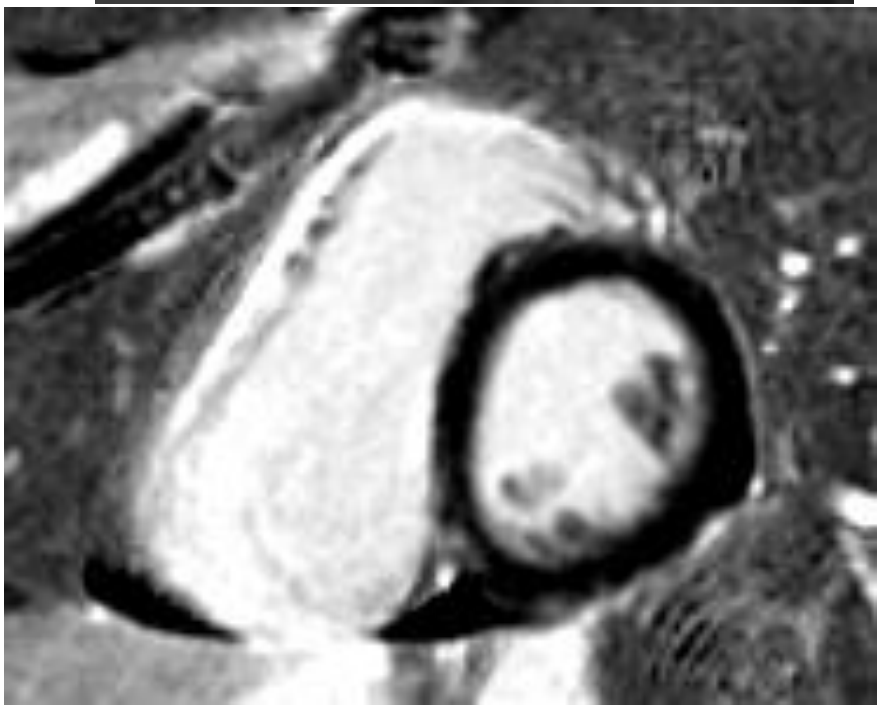
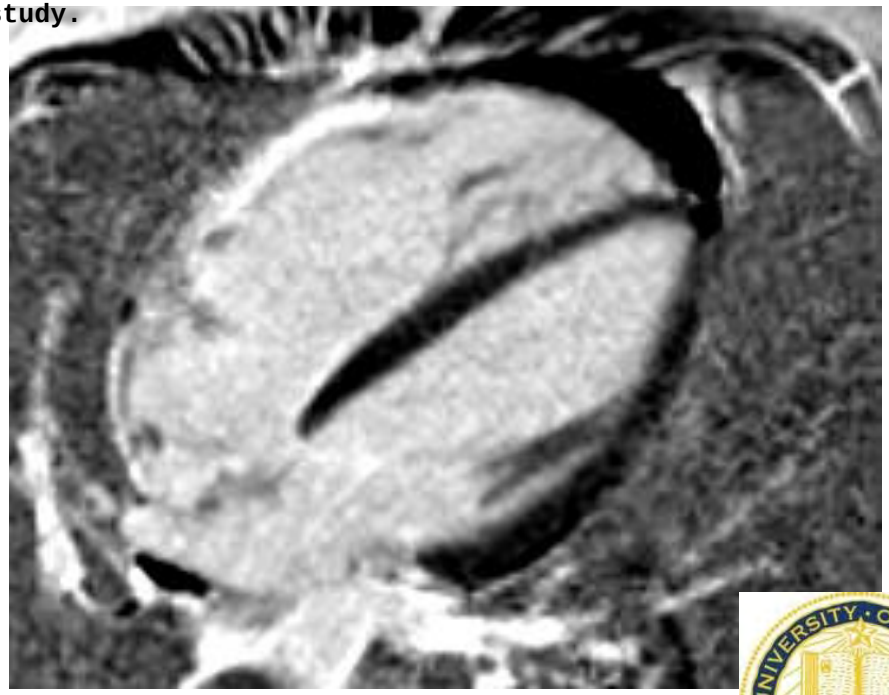
Cardiac MRI

IMPRESSION:

1. Mildly dilated right ventricle (RVEDVi 128.4 mL/m2) with moderate to severe systolic dysfunction (RVEF 30%).
2. Dyskinetic motion of the right ventricular basal to mid inferior and inferoanterior walls is noted.
3. Possible very small aneurysm of the mid inferoanterior wall.
4. Normal left ventricular size (LVEDVi 67.8 mL/m2) with low normal systolic function (LVEF 55%). No significant wall motion abnormalities are seen.
5. Extensive, nearly transmural, myocardial delayed enhancement of the right ventricle is noted.
6. No obvious left ventricular delayed enhancement is seen.
7. No obvious fatty infiltration or edema of the myocardium is noted on limited imaging.
8. No significant pericardial effusion.
9. **Per the 2020 International ("Padua") Criteria, 2 major criteria for arrhythmogenic cardiomyopathy are met on this study.**







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Diagnosis of arrhythmogenic cardiomyopathy: The Padua criteria

Domenico Corrado [a,*], Martina Perazzolo Marra [a], Alessandro Zorzi [a], Giorgia Beffagna [a], Alberto Cipriani [a], Manuel De Lazzari [a], Federico Migliore [a], Kalliopi Pilichou [a], Alessandra Rampazzo [b], Ilaria Rigato [a], Stefania Rizzo [a], Gaetano Thiene [a], Aris Anastasakis [c], Angeliki Asimaki [d], Chiara Bucciarelli-Ducci [e], Kristine H. Haugaa [f], Francis E. Marchlinski [g], Andrea Mazzanti [h], William J. McKenna [i], Antonis Pantazis [j], Antonio Pelliccia [k], Christian Schmied [l], Sanjay Sharma [m], Thomas Wichter [n], Barbara Bauce [a], Cristina Basso [a]

Table 1
"Padua criteria" for diagnosis of Arrhythmogenic Cardiomyopathy.

Category	Right ventricle (upgraded 2010 ITF diagnostic criteria)
I. Morpho-functional ventricular abnormalities	*By echocardiography, CMR or angiography:* *Major* • Regional RV akinesia, dyskinesia, or bulging *plus* one of the following: – global RV dilatation (increase of RV EDV according to the imaging test specific nomograms) – global RV systolic dysfunction (reduction of RV EF according to the imaging test specific nomograms) *Minor* • Regional RV akinesia, dyskinesia or aneurysm of RV free wall
II. Structural myocardial abnormalities	*By CE-CMR:Major* • Transmural LGE (stria pattern) of ≥1 RV region(s) (inlet, outlet, and apex in 2 orthogonal views) *By EMB (limited indications):Major* • Fibrous replacement of the myocardium in ≥1 sample, with or without fatty tissue
III. Repolarization abnormalities	*Major* • Inverted T waves in right precordial leads (V_1,V_2, and V_3) or beyond in individuals with complete pubertal development (in the absence of complete RBBB) *Minor* • Inverted T waves in leads V1 and V2 in individuals with completed pubertal development (in the absence of complete RBBB) • Inverted T waves in V1,V2,V3 and V4 in individuals with completed pubertal development in the presence of complete RBBB.
IV. Depolarization abnormalities	*Minor* • Epsilon wave (reproducible low-amplitude signalsbetween end of QRS complex to onset of the T wave) in the right precordial leads (V1 to V3) • Terminal activation duration of QRS ≥55 ms measured from the nadir of the S wave to the end of the QRS, including R', in V1, V2, or V3 (in the absence of complete RBBB)
V. Ventricular arrhythmias	*Major* • Frequent ventricular extrasystoles (>500 per 24 h), non-sustained or sustained ventricular tachycardia of LBBB morphology *Minor* • Frequent ventricular extrasystoles (>500 per 24 h), non-sustained or sustained ventricular tachycardia of LBBB morphology with inferior axis ("RVOT pattern")

Definite "dominant right" variant=
- 2 Major
- 1 Major and 2 Minor
- 4 Minor from different categories

Our patient…
- 4 Major
- 2 Minor

Clinical Diagnosis of "Definite" Dominant Right Arrhythmogenic Cardiomyopathy

- Genetic Testing pending…

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Syncope in a 17-year-old girl during a high school soccer game

"Definite" RV dominant Arrhythmogenic Cardiomyopathy by Padua Criteria

What next?

- **Medications?**
- **ICD Implant?**
- **Other Interventions→ EP Study/Ablation? Cath? Biopsy**
- **Return to Soccer?**
- **NCAA eligibility? Scholarship/School implications**

- **RESTRICTED FROM SOCCER DURING WORKUP**
- Started on Flecainide 50 mg BID
- 14 day ambulatory monitor with 9.9% PVCs and 1947 nonsustained VT runs. 1 sustained VT for 40 seconds
- Flecainide increased to 100 mg BID
- 14 day ambulatory monitor with 11.2% PVCs, but 1 run of nonsustained VT and no sustained VT
- Repeat treadmill on flecainide 100 mg BID → continued frequent PVCs and NSVT
- Started on nadolol 10 mg → 20 mg PO daily.

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GENETIC TESTING

RESULT: UNCERTAIN

Variant(s) of Uncertain Significance identified.

GENE	VARIANT	ZYGOSITY	VARIANT CLASSIFICATION
PKP2	c.2093C>A (p.Thr698Lys)	heterozygous	Uncertain Significance

About this test

This diagnostic test evaluates 100 gene(s) for variants (genetic changes) that are associated with genetic disorders. Diagnostic genetic testing, when combined with family history and other medical results, may provide information to clarify individual risk, support a clinical diagnosis, and assist with the development of a personalized treatment and management strategy.

PKP2, Exon 10, c.2093C>A (p.Thr698Lys), heterozygous, Uncertain Significance

- This sequence change replaces threonine, which is neutral and polar, with lysine, which is basic and polar, at codon 698 of the PKP2 protein (p.Thr698Lys).
- This variant is not present in population databases (gnomAD no frequency).
- This variant has not been reported in the literature in individuals affected with PKP2-related conditions.
- ClinVar contains an entry for this variant (Variation ID: 664298).
- An algorithm developed to predict the effect of missense changes on protein structure and function (PolyPhen-2) suggests that this variant is likely to be disruptive.
- In summary, the available evidence is currently insufficient to determine the role of this variant in disease. Therefore, it has been classified as a Variant of Uncertain Significance.

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HRS Consensus Statement

2024 HRS expert consensus statement on arrhythmias in the athlete: Evaluation, treatment, and return to play

Rachel Lampert, MD, FHRS, (Chair),[1,*] Eugene H. Chung, MD, MPH, MSc, FHRS, (Vice-Chair),[2,*] Michael J. Ackerman, MD, PhD,[3,*] Alonso Rafael Arroyo, MD,[15,†] Douglas Darden, MD,[4,*] Rajat Deo, MD,[5,*] Joe Dolan,[‡] Susan P. Etheridge, MD, FAHA, FHRS, FACC, CEP-S,[6,§] Belinda R. Gray, MBBS, PhD, FHRS, CCDS,[7,*] Kimberly G. Harmon, MD,[8,¶] Cynthia A. James, PhD, CGC,[9,*] Jonathan H. Kim, MD, MSc, FACC,[10,#] Andrew D. Krahn, MD, FHRS,[11,*] Andre La Gerche, MBBS, PhD,[12,**] Mark S. Link, MD, FHRS,[13,*] Ciorsti MacIntyre, MD,[3,*] Lluis Mont, MD, PhD, FEHRA,[14,††] Jack C. Salerno, MD, FHRS,[16,‡‡] Maully J. Shah, MBBS, FHRS, CCDS, CEPS-P[17,‡‡]

Figure 2
Model for shared decision-making for athletes with cardiovascular disease. In the team-physician-led decision-making process, physicians incorporate shared decision-making, guided by respect for patients' goals and preferences, while integrating collaborative discussion among the athlete, family, treating physician, team physician, additional experts, and other institutional stakeholders (athletic departments and athletic trainers) in balancing risk-tolerances. SCA = sudden cardiac arrest. Reprinted with permission from Martinez et al.[53]

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Shared Decision-Making
Genotype: Low-risk? High-risk? Or Genotype negative?

Recommendations for complex ventricular arrhythmias

COR	LOE	Recommendations
2a	C-LD	8. In athletes with ventricular arrhythmias and nonfamilial and/or genotype-negative phenotype-positive ARVC (presumed exercised induced), catheter ablation and/or ICD is reasonable after appropriate risk stratification.[307]

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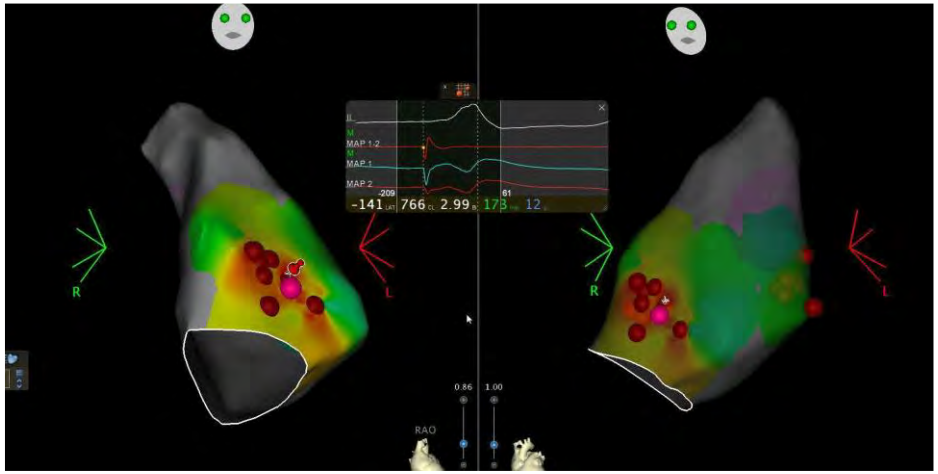
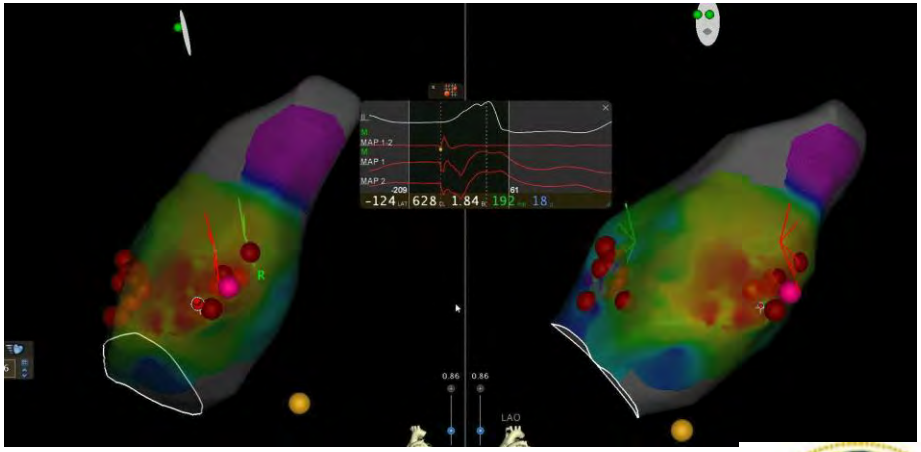
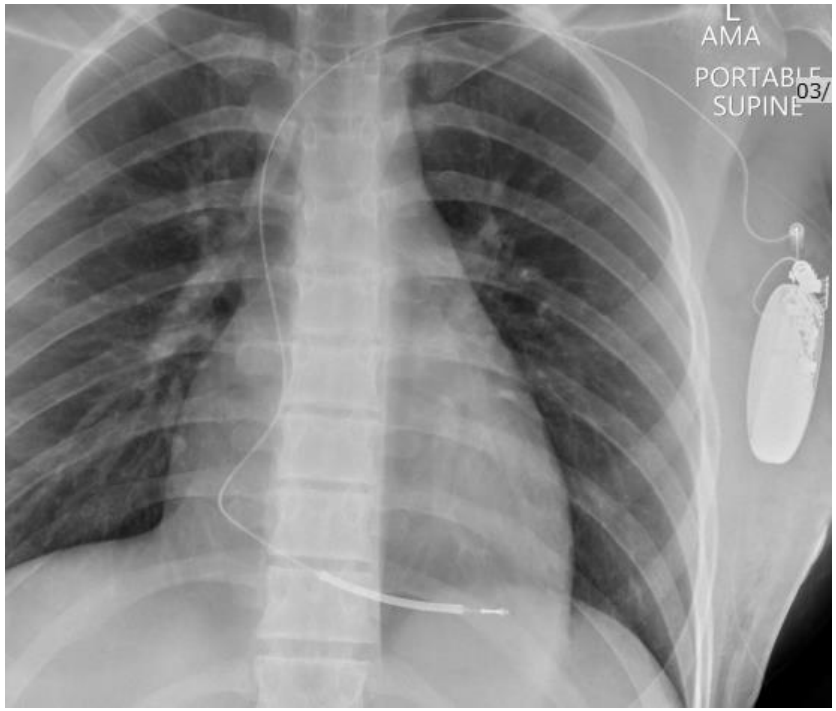
EPS and ablation of 2 distinct focuses in the RVOT





And…

Implantation of a transvenous, single chamber ICD



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Shared Decision Making
Genotype: Low-risk? High-risk? Or Genotype negative?

Recommendations for management specific to athletes with arrhythmogenic and dilated cardiomyopathies

1	B-NR	3. In athletes with phenotype-positive ACM, sports participation should be tailored to patient's genotype and the intensity and duration of sport.[27,425–429]
2b	C-LD	4. In athletes with phenotype-positive ACM and a lower-risk genotype, participation in vigorous endurance sports may be considered.[439]
3: Harm	B-NR	5. In athletes with phenotype-positive ACM and higher-risk genotypes, participation in vigorous endurance sports is potentially harmful.[27]
3: Harm	B-NR	6. In athletes with nonfamilial and/or genotype-negative phenotype-positive ARVC (presumed exercised induced), continuation of vigorous endurance sports is harmful.[305,328]

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2024 HRS expert consensus statement on arrhythmias in the athlete: Evaluation, treatment, and return to play

Rachel Lampert, MD, FHRS, (Chair),[1,*] Eugene H. Chung, MD, MPH, MSc, FHRS, (Vice-Chair),[2,*] Michael J. Ackerman, MD, PhD,[3,*] Alonso Rafael Arroyo, MD,[15,†] Douglas Darden, MD,[4,*] Rajat Deo, MD,[5,*] Joe Dolan,[‡] Susan P. Etheridge, MD, FAHA, FHRS, FACC, CEP-S,[6,§] Belinda R. Gray, MBBS, PhD, FHRS, CCDS,[7,*] Kimberly G. Harmon, MD,[8,¶] Cynthia A. James, PhD, CGC,[9,*] Jonathan H. Kim, MD, MSc, FACC,[10,#] Andrew D. Krahn, MD, FHRS,[11,*] Andre La Gerche, MBBS, PhD,[12,**] Mark S. Link, MD, FHRS,[13,*] Ciorsti MacIntyre, MD,[3,*] Lluis Mont, MD, PhD, FEHRA,[14,††] Jack C. Salerno, MD, FHRS,[16,‡‡] Maully J. Shah, MBBS, FHRS, CCDS, CEPS-P[17,‡‡]

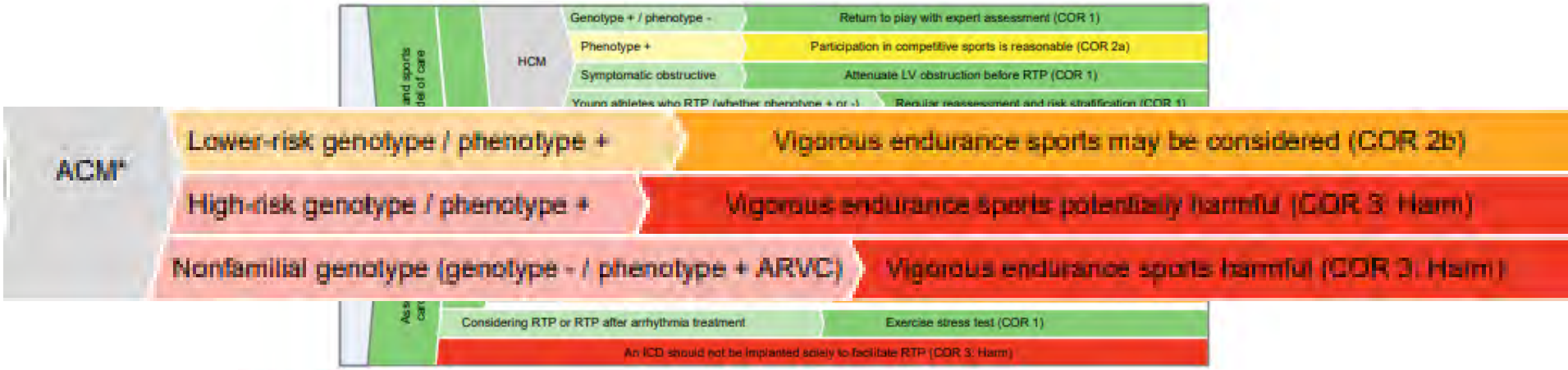

Figure 13
Recommendations for athletes with inherited cardiomyopathies returning to play. Colors correspond to the class of recommendation (COR) in Table 1. *Tailor management to genotype. ACM = arrhythmogenic cardiomyopathy; ARVC = arrhythmogenic right ventricular cardiomyopathy; DCM = dilated cardiomyopathy; GDMT = guideline-directed medical therapy; HCM = hypertrophic cardiomyopathy; ICD = implantable cardioverter-defibrillator; LV = left ventricular; LVEF = left ventricular ejection fraction; RTP = return to play.

CHOC Children's.

THE UNIVERSITY OF CALIFORNIA IRVINE

Rady Children's Health

Syncope in a 17-year-old girl during a high school soccer game

- On flecainide 100 mg PO BID and nadolol 20 mg daily after ablation of 2 PVC populations and implant of single-chamber ICD…
- Repeat treadmill with increasing single PVCs with increasing HR, couplets and triplets at max HR 125 bpm (betablocker effect). No VT
- Repeat ambulatory monitor with 5% PVCs, no VT. Max HR 153 bpm.

Who would let her play?

A. No

B. Yes, but only after informed discussion and review of literature and clear delineation of risks and acknowledgement of understanding of those risks

CHOC Children's.

THE UNIVERSITY OF CALIFORNIA IRVINE

Rady Children's Health

Arrhythmogenic Cardiomyopathy in a Teenage Elite Soccer Player: What I Did…

“After the procedure [stress test on nadolol 20 mg and flecainide 100 mg BID], I sat down with *****, her mother and her grandmother and reviewed this study. We also reviewed more data on arrhythmogenic cardiomyopathy and exercise. Finally we reviewed the recently published 2024 HRS Sports Cardiology and Return to Play document (*Heart Rhythm* May 2024). This specifies that with **symptomatic PKP2 + and phenotype + arrhythmogenic cardiomyopathy** that high level exertion **is "likely harmful."**

We discussed that although ***** is likely now medically treated for arrhythmias and her arrhythmia/sudden cardiac death risk is low, **high-level exercise will almost certainly accelerate her underlying disease**. We discussed that this could mean **worsening arrhythmias requiring escalation of medical therapies and potential invasive ablation procedures, appropriate ICD shocks, escalation of ventricular scarring and worsening ventricular function requiring heart failure therapies, and potentially even future heart transplant.**

That being said, **using "shared-decision making" and a "shared risk" approach** described in published guidelines, Emily **may return** to training and competitive soccer while **acknowledging the potential harm and escalation of her underlying arrhythmogenic cardiomyopathy.**

I recommended an advanced **genetic-cardiomyopathy specialty consultation**, and with the family's permission, I will reach out to colleagues and experts across the country for other opinions and recommendations.”

CHOC Children's.

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Rady Children's Health

SADS case Presentation

Abdullah Sarkar MD

Claire Newlon MD

Yaniv Bar-Cohen MD

Jeremy Moore MD

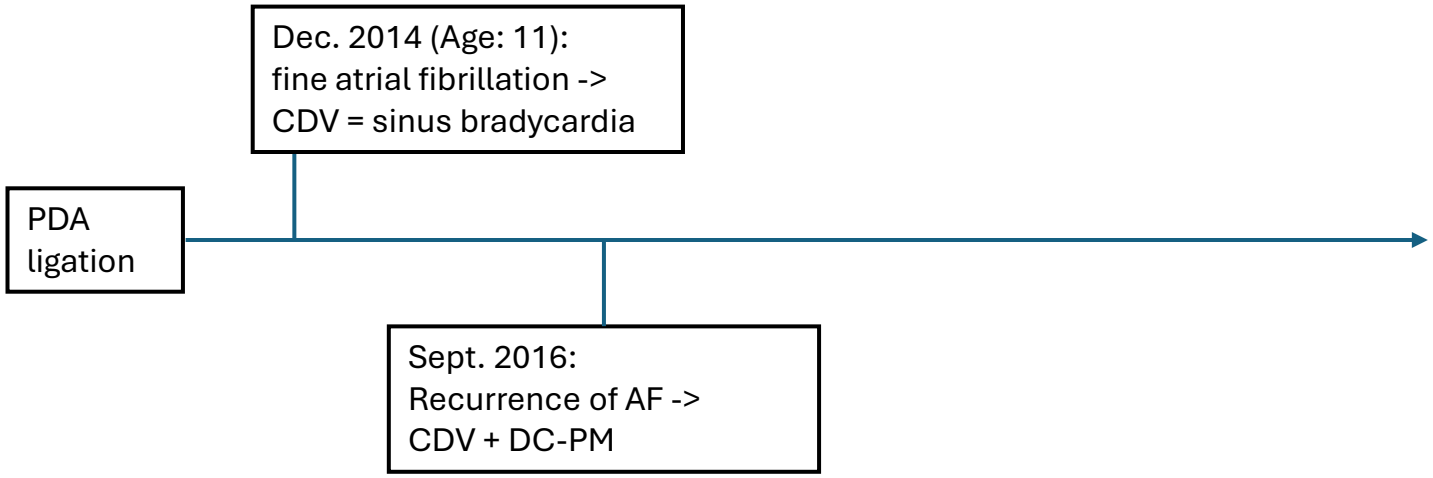
Case Profile

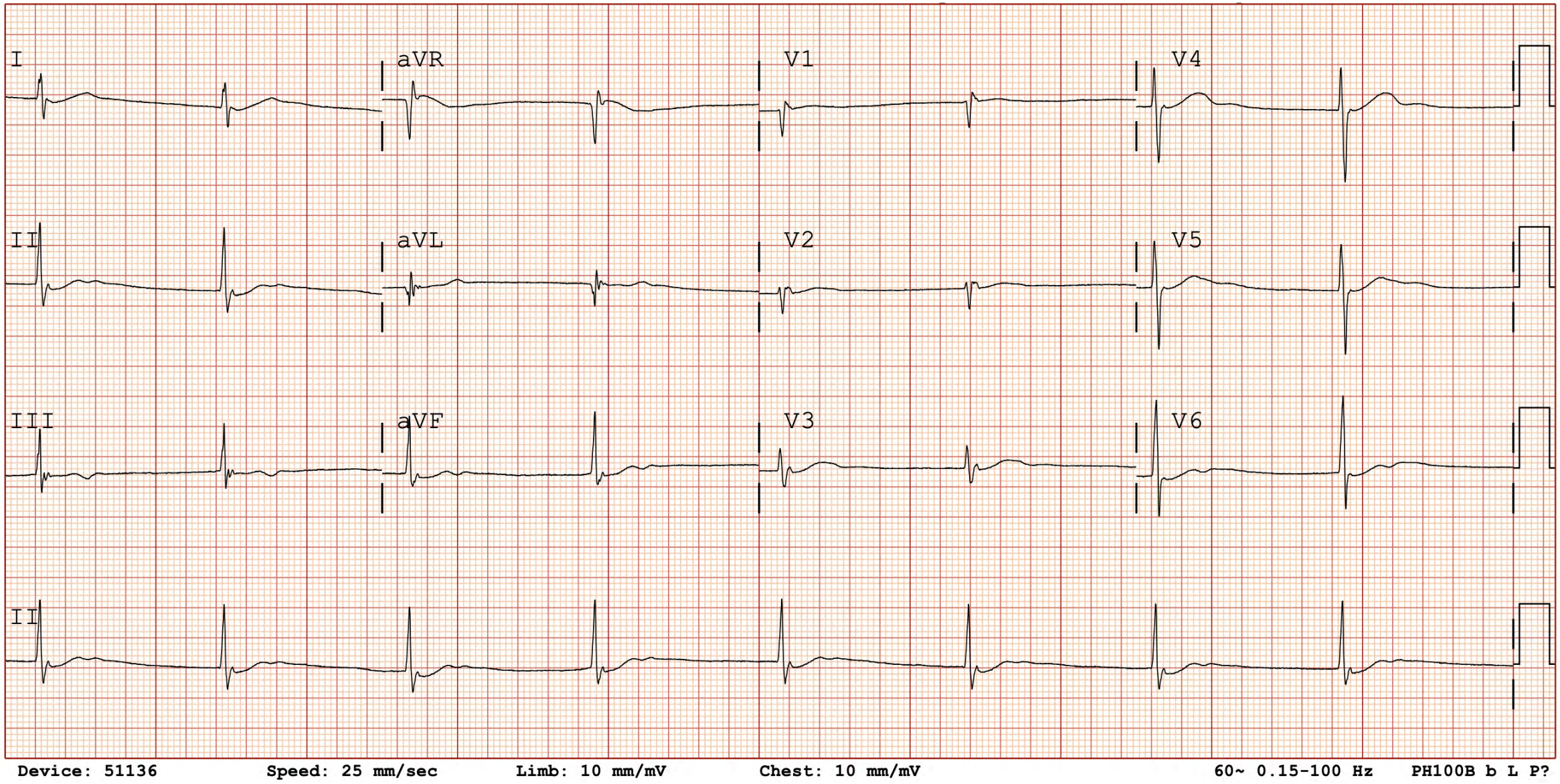
- 21-year-old female was referred to our center for management of persistent AF.

- Prior history of surgical PDA ligation as an infant.

- She was noted to have sinus node dysfunction and paroxysmal AF at age 13 years resulting in dual chamber pacemaker placement.

Clinical Timeline

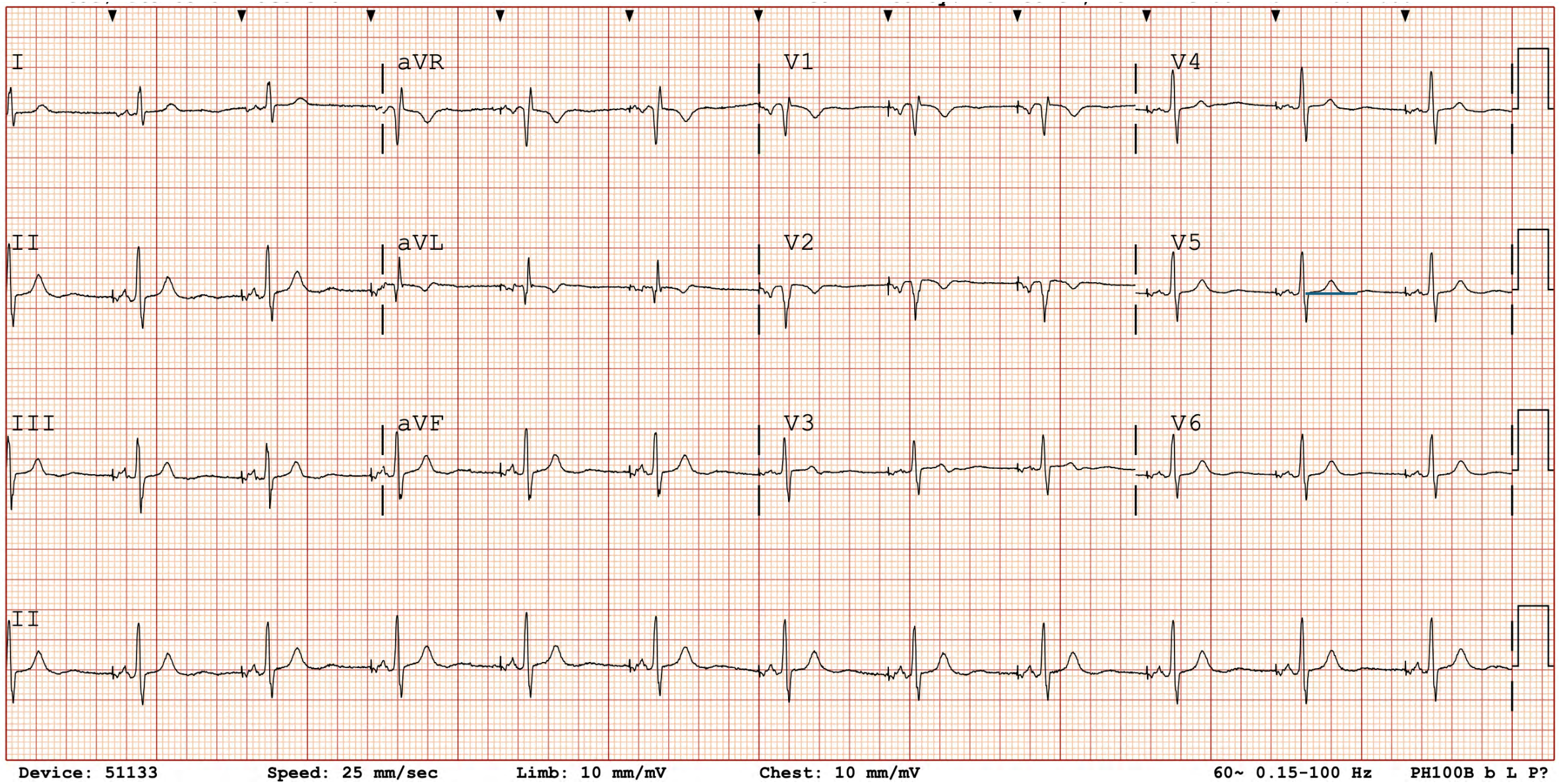



I
aVR
V1
V4
II
aVL
V2
V5
III
aVF
V3
V6
II
Device: 51136
Speed: 25 mm/sec
Limb: 10 mm/mV
Chest: 10 mm/mV
60~ 0.15-100 Hz
PH100B b L P?

ARS: Question 1

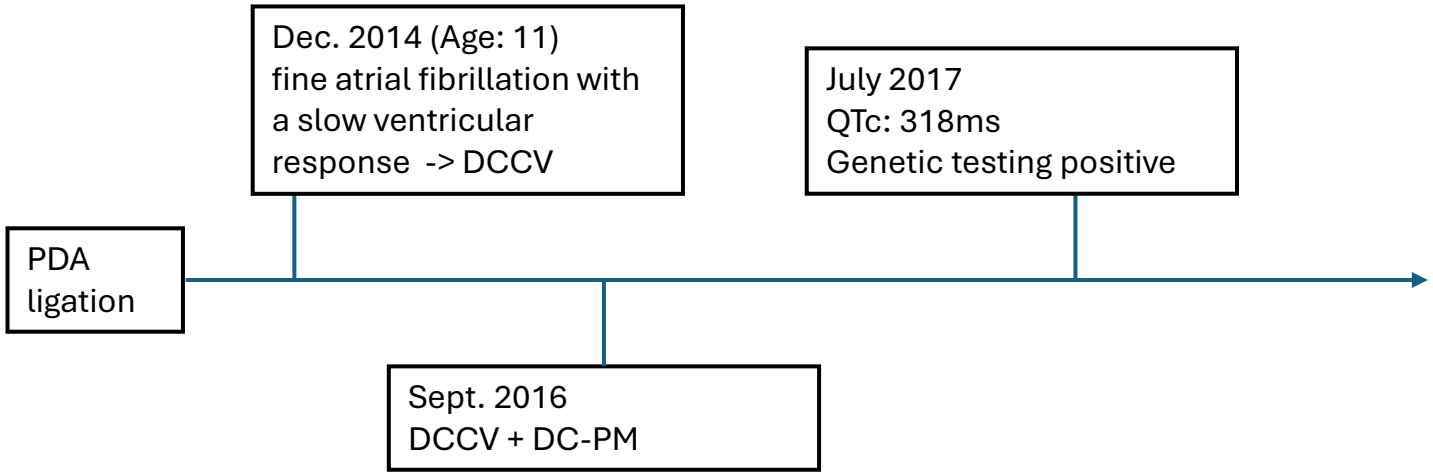
- In the setting of a child with bradycardia and AF, what differential would you consider:

1. Brugada Syndrome
2. Concealed accessory pathway
3. Short-QT syndrome
4. Titin cardiomyopathy


I
aVR
V1
V4
II
aVL
V2
V5
III
aVF
V3
V6
II
Device: 51133
Speed: 25 mm/sec
Limb: 10 mm/mV
Chest: 10 mm/mV
60~ 0.15-100 Hz
PH100B b L P?

QTC: 318ms

Clinical Events



PM check: 1/5/17
Pacemaker/ICD Events:

1 episode of ventricular ectopy / slow VT
(4 beats, CLs 398 – 500) 829 ms, 434 ms, 398 ms, 500 ms).

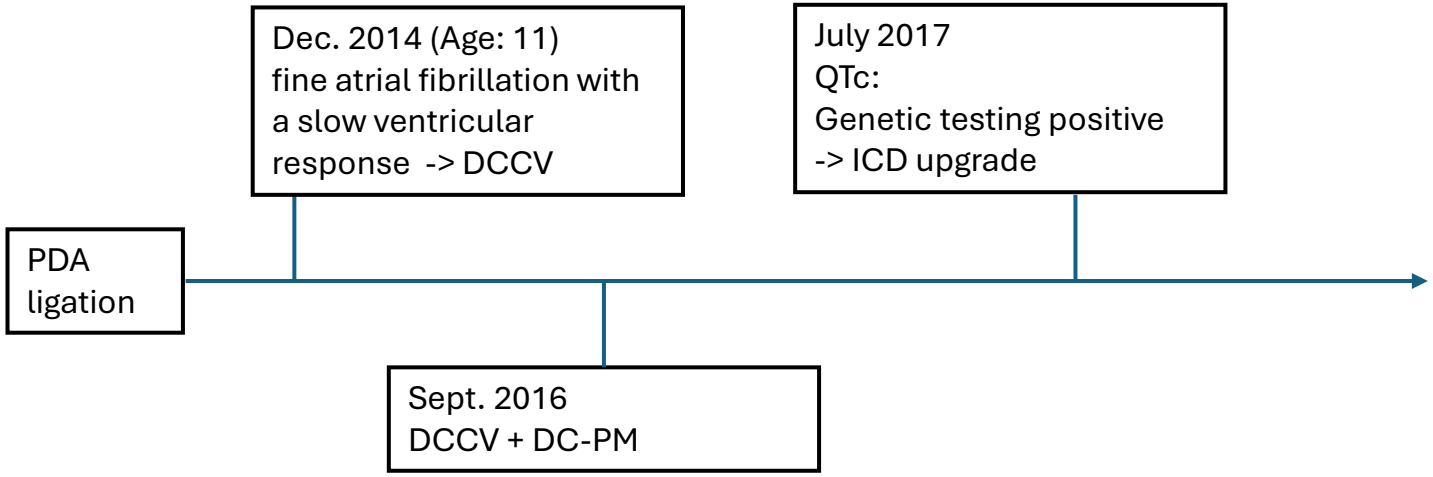
Additionally, runs of atrial tachycardia seen on EGM.

ARS: Question 2

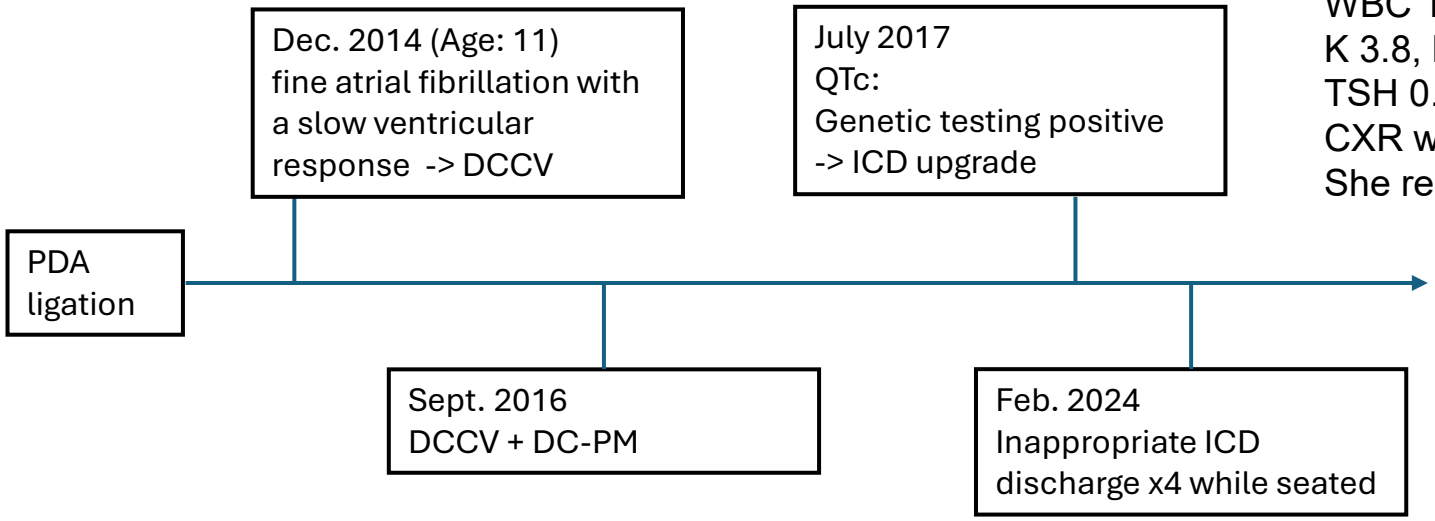
- Gene testing result: KCNQ1 c.421G>A (p.Val141Met), what would you do next?

1. Upgrade device to defibrillator now
2. Restrict from competitive sports
3. Start Quinidine
4. Continue clinical monitoring

Clinical Events



Clinical Events



Labs obtained:
WBC 11.7, H/H 12.1/36.3, Plt 298, PT 13.2/INR 1.03, aPTT 26.9, Na 139, K 3.8, BUN/Cr 14/0.69, Mg 1.7, lactate 1.3 mmol/L, troponin 0.035 ng/mL, TSH 0.916, FT4 1.09.
CXR without focal consolidation.
She received magnesium repletion and received a Heparin bolus.

Failure of DCCV for AF using amiodarone, procainamide, ibutilide, and dual defibrillation shocks

Significant bradycardia and increased ventricular pacing burden with beta-blocker therapy (shown in next slides).

Female Hispanic

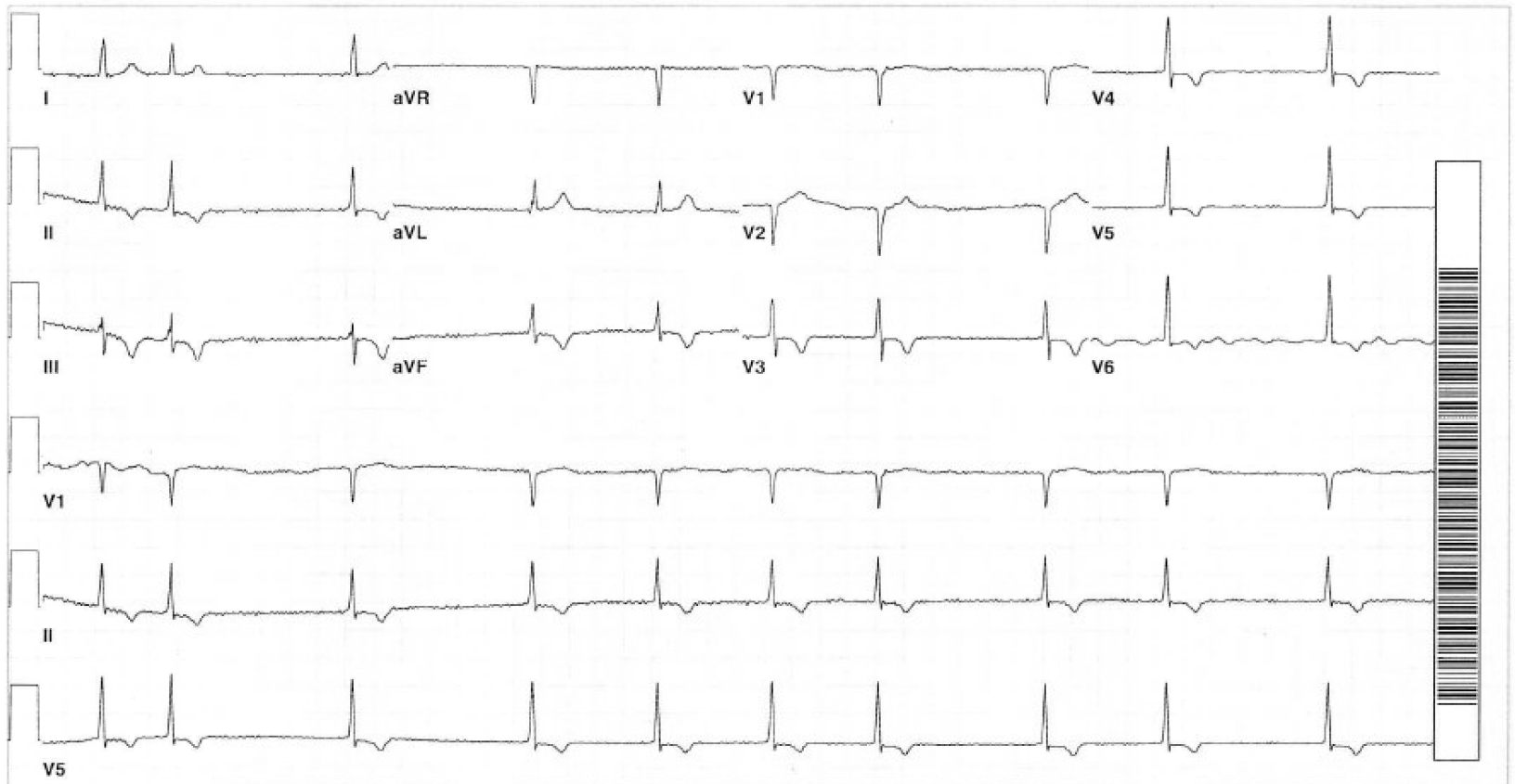
Room:WMP330B
Loc:48

PR interval		ms	Abnormal Q suggests anterior infarct
QRS duration	78	ms	Abnormal T, consider ischemia, diffuse leads
QT/QTcB	337/345	ms	12 Lead; Mason-Likar
P-R-T axes	* 21	-63	Abnormal ECG

V1 3D

Technician:
Test ind:

Unconfirmed



25mm/s 10mm/mV 100Hz 10.1.5 12SL NO SERIAL CID: 0

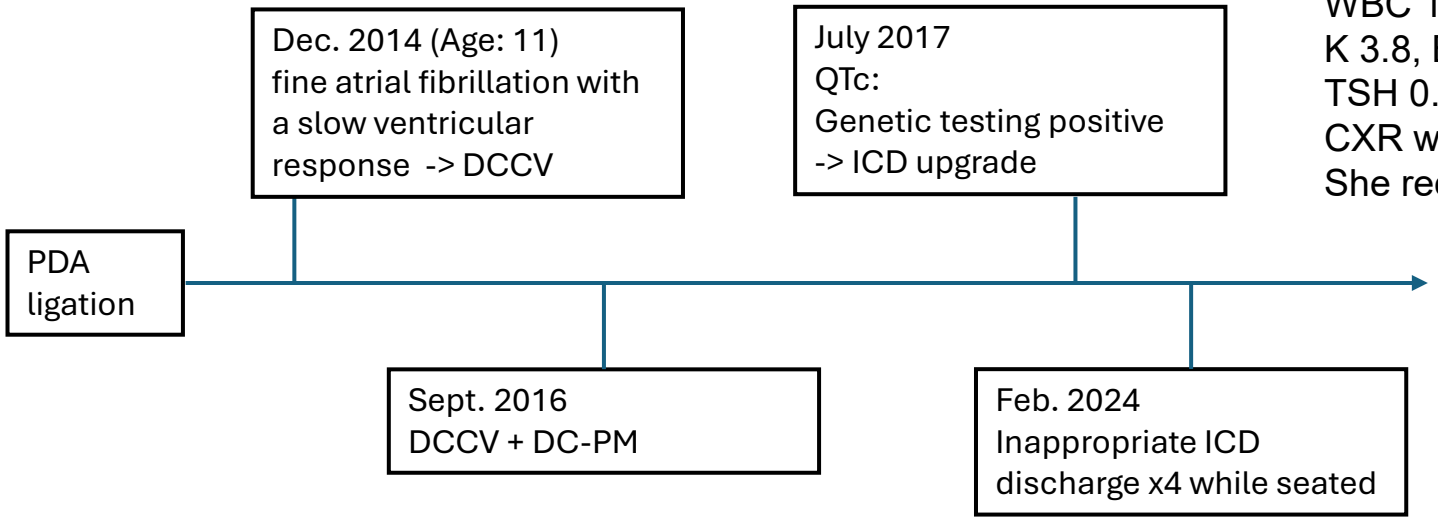
EID: EDT: ORDER: ACCOUNT: 90204620230

ARS: Question 3

- Given inappropriate shocks related to rapidly conducted AF, inability to achieve rhythm control, and poor tolerance of AV nodal agents, what would you do next?

1. Conduction system pacing + AV node ablation
2. Pursue rate control (despite VVI pacing)
3. Catheter ablation
4. Surgical Maze operation

Clinical Events



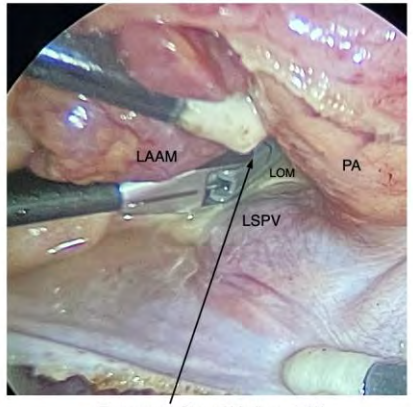
Labs obtained:
WBC 11.7, H/H 12.1/36.3, Plt 298, PT 13.2/INR 1.03, aPTT 26.9, Na 139, K 3.8, BUN/Cr 14/0.69, Mg 1.7, lactate 1.3 mmol/L, troponin 0.035 ng/mL, TSH 0.916, FT4 1.09.
CXR without focal consolidation.
She received magnesium repletion and received a Heparin bolus.

Failure of DCCV for AF using amiodarone, procainamide, ibutilide, and dual defibrillation shocks

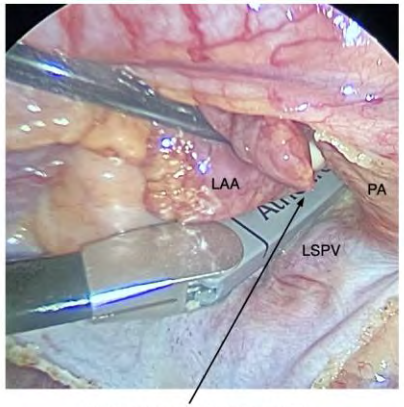
➔ atenolol, rivaroxaban
➔ referred for ablation

Epicardial Ablation

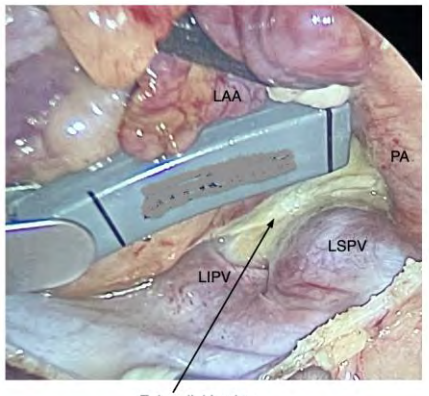
- Patient remained in persistent AF, 5 months.
- The posterior pericardium was accessed via subxiphoid approach.
- A unipolar vacuum-assisted linear RF ablation catheter delivered a series lesions covering the posterior left atrium.
- Confluent scar was confirmed by high-density electroanatomic mapping.
- An 85 mm clip was placed for left atrial appendage exclusion.
- Cardioversion remained unsuccessful despite amiodarone load.



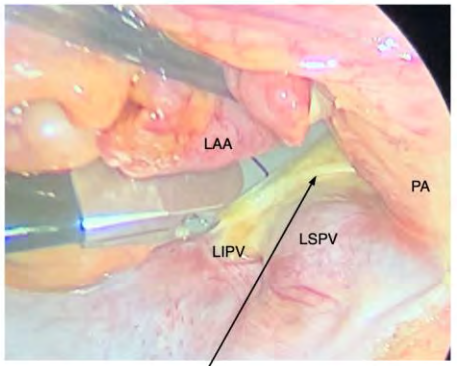
Transverse Sinus Ablatiion - 30W



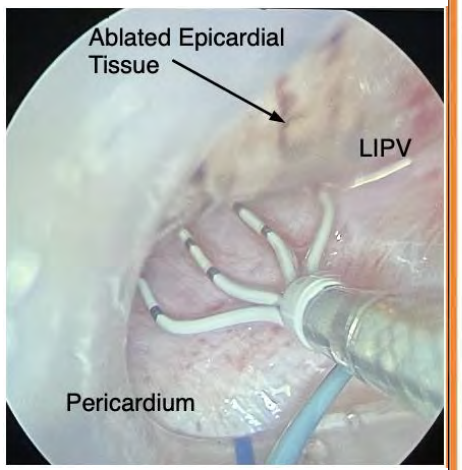
LAA Base / LSPV Ablation - 30W



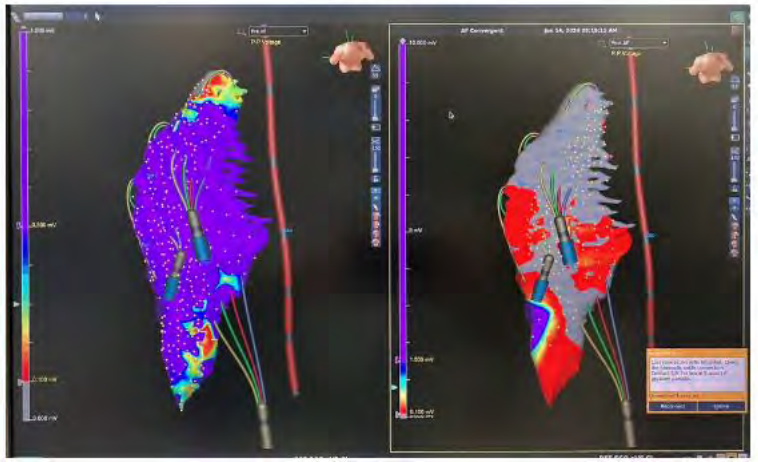
Epicardial Lesion



Ablated Ligament of Marshall

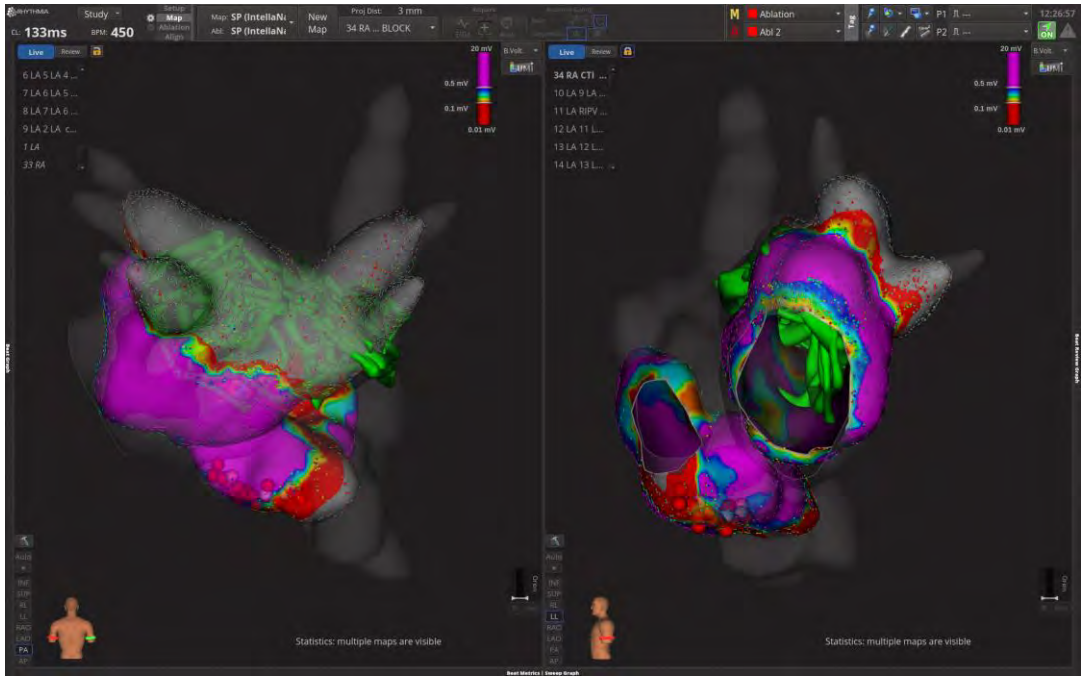


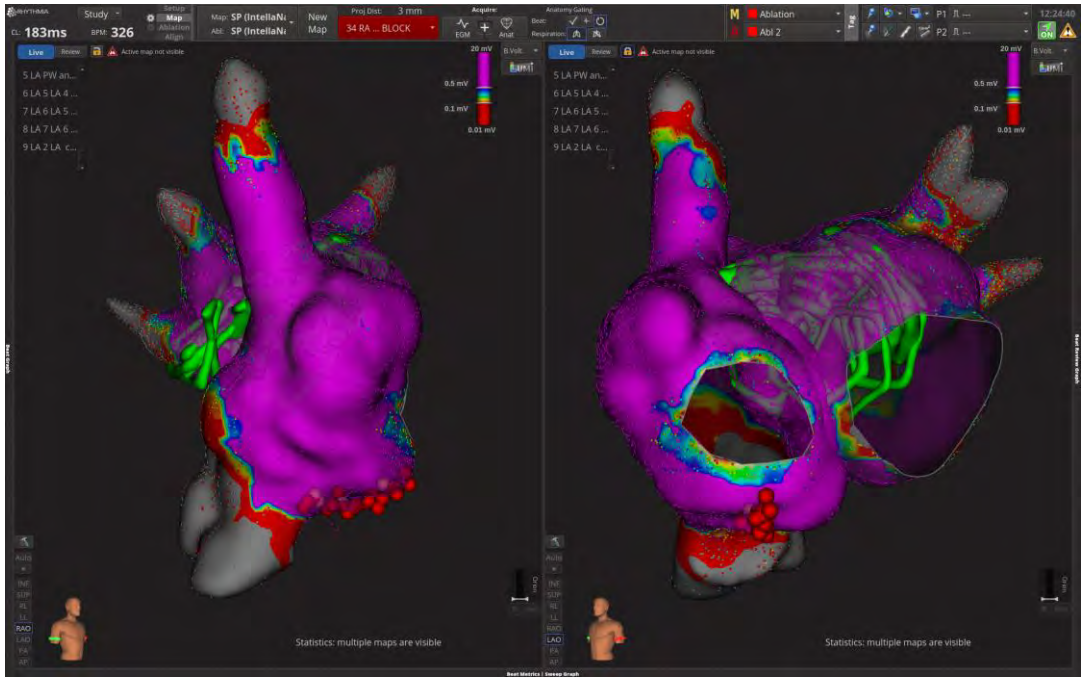
Pre / Post

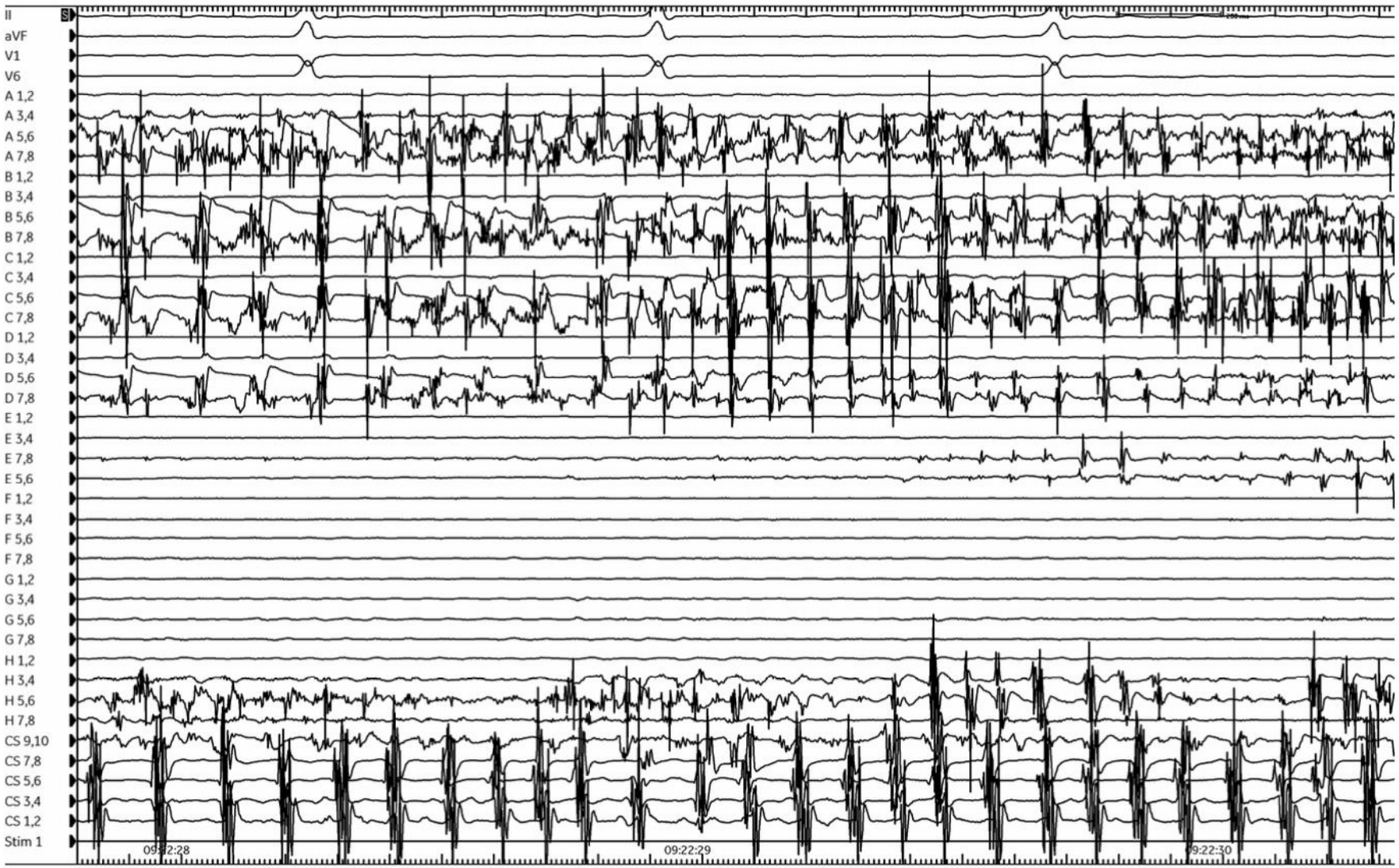


Endocardial Ablation

- Patient returned six weeks later in rate-controlled AF, again, unresponsive to synchronized cardioversion (200J).
- A 3D map of the left atrium demonstrated densely scarred posterior wall with no EGMs.
- Pulmonary vein and posterior wall isolation were completed with pulsed-field ablation.







SS. Baseline through Orion

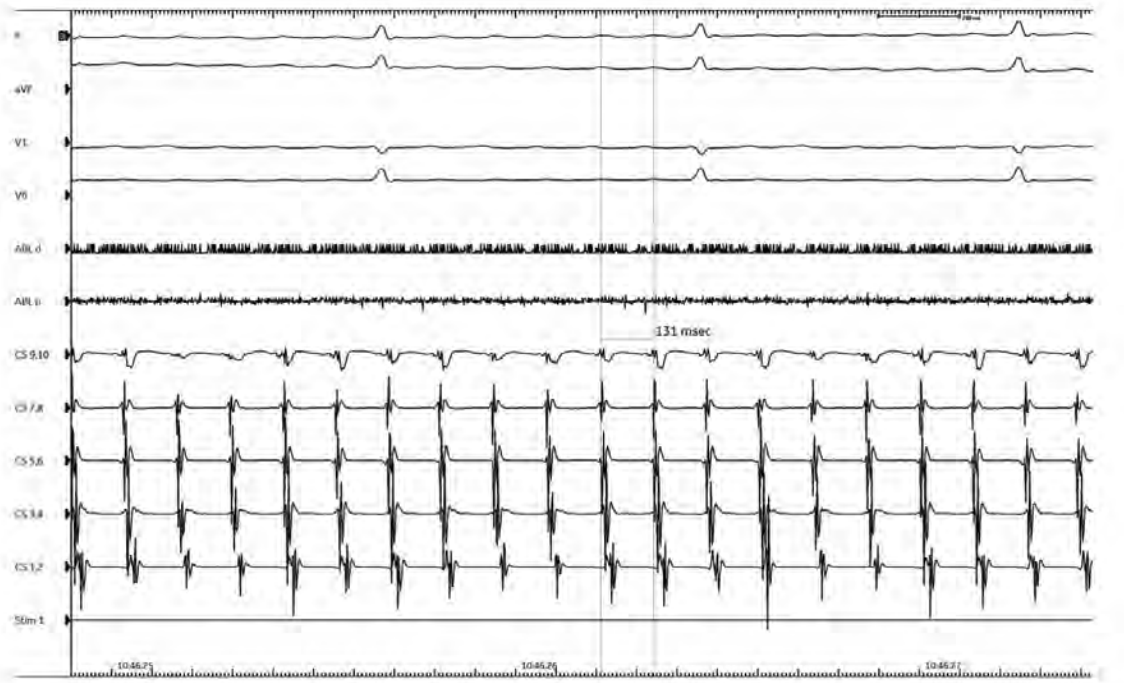
Sweep speed: 400 mm/sec

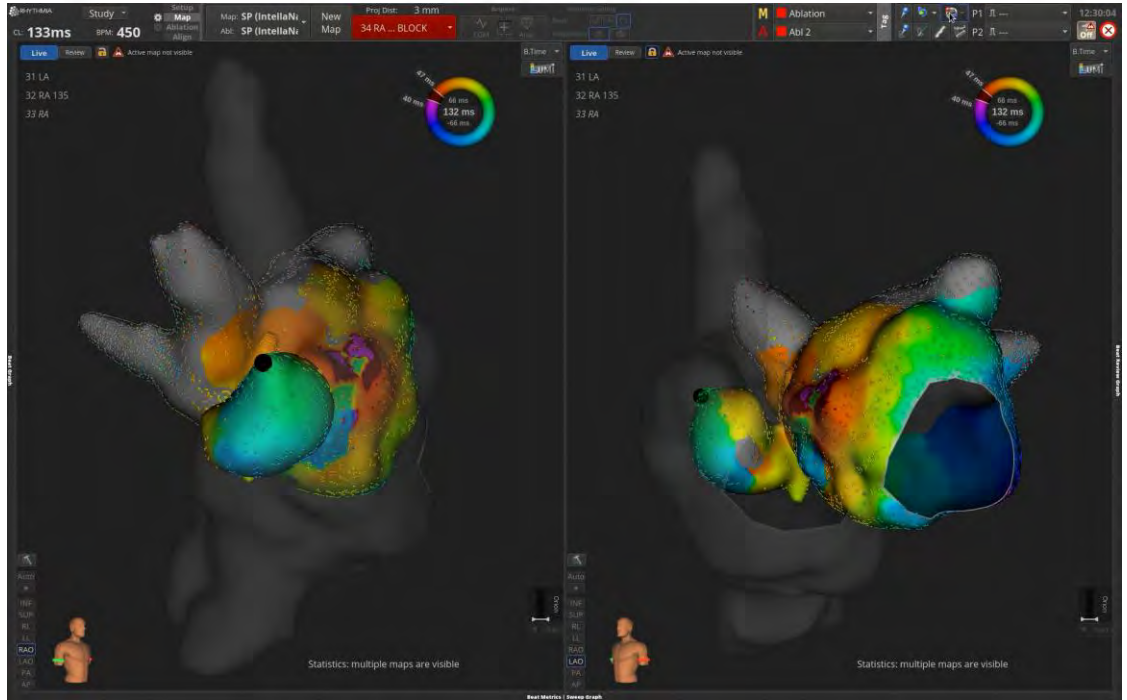
Ultra-rapid fibrillatory waves with unipolar EGMs = 35-55 ms encountered at LA roof and lateral wall

Endocardial Ablation

- Repeat cardioversion (200J) then resulted in an organized ultra-rapid atrial tachycardia (CL 130 ms) that could be reproducibly mapped to the atrial septum but terminated with catheter manipulation.

- CTI ablation was performed, and the patient was discharged home on sotalol with atrial paced rhythm.





Discussion

- Case of 21yo F with SQTS (KCNQ1 c.421G>A (p.Val141Met), sinus node dysfunction, and persistent atrial fibrillation refractory to several anti-arrhythmic drugs and multiple cardioversion attempts.

- Cardiac MRI demonstrated a structurally normal heart.

- Epi-endo catheter ablation (“convergent procedure”) resulted in cessation of AF on short-term follow up of 8 months.

Volume 43, Issue 40
21 October 2022

Article Contents

JOURNAL ARTICLE GUIDELINES

2022 ESC Guidelines for the management of patients with ventricular arrhythmias and the prevention of sudden cardiac death: Developed by the task force for the management of patients with ventricular arrhythmias and the prevention of sudden cardiac death of the European Society of Cardiology (ESC) Endorsed by the Association for European Paediatric and Congenital Cardiology (AEPC) FREE

Risk stratification, SCD prevention and treatment of VA		
ICD implantation is recommended in patients with a diagnosis of SQTS who: (a) are survivors of an aborted CA and/or (b) have documented spontaneous sustained VT.[1063]	I	C
ILR should be considered in young SQTS patients.	IIa	C
ICD implantation should be considered in SQTS patients with arrhythmic syncope.	IIa	C
Quinidine may be considered in (a) SQTS patients who qualify for an ICD but present a contraindication to the ICD or refuse it, and (b) asymptomatic SQTS patients and a family history of SCD.[1069–1071]	IIb	C
Isoproterenol may be considered in SQTS patients with an electrical storm.[1075]	IIb	C
PES is not recommended for SCD risk stratification in SQTS patients.	III	C

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Long-Term Follow-Up of a Pediatric Cohort With Short QT Syndrome

Table 3 Characteristics of All Patients

Variable	Total (n = 25)	Symptomatic* (n = 14)	Asymptomatic (n = 11)	p Value
Patient age at presentation (yrs)	15 (9–18)	15 (8–17)	17 (9–18)	0.621
Age <12 yrs	9 (36%)	4 (28.6%)	5 (45.5%)	0.434
Male	21 (84%)	11 (78.6%)	10 (90.9%)	0.604
Follow-up duration (yrs)	5.9 (4.4–7.1)	5.7 (4.8–7.4)	6.1 (3.2–6.9)	0.460
Symptoms				
Aborted SCD	6 (24%)	6 (43%)	—	
Unheralded syncope	4 (16%)	4 (28.5%)	—	
Palpitations†	4 (16%)	4 (28.5%)	—	
Modified Gollob score	5 (4–5)	5 (4–6)	4 (4–5)	**0.044**
Genetic mutation				
KCNH2	2 (8%)	2 (14%)	0	
KCNJ2	2 (8%)	2 (14%)	0	
KCNQ1	1 (4%)	1 (7%)	0	
ECG parameters				
QT (ms)	290 (280–300)	280 (200–300)	295 (280–320)	0.333
QTc (ms)	312 (286–335)	306 (252–329)	330 (292–335)	0.207
J point-to-T peak interval (ms)	140 (119–160)	130 (80–160)	140 (120–160)	0.344
J point-to-T peak interval <120 (ms)	7 (28%)	6 (42.9%)	1 (9.1%)	0.090
Early repolarization	12/24 (50%)	6/14 (43%)	6/10 (60%)	0.680
Family history				0.620
SQTS	8 (32%)	4 (28.6%)	4 (36.4%)	
SCD	4 (16%)	3 (21.4%)	1 (9.1%)	
SCD and SQTS	9 (36%)	4 (28.6%)	5 (45.5%)	
Negative	4 (16%)	3 (21.4%)	1 (9.1%)	
ICD	11 (44%)	8 (57.1%)	3 (27.3%)	0.227
Appropriate shocks	2 (18%)	2 (25%)	0	
Inappropriate shock	7 (63.6%)	4 (50%)	3 (100%)	
Complications‡	9 (81.8%)	6 (75%)	3 (100%)	

Values are median (interquartile range) or n (%). *Only patients with aborted sudden cardiac death, syncope, or documented ventricular or atrial fibrillation at presentation or during follow-up were considered symptomatic for short QT syndrome. †Palpitations and atrial fibrillation or supraventricular tachycardia. ‡Including inappropriate shocks.

ECG = electrocardiography; ICD = implanted cardiac defibrillator; J point-to-T peak interval = interval in milliseconds measured on standard electrocardiography ECG from the J-point to the peak T-wave voltage; SCD = sudden cardiac death. Other abbreviations as in Table 1.

2005

De novo *KCNQ1* mutation responsible for atrial fibrillation and short QT syndrome in utero Get access

Kui Hong , David R. Piper , Aurora Diaz-Valdecantos , Josep Brugada , Antonio Oliva , Elena Burashnikov , José Santos-de-Soto , Josefina Grueso-Montero , Ernesto Diaz-Enfante , Pedro Brugada ... Show more

AF in utero with concomitant bradycardia, short QT interval.

2008

Mechanisms by which atrial fibrillation-associated mutations in the S1 domain of KCNQ1 slow deactivation of I_{Ks} channels

Lioara Restier, Lan Cheng, Michael C. Sanguinetti

p.V141 causes AF and SQTS.

2012

Characterization of KCNQ1 atrial fibrillation mutations reveals distinct dependence on KCNE1

Priscilla J. Chan,[1] Jeremiah D. Osteen,[1] Dazhi Xiong,[1] Michael S. Bohnen,[1] Darshan Doshi,[2] Kevin J. Sampson,[1] Steven O. Marx,[1,2] Arthur Karlin,[3,4] and Robert S. Kass[1]

markedly shorten APD.

2013

Long-Term Follow-Up of a Pediatric Cohort With Short QT Syndrome

Juan Villafañe, MD,* Joseph Atallah, MD, CM, SM,† Michael H. Gollob, MD,‡

3 of 25 patients had SQTS and AF.

2014

Short QT Syndrome Manifesting with Neonatal Atrial Fibrillation and Bradycardia

Subject Area: Cardiovascular System

Juan Villafañe; Peter Fischbach; Roman Gebauer

2 neonates with AF, slow ventricular response, SQTS. p.V141M mutation in the *KCNQ1* gene.

HeartRhythm Case Reports
Volume 1, Issue 4, July 2015, Pages 193-197

Short QT and atrial fibrillation: A *KCNQ1* mutation–specific disease. Late follow-up in three unrelated children

Georgia Sarquella-Brugada MD [*], Oscar Campuzano PhD [†‡], Anna Iglesias MSc [†], Josefina Grueso MD, PhD [§], David J. Bradley MD [‖], Gunter Kerst MD, PhD [¶], Daniel Shmorhun MD, PhD [**], Josep Brugada MD, PhD [*††], Ramon Brugada MD, PhD [†‡‡‡]

Patient 1
- Intrauterine AF
- At birth, short QTc and AF refractory to CDV
- Age 2.5, symptomatic sinus pauses -> PM
- 1 year later with DCM -> epicardial LV lead
- Age 8, SCD

Patient 2
- Fetal bradycardia
- CS delivery pre-term, short QTc and AF refractory to CDV + quinidine
- Epicardial DDD device. Slightly dilated LV on follow up, 8 years.

Patient 3
- Fetal bradycardia
- Elective CS delivery, short QTc and AF
- Age 0-4, after initial failure to CDV, recurrence on amiodarone then flecainide
- Age 9, remains in AF, mild LV dilatation, severe aortic root dilatation

Thank you

Familial Idiopathic Ventricular Fibrillation

Shankar Baskar, MD, FHRS
Pediatric & Congenital Electrophysiology
Assistant Professor of Pediatrics
Cincinnati Children's Hospital, Cincinnati, OH

Cincinnati Children's
changing the outcome together

Proband

- 16-year-old female with no prior history and who is a refugee from Ethiopia collapsed at home.
- She had no prior recent illness and was not active and had interacted with the family 10 minutes before being found collapsed.
- She was in VF upon EMS arrival and CPR was initiated. She achieved ROSC in the ED after receiving multiple antiarrhythmics (lidocaine, amiodarone and esmolol) and multiple shocks with a prolonged downtime.
- Echo with moderate biventricular dysfunction but structurally normal heart in the context of prolonged downtime
- An ECG was unable to be obtained with an estimated QTc of 470 msec on telemetry.
- Frequent PVCs were noted with coupling intervals of 300 – 400 msec, that initiated runs of polymorphic VT (PVT)
- She was transferred to the PICU and continued to have refractory PVT and VF, ultimately resulting in her death.

Proband – Patient #1

16-year-old female, refugee from Ethiopia, previously healthy

Event: Sudden collapse at home

EMS: Found in **VF**, received CPR, multiple shocks, and antiarrhythmics (lidocaine, amiodarone, esmolol)

ROSC achieved in ED after prolonged downtime

Echo: Moderate biventricular dysfunction, no structural abnormality

Telemetry: QTc ~470 ms, frequent **PVCs** (CI 300–400 ms) triggering polymorphic VT

Outcome: Refractory VF despite escalation; patient died

Autopsy: Unremarkable

Genetics: Heterozygous **VUS in TRDN** (c.2030T>G, p.Val677Gly)

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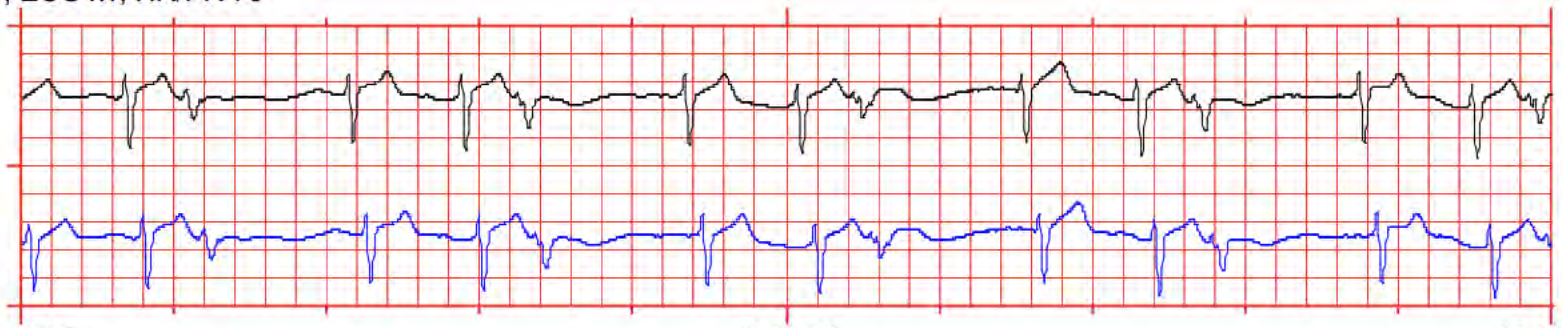
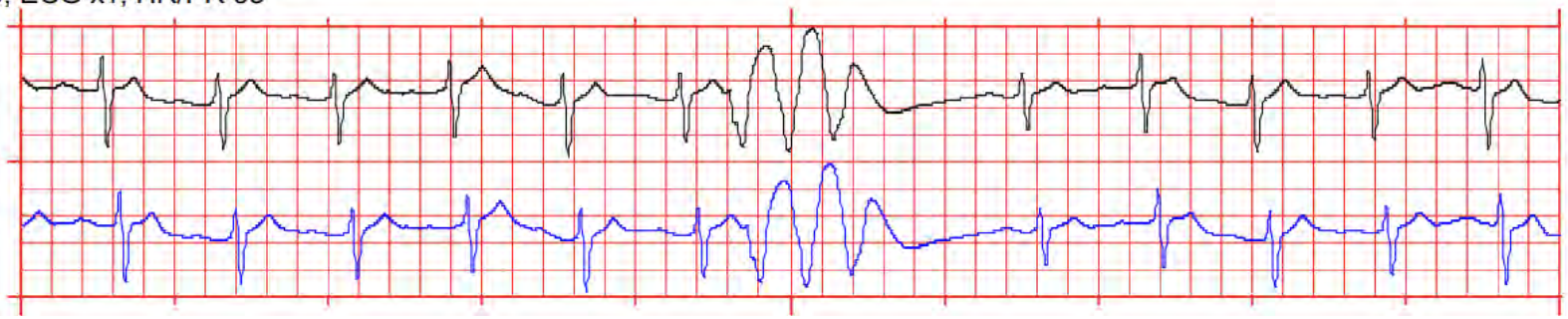
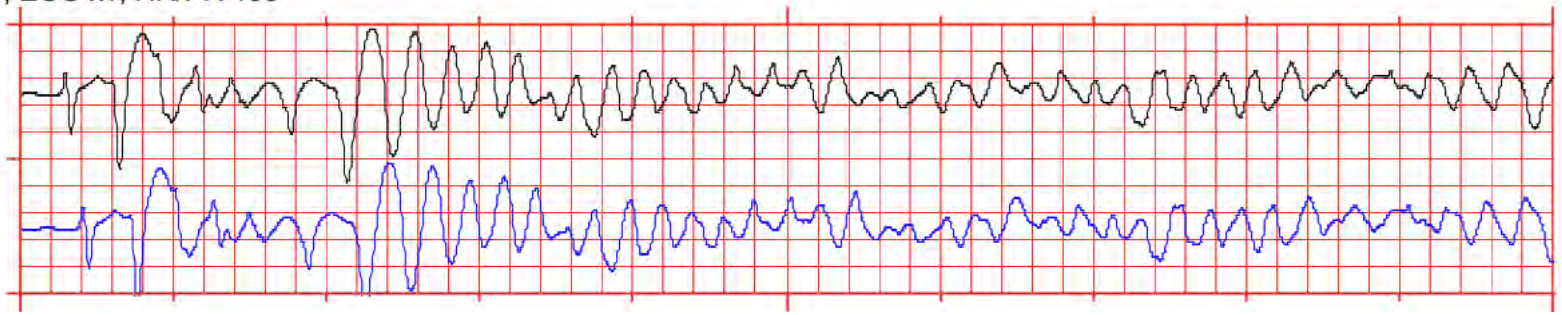
MFC, ECG x1, HR/PR 76



MFC, ECG x1, HR/PR 93



MFC, ECG x1, HR/PR 103



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changing the outcome together

Family H/o

No known family history of sudden death or cardiac devices

Mother: Normal ECG, Echo, GXT

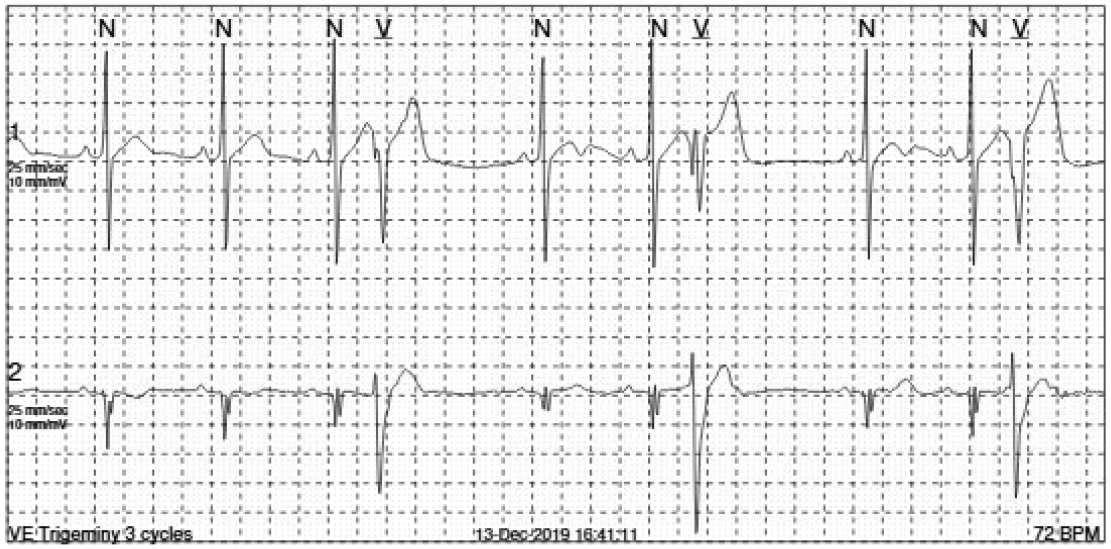
Father: Normal Echo, Holter, Exercise test; **T-wave inversion** in lateral leads

Patient #2 (Older Brother)

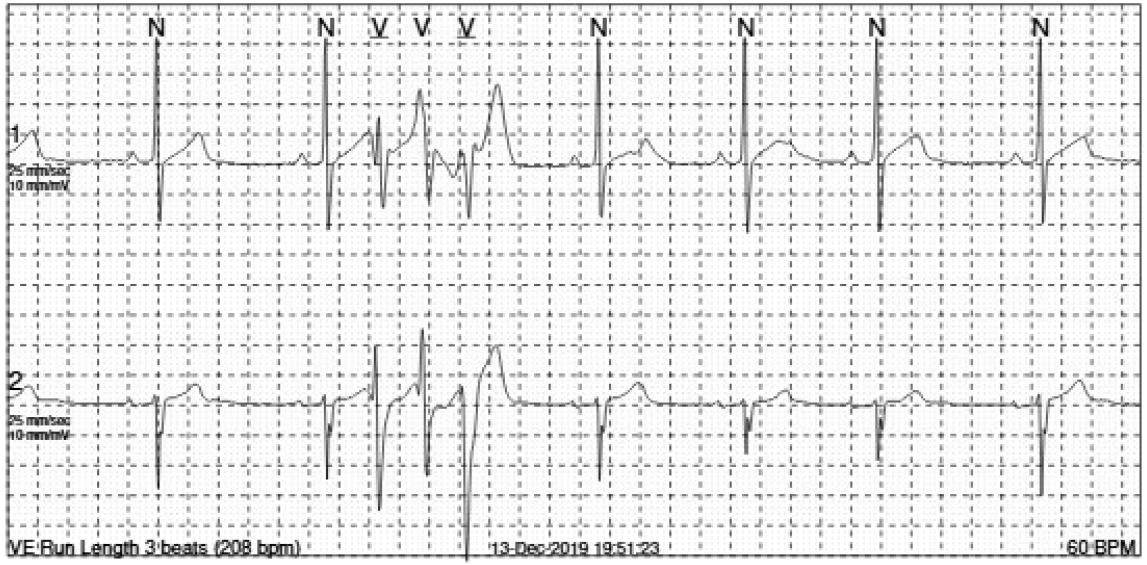
19-year-old male, previously healthy

Initial screening: Normal ECG, Echo; Holter – occasional PVCs; Exercise test – PVCs suppressed with exertion

Bigeminy

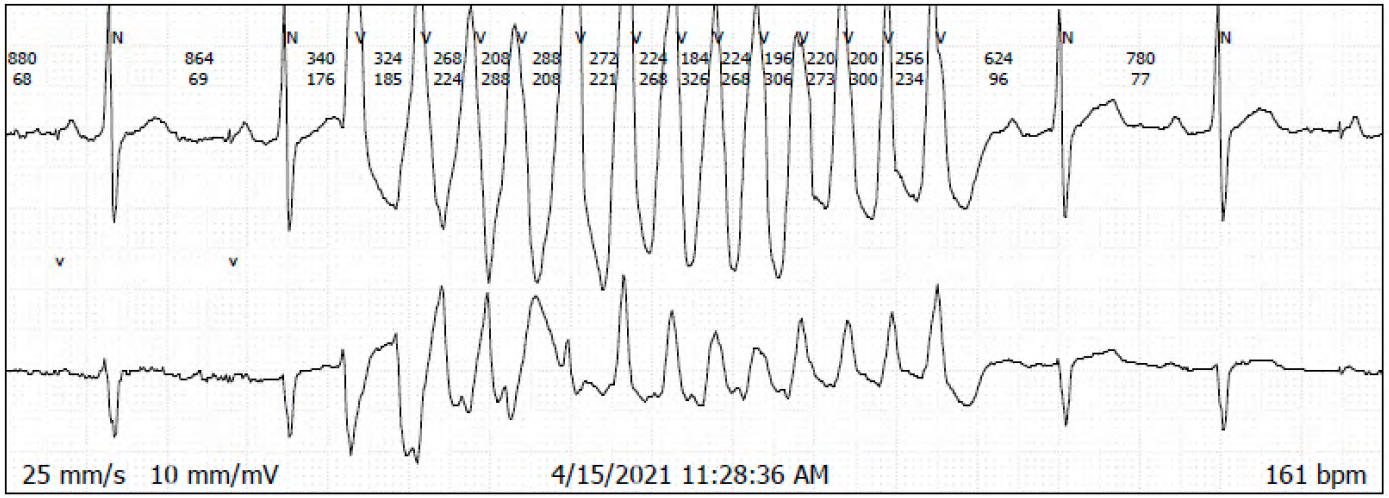


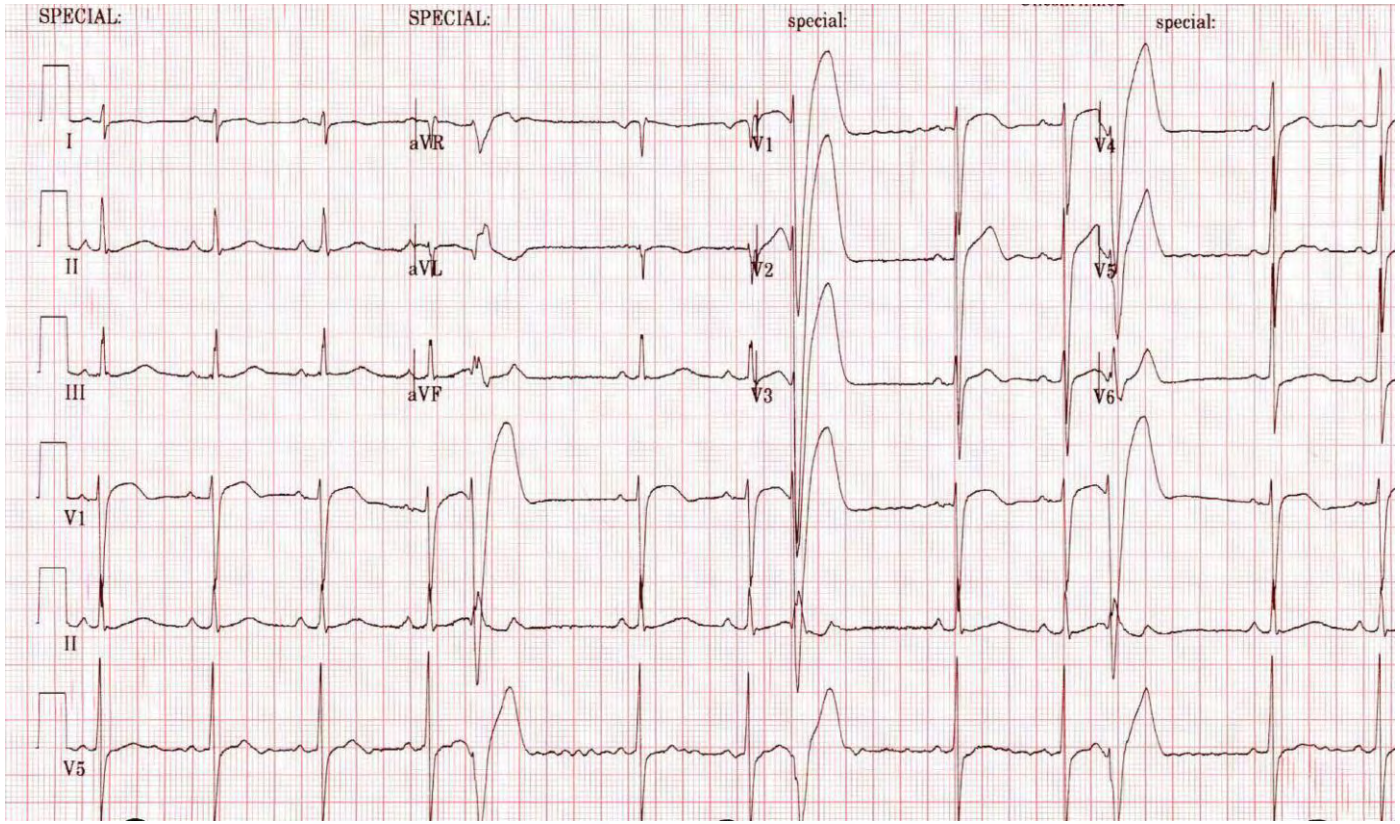
Longest/ Fastest Run of VT



- **SCA** during church (standing) 1 year later, resuscitated from VF arrest
- **VF storm** in adult CV-ICU, required **VA ECMO**, and on amiodarone/lidocaine. Noted to have **frequent PVCs**.
- **Dual Chamber ICD** placed after transfer to CCHMC. Transitioned to **flecainide/calcium-channel blocker** due to concerns for **short-coupled PVC induced VF**.
- Had an appropriate shock while on this therapy after discharge.
- Transitioned to **quinidine** and calcium channel blocker
- No recurrence of VT or PVCs, for past 4 years.
- **Whole genome testing negative**.

Event: 1 Min RR = 0.18 s





Patient #3 (Younger Sister)

14-year-old female, asymptomatic

Workup: Normal ECG, Echo, MRI; Holter – rare PVCs

Exercise test: Frequent PVCs at peak HR

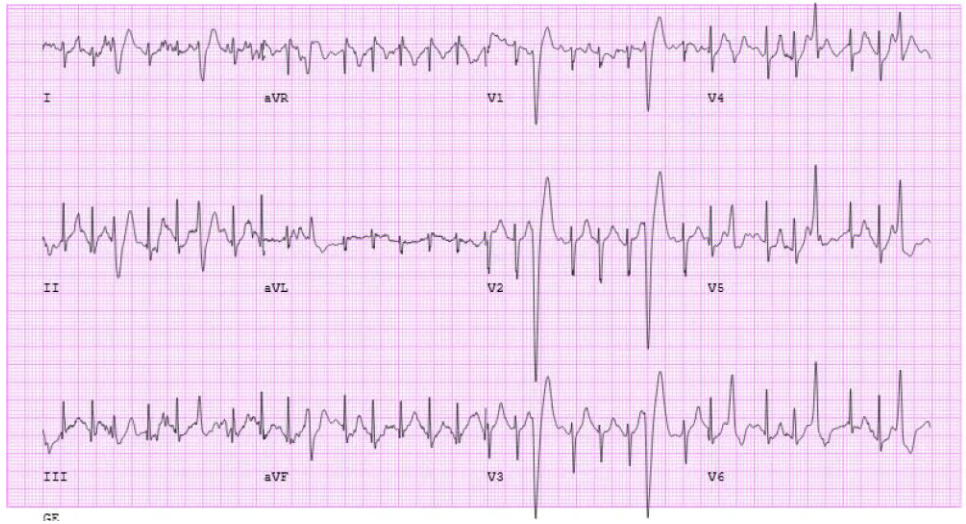
Genetics: TRDN VUS negative; **TTN splice variant** (likely pathogenic)

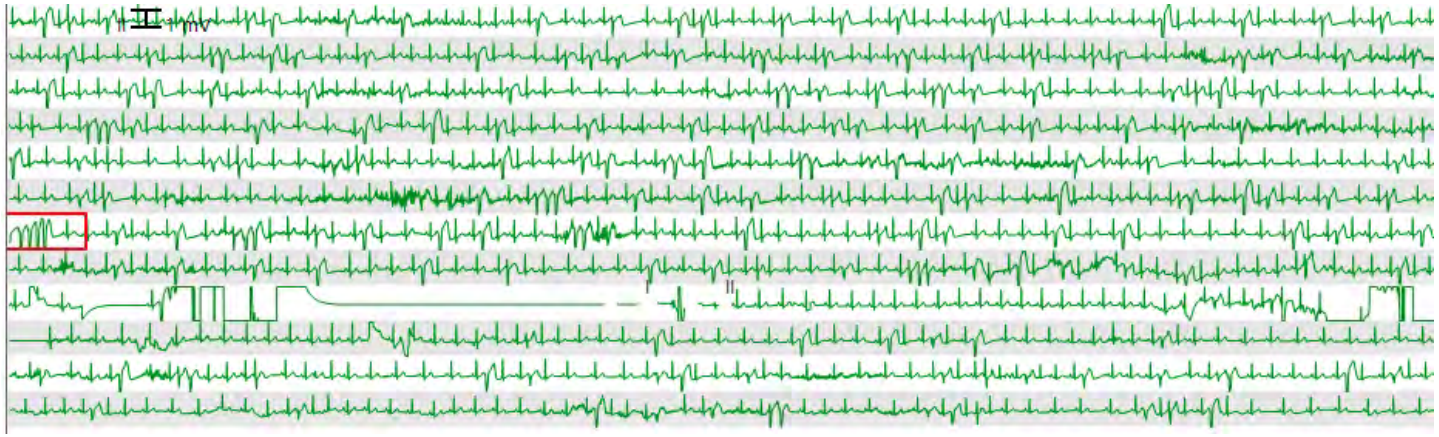
Management: Started **nadolol**, declined ILR/ICD

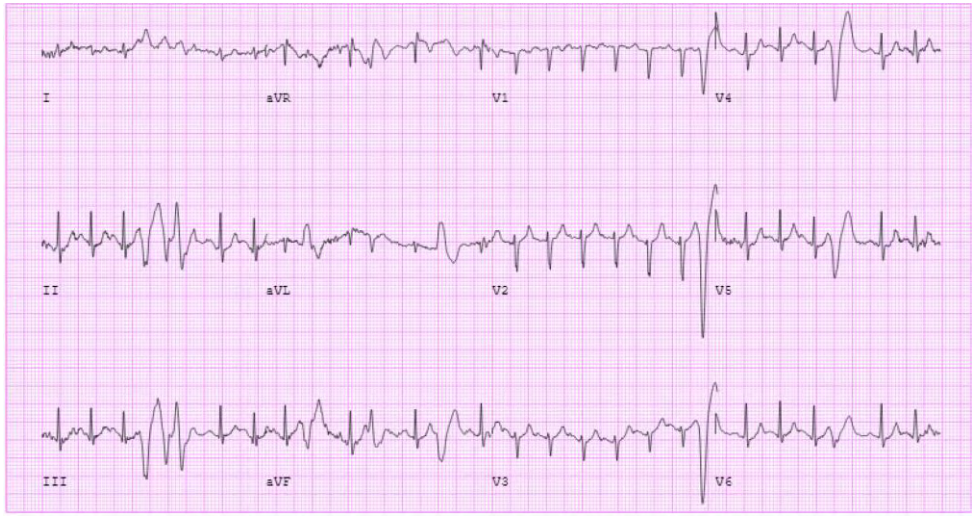
Later noted **NSVT** on stress test

Refused ICD repeatedly; started **quinidine** but had **poor compliance**

Outcome: **Died suddenly**; unsuccessful resuscitation in outside ER


I
aVR
V1
V4
II
aVL
V2
V5
III
aVF
V3
V6




I
aVR
V1
V4
II
aVL
V2
V5
III
aVF
V3
V6

Younger Siblings

- 3-year-old sister
  - Normal Echo, ECG and Holter
- 16-month-old sister
  - Normal echo, ECG and Holter

Discussion & Questions

1. Diagnosis Considerations
    a) Short-Coupled PVC induced VF
    b) Idiopathic VF with familial clustering
    c) Others ?
2. Further management/evaluation of patient #2
    a) Role of EP testing
    b) PVC ablation in case of recurrence or Quinidine intolerance
3. Management of younger siblings
    a) Close clinical follow up
    b) Consider ILR placement
    c) Pre-emptive quinidine therapy
    d) Discuss timing/criteria for ICD placement

SCA in a 14-year-old boy

Chris Anderson MD, FAAP, CEPS-PC

SADS FOUNDATION
SUDDEN ARRHYTHMIA DEATH SYNDROMES

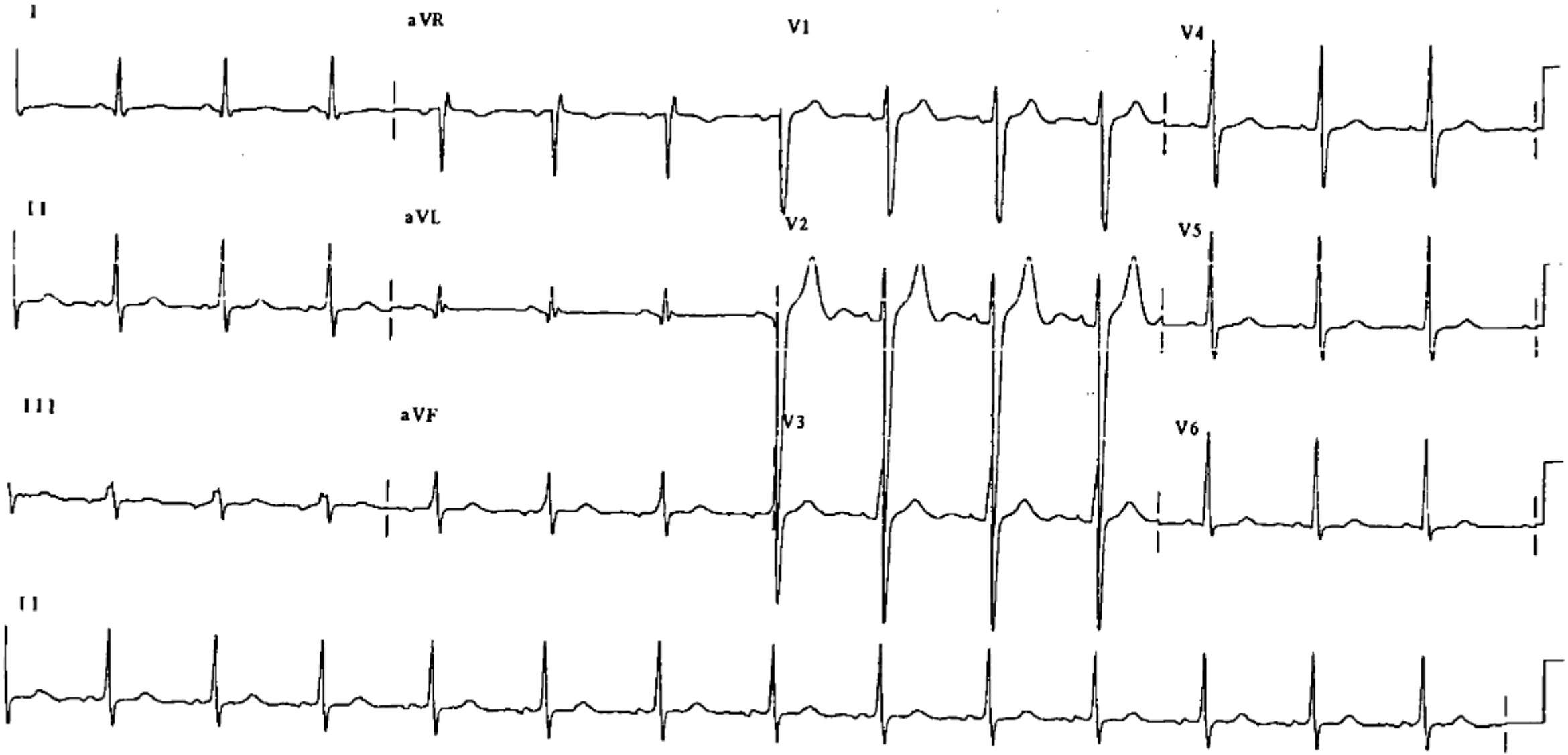
PACES The Pediatric & Congenital Electrophysiology Society

Providence Sacred Heart CHILDREN'S Hospital

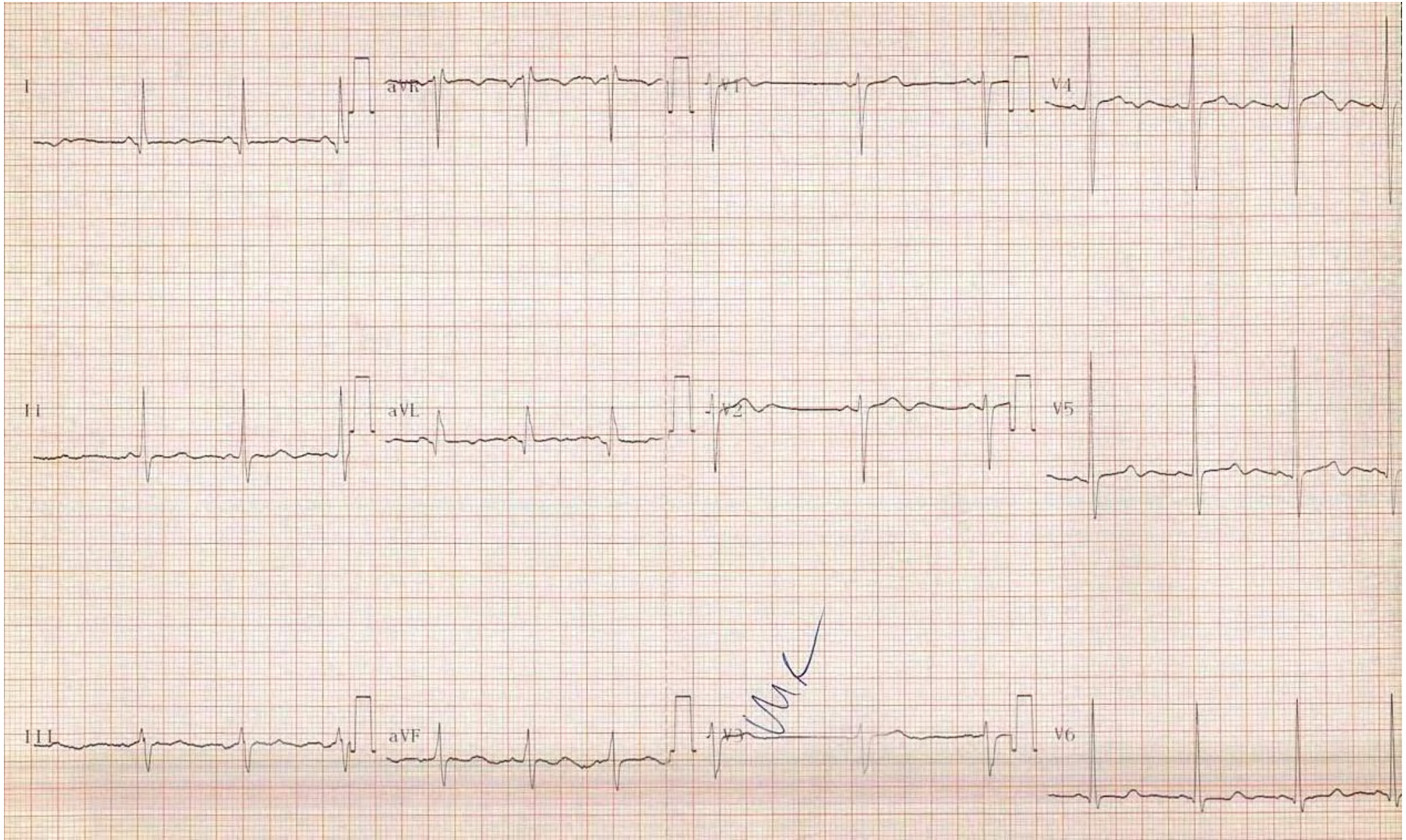
Brief History & Physical

- An asymptomatic 14 yo male presented for evaluation following his younger brother's sudden death while riding a motorcycle in a motocross competition
- Brother's autopsy was unrevealing
- FH also remarkable for a maternal cousin with congenital heart disease (supravalvar AS and bilateral branch PS – non-Williams).
- Both parents had normal ECGs
- Exam is normal

12-lead ECG at presentation:



12-lead ECG at presentation:



Other cardiac testing:

- Normal echocardiogram
- Normal 24-hour Holter monitor
- Exercise treadmill testing: “few seconds” of rapidly conducted AF up to a HR of 240 bpm with slight QRS aberrancy near peak exercise

~Metoprolol initiated~

- EPS including AF induction, isoproterenol infusion, programmed ventricular stimulation:
  - No AP or other abnormal conduction pathways
  - Shortest RR interval during induced self-limited AF 320 ms
  - No inducible VT
  - QTc at baseline measured 386 ms, and 496 ms on isoproterenol
- Additional ECGs: longest QTc 470 msec
- Genetic testing recommended

We have received your request for benefits for the FAMILION test. This notice is to inform you that the request for benefits has been denied based upon our review of your policy.

Under the terms of your policy, benefits are not provided for the proposed service, supply, drug or other charges that are "Experimental or Investigational". Your policy defines Experimental or Investigational as the use of any treatment, procedure, facility, equipment, drug, device or supply that: 1) Is not yet generally recognized by physicians practicing within the state of Idaho as accepted medical practice, or 2) Requires federal or other governmental approval, for other than experimental and/ or investigational purposes, and such approval has not been granted at the time the treatment, procedure, facility, equipment, drug, device or supply is used.

The requesting provider, Genaissance Pharmaceuticals has been advised of this determination.

For further clarification, please see your Group's Exclusions and Limitations section of the contract, Evidence of Coverage, Summary of Benefits, and/or Plan Administrator.

INQUIRY AND APPEALS PROCEDURES

INFORMAL INQUIRY

For any initial questions concerning this matter, an Insured should call or write Blue Cross of Idaho's Customer Services Department. Contact information is provided on the back of the patient's ID card.

FORMAL APPEAL

An Insured who wishes to formally appeal a Pre-Service Claim decision by Blue Cross of Idaho may do so through the following process:

A written appeal must be sent to the Appeals and Grievance Coordinator within one hundred and eighty (180) days after receipt of the notice of Adverse Benefit Determination. Urgent pre-service appeals, and the documents in support of such appeal may be submitted by phone or facsimile. The appeal should state the reasons why the Insured contends Blue Cross of Idaho's decision was incorrect. Any written comments, documents or other relevant information may be submitted with the appeal.

Sudden Cardiac Arrest

- Poor pt tolerance of metoprolol with depression—dose decreased to 25 mg daily
- One week before 16th birthday, SCA while standing at mid-court during a free throw
- Prodrome of lightheadedness, dizziness, and blurry vision.
- A physician in the stands performed CPR, and an AED was retrieved and delivered a shock for coarse VF (confirmed on review of AED data), converting on the first shock.
- The pt experienced full neurologic recovery
- “Borderline” QTc prolongation of 470 msec in the first 24 hours post-arrest; QTc 425 msec at discharge.
- Cardiac MRI and echo showed mild LV dysfunction post-arrest with LVEF 50%, resolved back to normal with time
- Dual chamber transvenous ICD was implanted without complication, and metoprolol dose increased back to 50 mg daily.

At this point, which of the following is the most likely clinical diagnosis?

A. Brugada syndrome
B. Catecholaminergic polymorphic ventricular tachycardia
C. Early repolarization syndrome
D. Long QT syndrome
E. Idiopathic ventricular fibrillation

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D. Long QT syndrome
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No definite correct response here—of the above, B and D are both reasonable options

Follow-Up

- Developed clinical depression
- Multiple ICD shocks from rapid conduction during AF, PTSD within the first year
- Was diagnosed with clinical LQTS at another center
- Much better controlled with combination beta blocker and propafenone
- Genetic testing completed at the age of 31 (Ambry *RhythmNext*—42 gene analysis), which revealed two heterozygous TECRL "variants of unknown significance":
  - **p.G246* (c.736G>T)**—later reclassified as pathogenic
  - **p.L271del (c.812_814delTGT)**—later reclassified as likely pathogenic
- Diagnosis later changed to CPVT at that center

Which of the following are true regarding TECRL and TECRL-related disease? *(Select all that apply)*

A. Both loss-of-function and gain-of-function mutations have been found

B. Phenotypic expression may mimic CPVT

C. Phenotypic expression may mimic LQTS

D. TECRL-related disease is most commonly expressed in an autosomal dominant manner

E. The gene product of TECRL localizes to the contractile apparatus

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TECRL—an emerging genetic arrhythmia substrate

- **Trans-2,3-enoyl CoA Reductase-Like protein**
- Phenotypes:
  - LQTS-like syndrome
  - CPVT-like syndrome
  - AF, malignant ventricular rhythms
- High-risk arrhythmia substrate in homozygous and compound heterozygous mutations

Thank you!!
Questions & Discussion