CARDIO EGYPT 2018

EGYPTIAN SOCIETY OF CARDIOLOGY

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Case presentation

AUTOSOMAL–DOMINANT LEFT–SIDED ARRHYTHMOGENIC CARDIOMYOPATHY CAUSED BY A NOVEL DESMOPLAKIN MASKED AS AN ACUTE CORONARY SYNDROME

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Clinical History

- **GM,** 64 years old female in 2014 (1st presentation)
- Ambiguous history of familiar CAD
- Type II Diabetes Mellitus
- Dyslipidemia
- Previous smoker
- No alchool
- Menière syndrome, intestinal polyposis

GM 64 yo

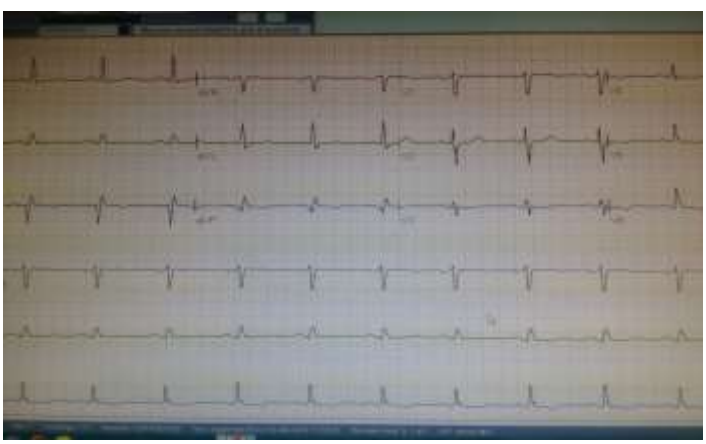
Clinical History

- September and November 2013 2 episodes of **typical precordial oppressive pain at rest**, lasting 15 min, with spontaneous resolution
- December 2013 pre-lipotimic episode linked to dyspnea and vertigo
- January 2014 frequent episodes of **precordial pain at rest**, linked to diaforesis and tachycardia, with spontaneous resolution in 15 min
- February 18, 2014 admission to HPG23 ER for several episodes of **precordial pain** in rapid succession

GM 64 yo

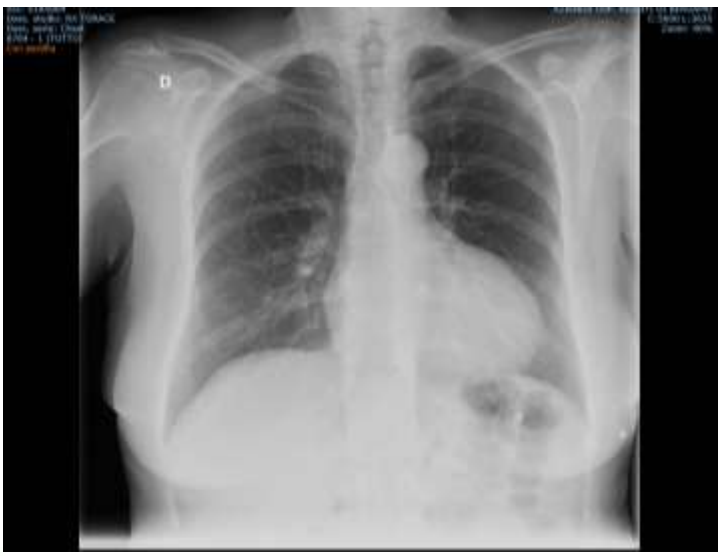
ECG

HR 85 bpm, incomplete left bundle branch block, **Q wave in inferior leads**, **ST-T abnormalities in infero-lateral leads**



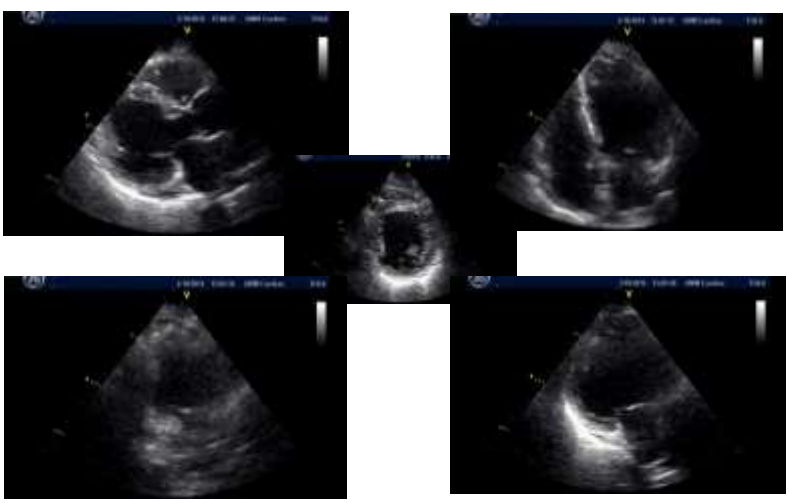
GM 64 yo

Chest X-ray



GM 64 yo

ECHO



Globous and enlarged LV, infero-posterior and lateral hypokinesis, LVEF 40%. Normal RV.

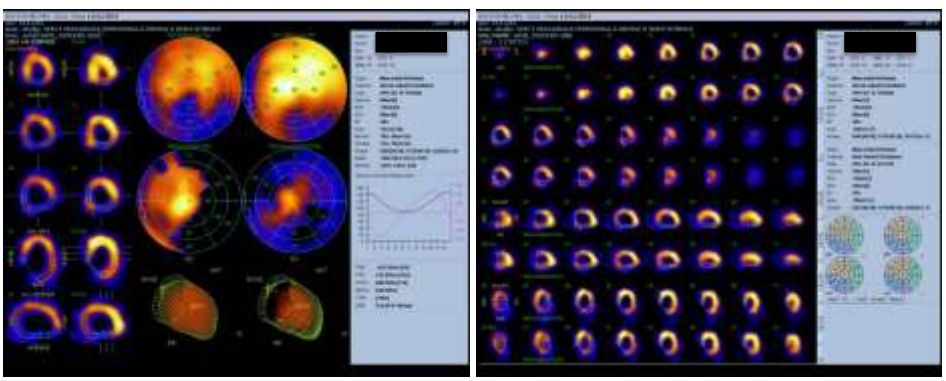
GM 64 yo

Blood chemistry

- Hb 13.7 g/dl, no iron deficiency
- Creatinine 0.63mg/dl
- eGFR 82 ml/kg/min, BUN 42mg/dL
- Na^{++} 142 mMol/L and K^{+} 4.6 mMol/L
- Total cholesterol 221 mg/dl, LDL 154 mg/dl
- Fasting glycemia 95 mg/dl, glycated Hb 6.5%
- Troponin I **0.07→0.1→0.07** ng/ml
- BNP 98 pg/ml

GM 64 yo

Perfusional Myocardial Scintigraphy Rest/Stress



Wide infero-lateral ischemia 30% (RC territory)
and mild LV systolic dysfunction (LVEF 40%)

GM, 64 yo female, precordial pain, T2DM, dyslipidemia, previous smoker

- A: Ischemic Cardiomyopathy?
- B: Diabetic Cardiomyopathy?
- C: Micro-vascular Dysfunction?

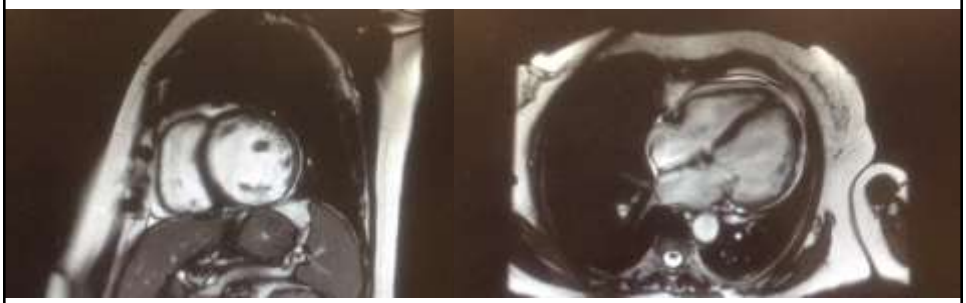
GM 64 yo

Coronary Angiography

- Coronary Angiography: normal coronary arteries
- Ventriculography: enlarged LV, inferior wall aneurysm with inferior akinesis and LV systolic dysfunction (EF 35%)

GM 64 yo

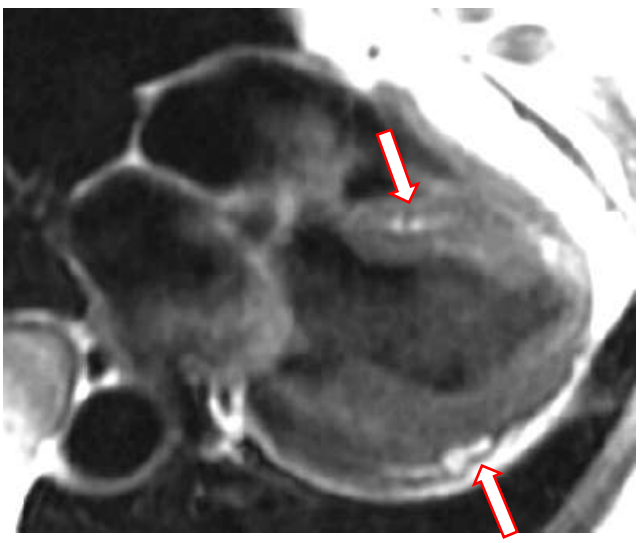
Cardiac MRI



LVEF 36%, primitive hypokinetic dilated cardiomyopathy, LV intramyocardial widespread **fibrosis** (non ischemic pattern) and **adipose tissue metaplasia areas** (inferior and septal wall)

GM 64 yo

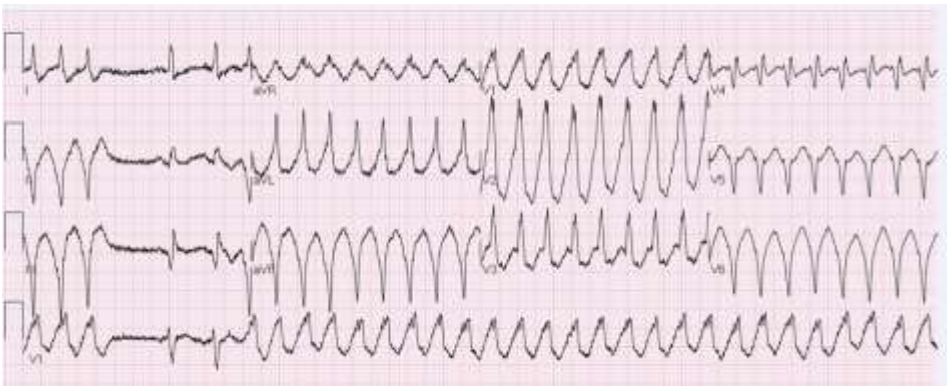
Cardiac MRI



GM 64 yo

24h HOLTER ECG-MONITORING

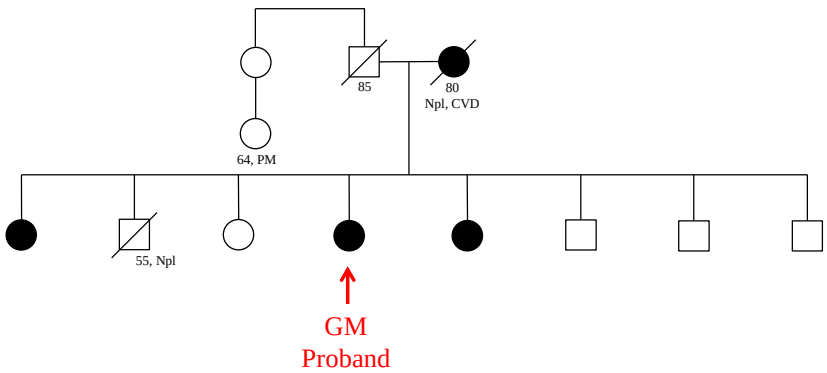
Frequent ventricular polymorphic ectopias (>5200), single, couple and hat-trick, also bigeminism.
One episode of NSVT.



GM, 64 yo female, precordial pain, T2DM, dyslipidemia, previous smoker

- A: Dilated Cardiomyopathy?
- B: Arrhythmogenic Ventricular Cardiomyopathy?
- C: (ongoing) Myocarditis ?

Extended evaluation of the Family Tree



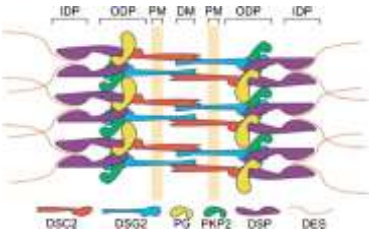
→ Cardiological evaluation + ECG + ECHO

→ Next Generation Sequencing (NGS) analysis of all known genes (n. 113) associated with cardiomyopathies was performed.

GM 64 yo

Next Generation Sequencing (NGS) analysis

Desmoplakin: normal



Van Tintelen et al. *Curr Opin Cardiol*. 2007;22:185–92

Desmoplakin: p.Thr356Lys

Loss of desmosomal integrity can substantially affect gap junctions, sodium channel function and electrical propagation, thereby promoting ventricular arrhythmias

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Chronic (and acute) inflammation as a response to myocardial injury

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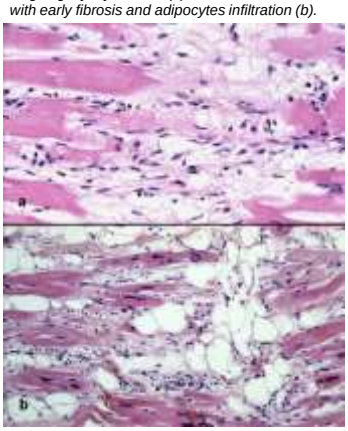
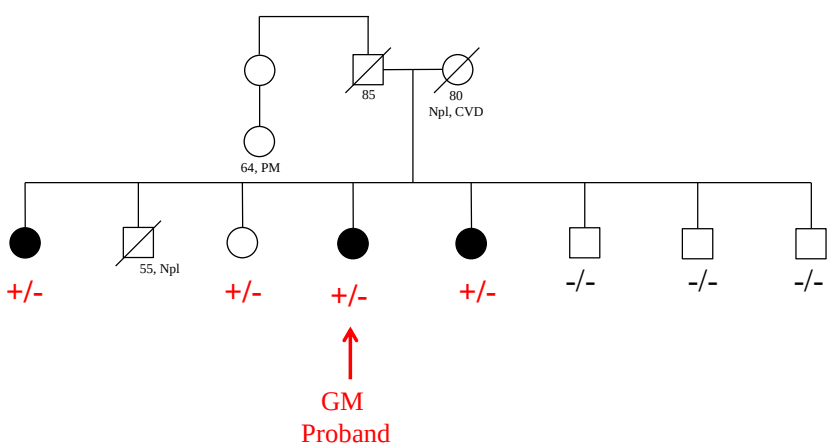
Myocyte cell death may occur via apoptosis or necrosis

Ongoing myocyte death (a) with early fibrosis and adipocytes infiltration (b).

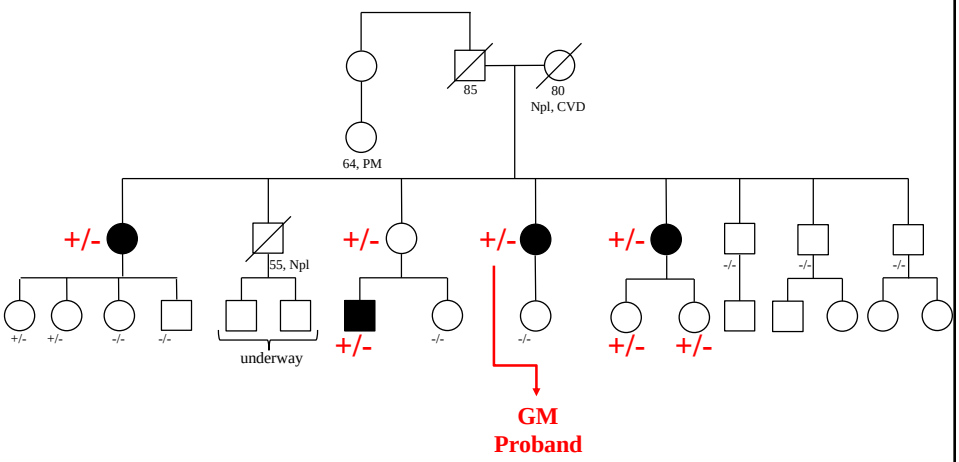


Basso et al. *Cardiovasc Pathol* 2005

Genetic analysis of proband's extended family



Genetic analysis of proband's extended family



GM 64 yo

Key points

- An atypical "acute coronary syndrome-like" manifestation of Left Dominant Arrhythmogenic Cardiomyopathy (LDAC), with arrhythmias of LV origin, lateral T-wave inversion and late gadolinium enhancement in the LV on C-MRI
- In the absence of CAD, inferior-lateral T-wave inversion is often considered a benign condition.
- Chest pain with enzyme release might be attributed to myocarditis.
- We hypothesized that these abnormalities might be manifestations of the "left-dominant" subtype of AC based on C-MRI findings.
- The extended familial screening allowed to identify other three asymptomatic LDAC cases, deserving a careful and regular follow-up

➡ Final diagnosis: Autosomal-dominant left-sided arrhythmogenic cardiomyopathy caused by mutation in desmoplakin.

$\mathbf{M}_{A(LDAC)}\ \mathbf{O}_{H}\ \mathbf{G}_{AD}\ \mathbf{E}_{G\text{-}DSP(p.Thr356Lys)}\ \mathbf{S}_{BII}$

Thank you for the attention

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