A novel de novo mutation in Lamin A/C gene in Emery Dreifuss Muscular Dystrophy patient with atrial standstill : A case report

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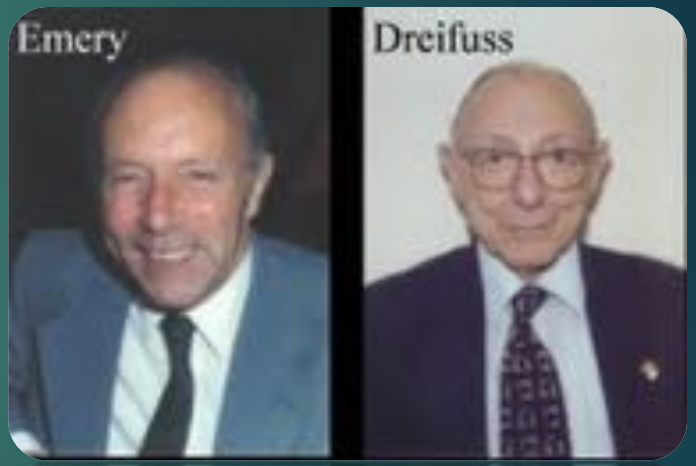
Introduction

Emery Dreifuss Muscular Dystrophy (EDMD)

1 : 100.000 of population

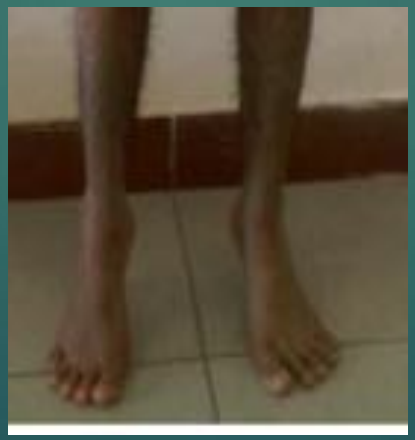
First described by Dreifuss and Hogan in 1961

Cardiac symptoms → first reported by Emery and Dreyfuss in 1966



Introduction

- Emerin mutation → X-Linked trait
- Lamin A/C mutation → Autosomal Dominant and Recessive



Atrial/ventricular arrhythmias

conduction abnormalities

systolic failure

Atrial paralysis

Case Report

History Taking

1994
Age 7

- Seen to have contracture deformities of both elbows, knees, and heel with muscle wasting
- No unifying diagnosis was made

Age 12

- She needs wheelchair to travel distances greater than 10 meters

Age 18

- First Cardiac abnormality was noted
- She presented to the physician due to palpitation and some episodes of presyncopal states.
- Holter monitoring showed low amplitude P waves and first-degree heart block with ventricle premature complex.

History Taking

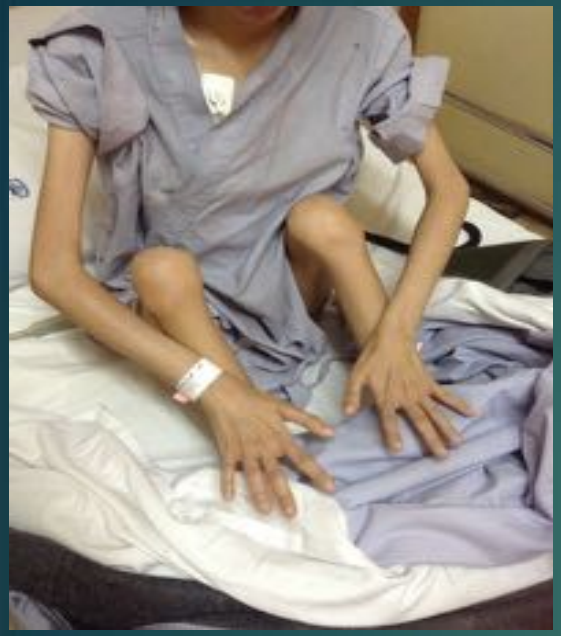
Age 26

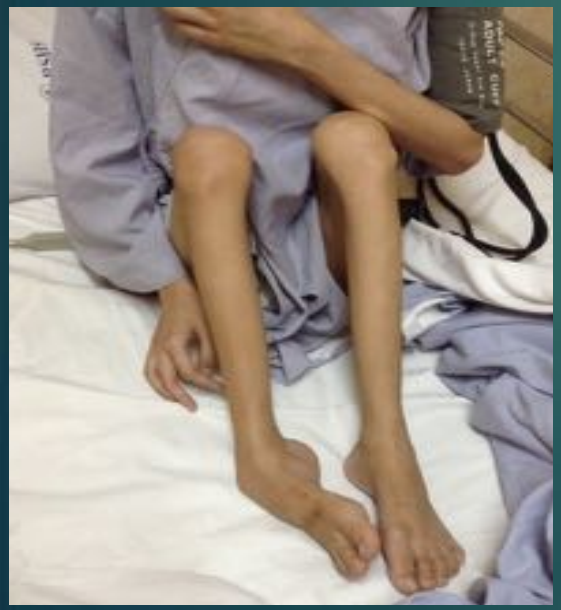
- She was referred to our hospital due an episode of syncope and the ECG showed persistent junctional rhythm
- Planned for PPM implantation

Age 27

- Six month after PPM implantation she was admitted to another hospital due embolic stroke

- Intellectual development was normal
- No other family members were reported to be affected with the same abnormalities.

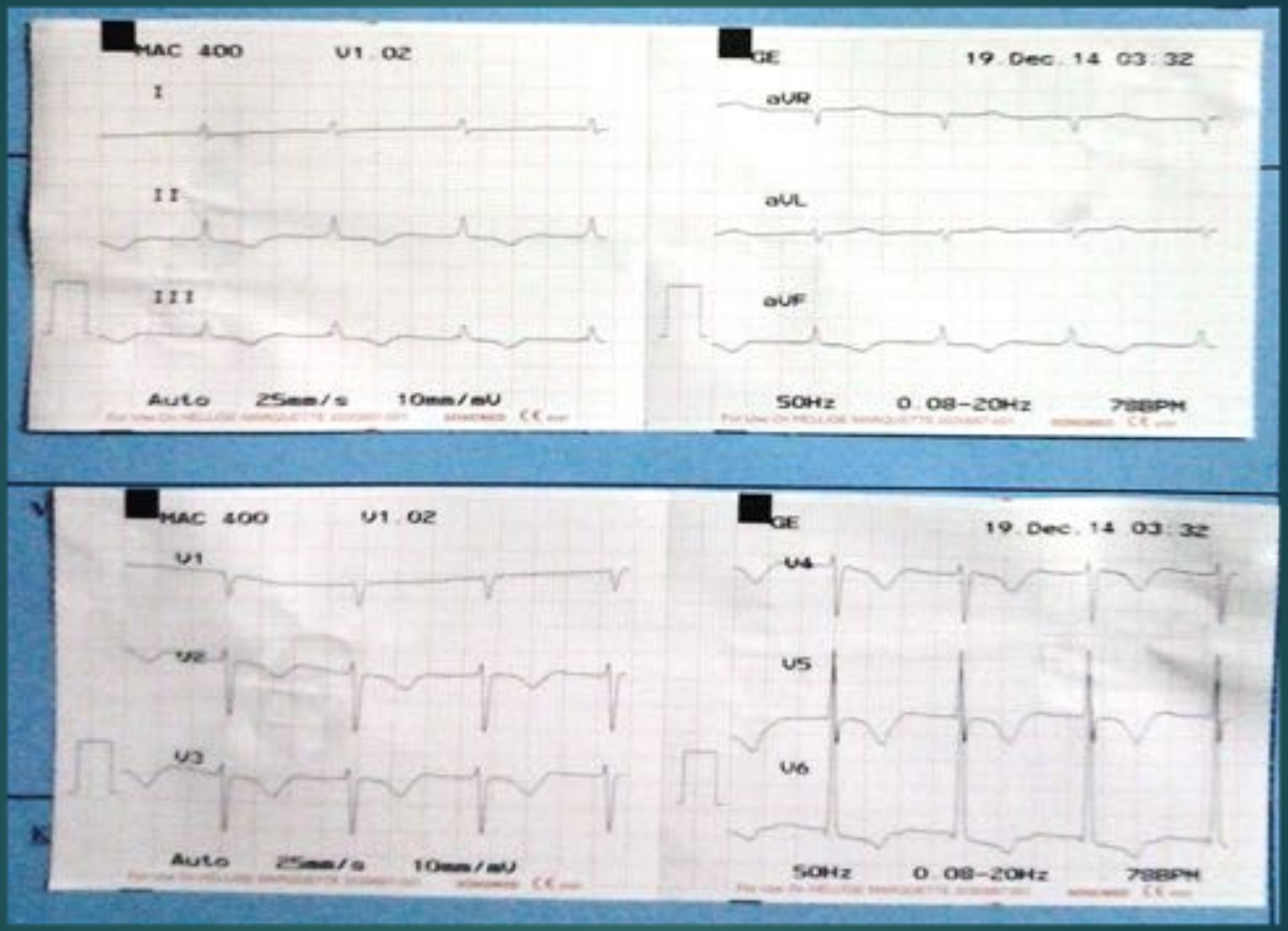




Physical examination and laboratory finding (before PPM implantation)

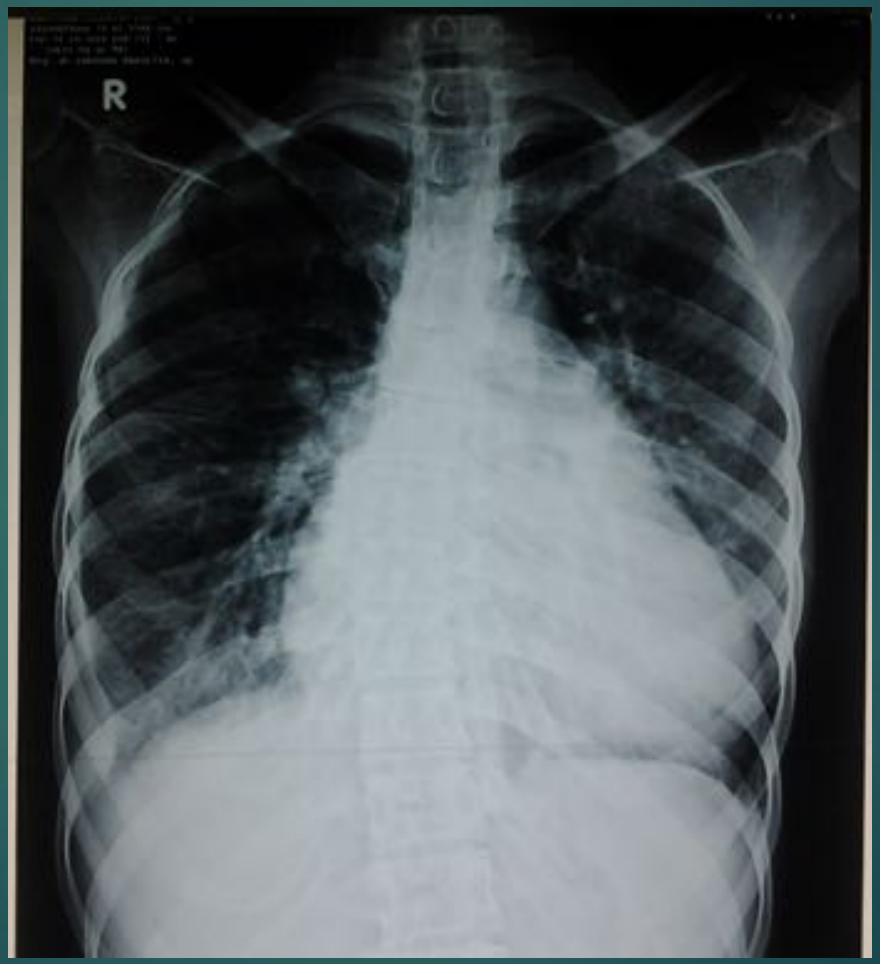
- Contracture of the elbows, knees, and heels tendon
- Muscle wasting
- Her heart rate = pulse : 40 beats/minutes (regular equal)
- High level of creatinine phosphokinase (709 U/L)

ECG (Age 26)

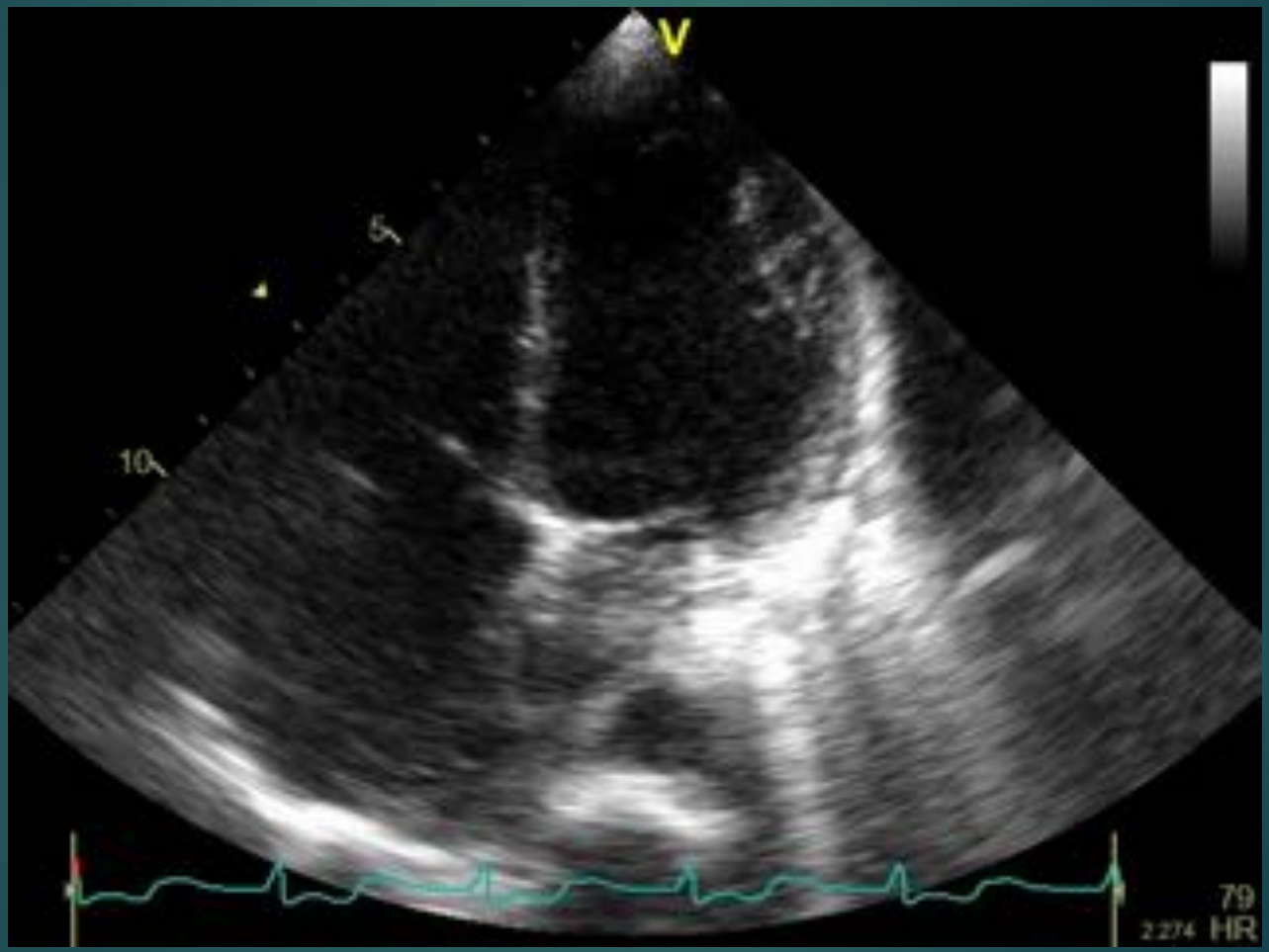


Showed a conduction disturbance with junctional rhythm

Chest X-Ray



Transthoracic Echocardiography



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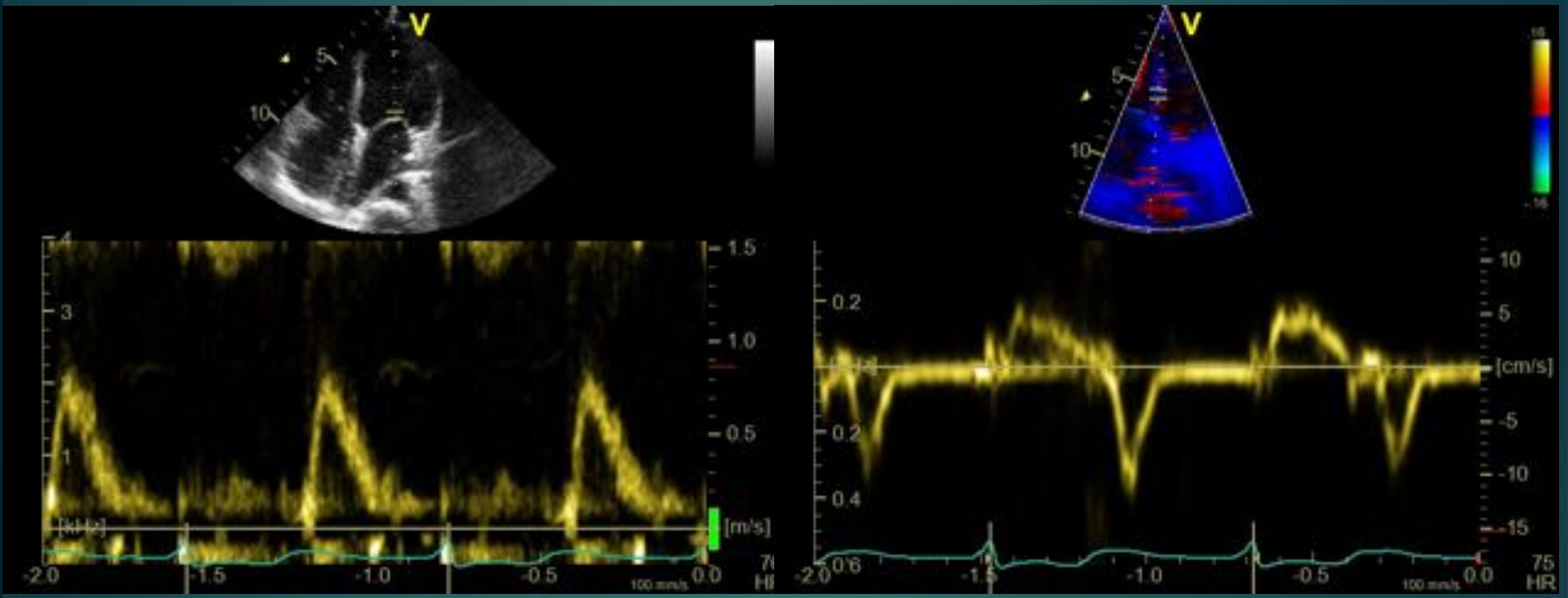
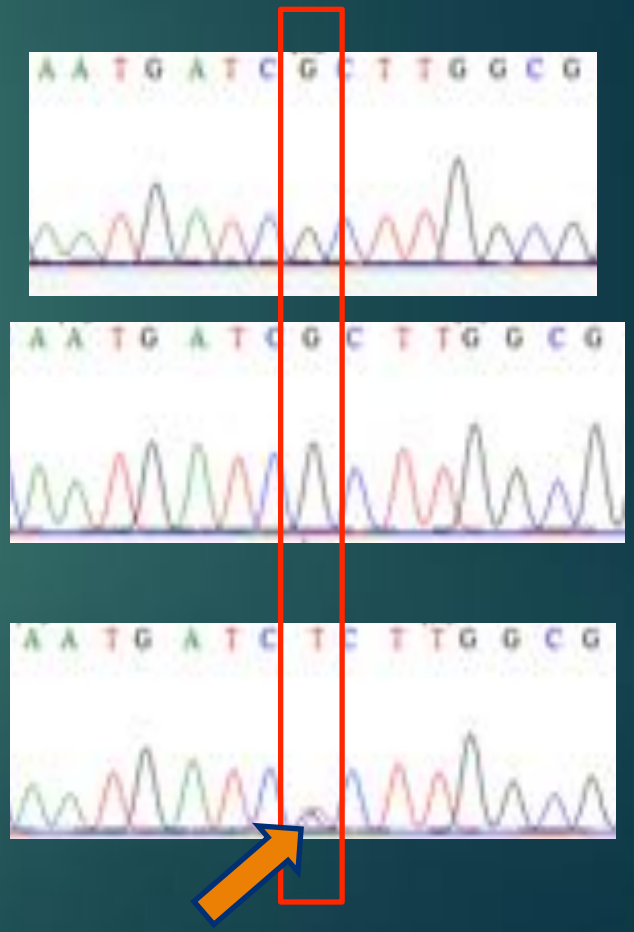


Permanent Pacemaker Implantation

- We planned to implant the DDDR
- The atrium can not be sensed nor paced
- The ventricle was easily paced with 0.5mA and the mode was changed into single ventricle pacing system (VVIR).

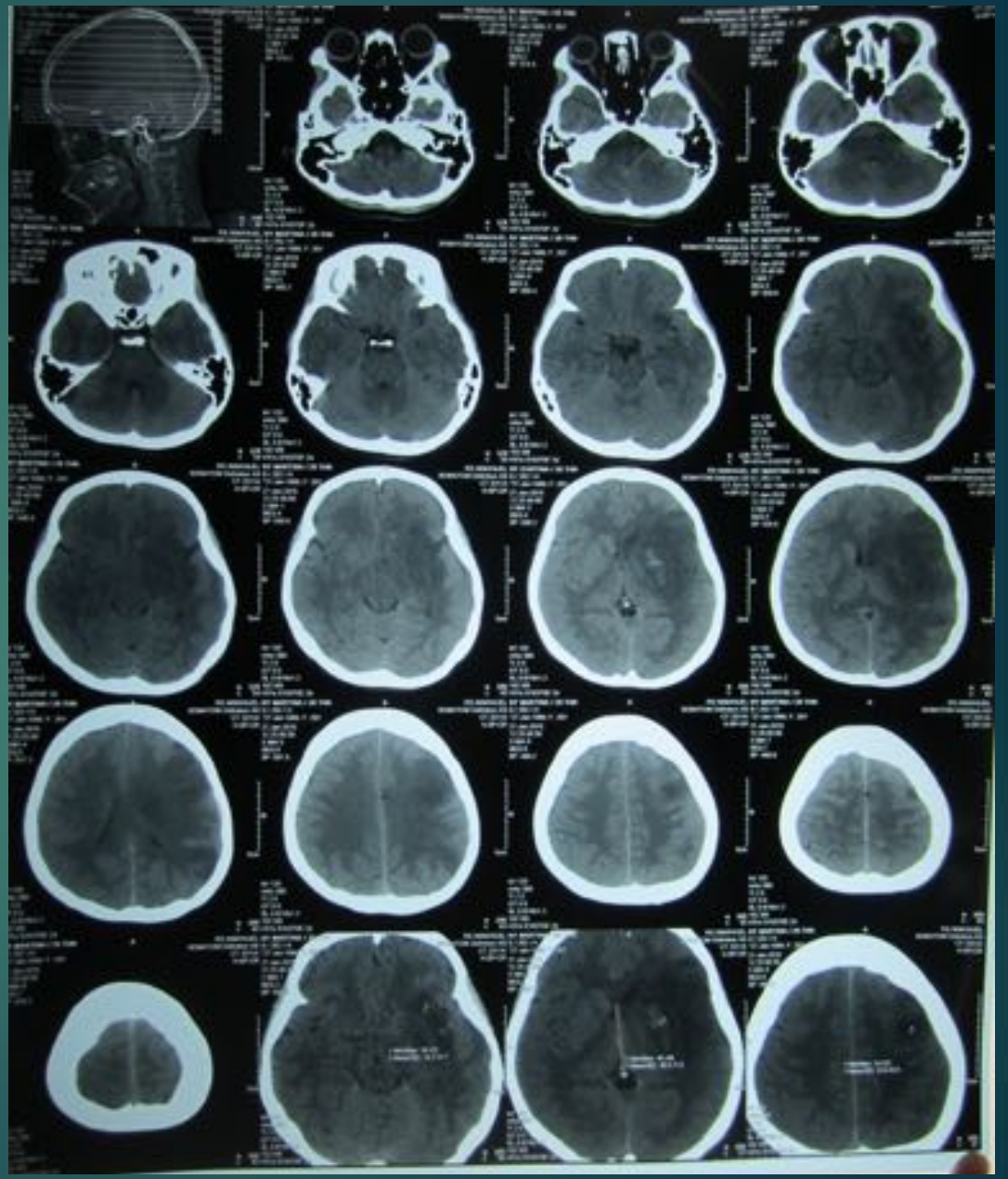
Electropherogram of molecular analysis in trios

- Heterozygous missense c.122G>T, (p.Arg41Leu) mutation.
- The mutation had occurred de novo (red box).

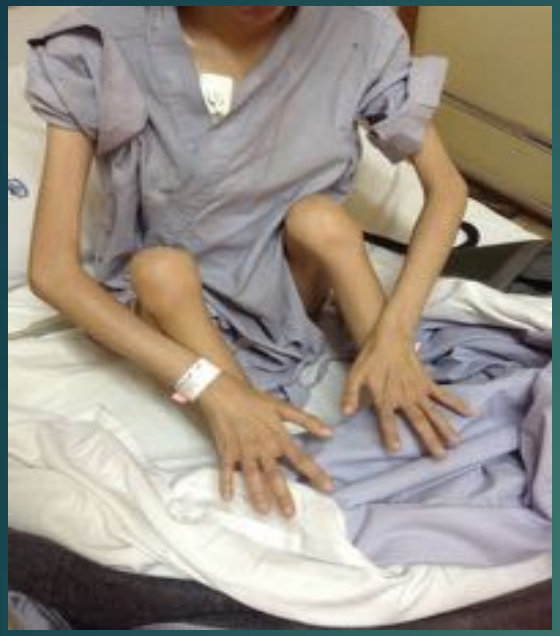


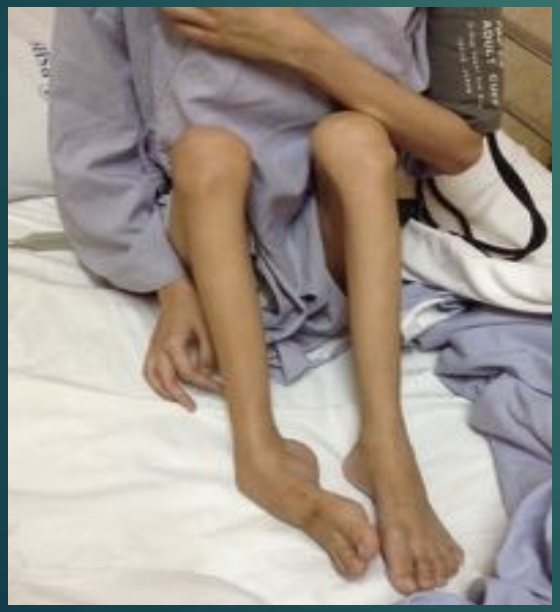
Head CT Scan

- Embolic stroke at the base of the left media cerebral artery (M1)
- Likely to come from the heart



DISCUSSION





ECG

Progressed by the age

Echo

No atrium mechanical activity

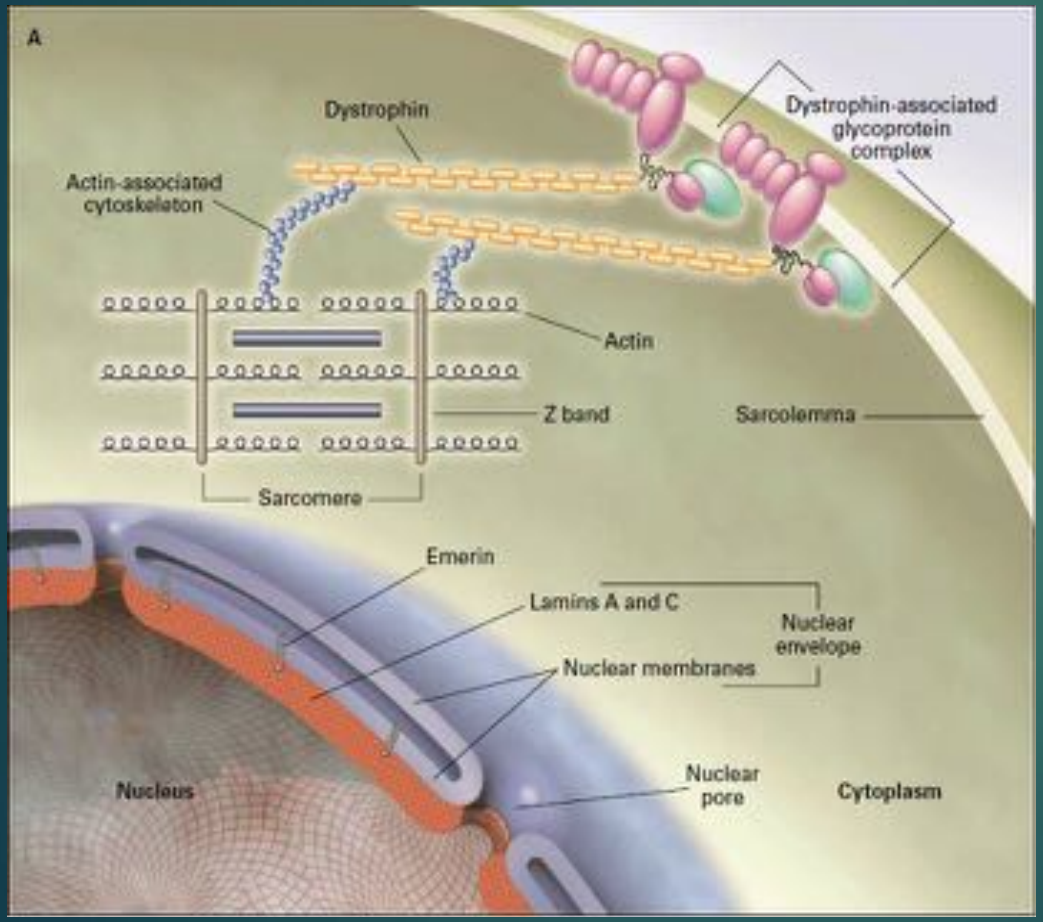
PPM implantation

The atrium can not be paced nor sensed

Atrial Standstill

It consistance with the long term follow up study on a large longitudinal series on 18 EDMD patients by Boriani G et al and a 40 year retrospective study by Emery AE that suggested that atrial stand still is an uncommon complication but almost pathognomonic of EDMD.

Why Lamin A/C Gene ?

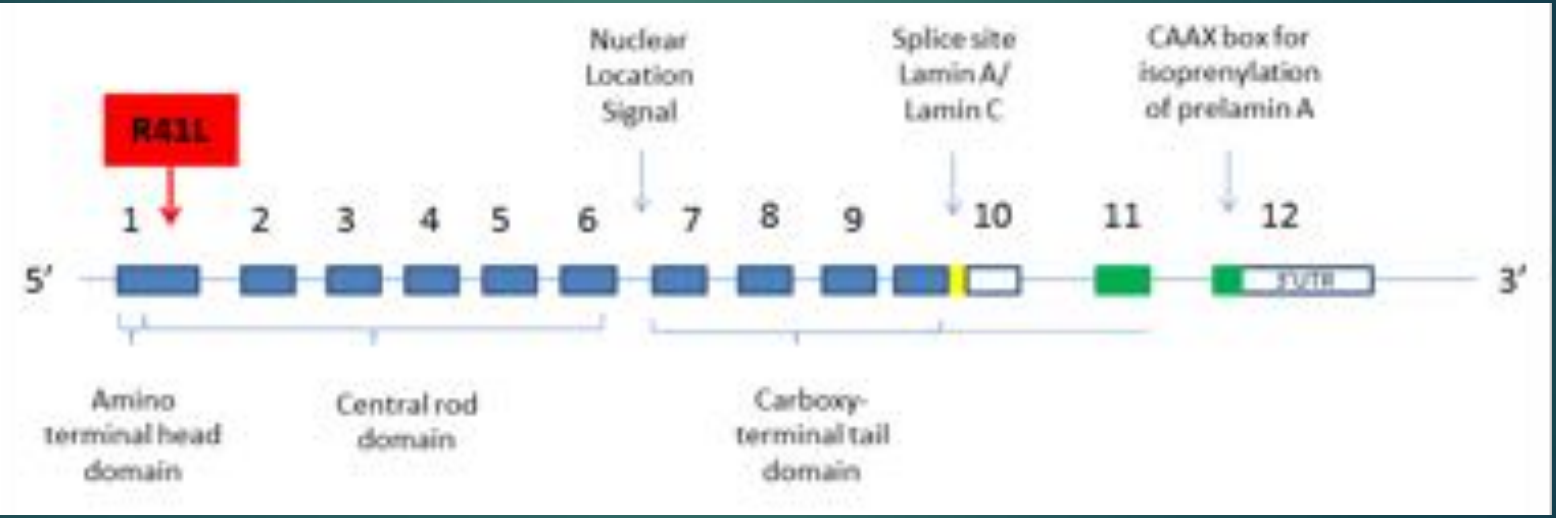


mechanical stress hypothesis

Pathophysiology

gene expression hypothesis

- 24 mutations in the Lamin A/C gene have been reported
- The particular mutation detected in our patient (c.122G>T,p.Arg41Leu) has not been reported before.



This mutation is located in α-helical central rod domain of lamin A and C protein structure

Felice et al

- The mutation in the rod domain of the lamin A/C gene may cause the full clinical spectrum of EDMD-AD

Fatkin et al

- The mutations at the rod region cause isolated myocardial disease while the missense mutation in the tail region cause EDMD

Conclusion

- We report a novel de novo mutation in *LMNA* gene following autosomal dominant form of EDMD.
- Functional analysis study for the future is needed to determine genotype-phenotype correlation.

Thank You