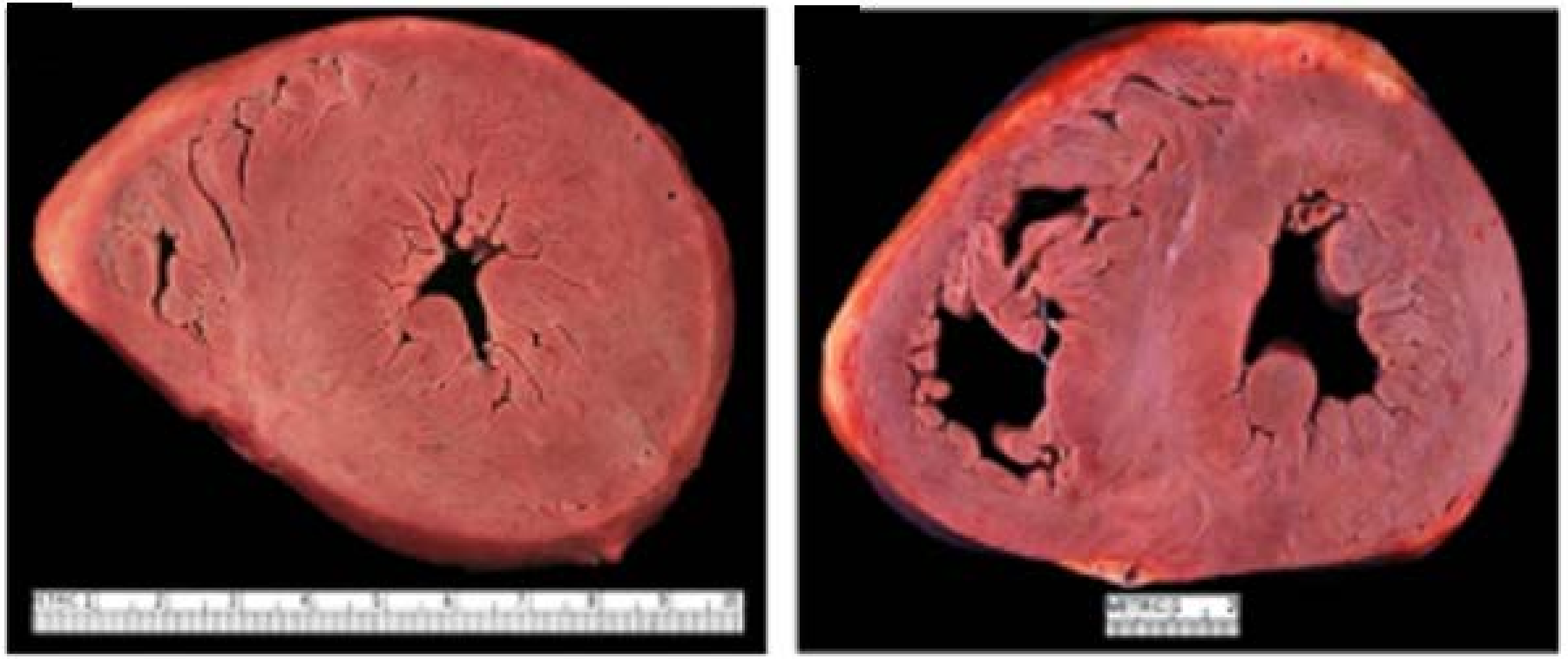
FENOCOPIAS DE MIOCARDIOPATÍA HIPERTRÓFICA.



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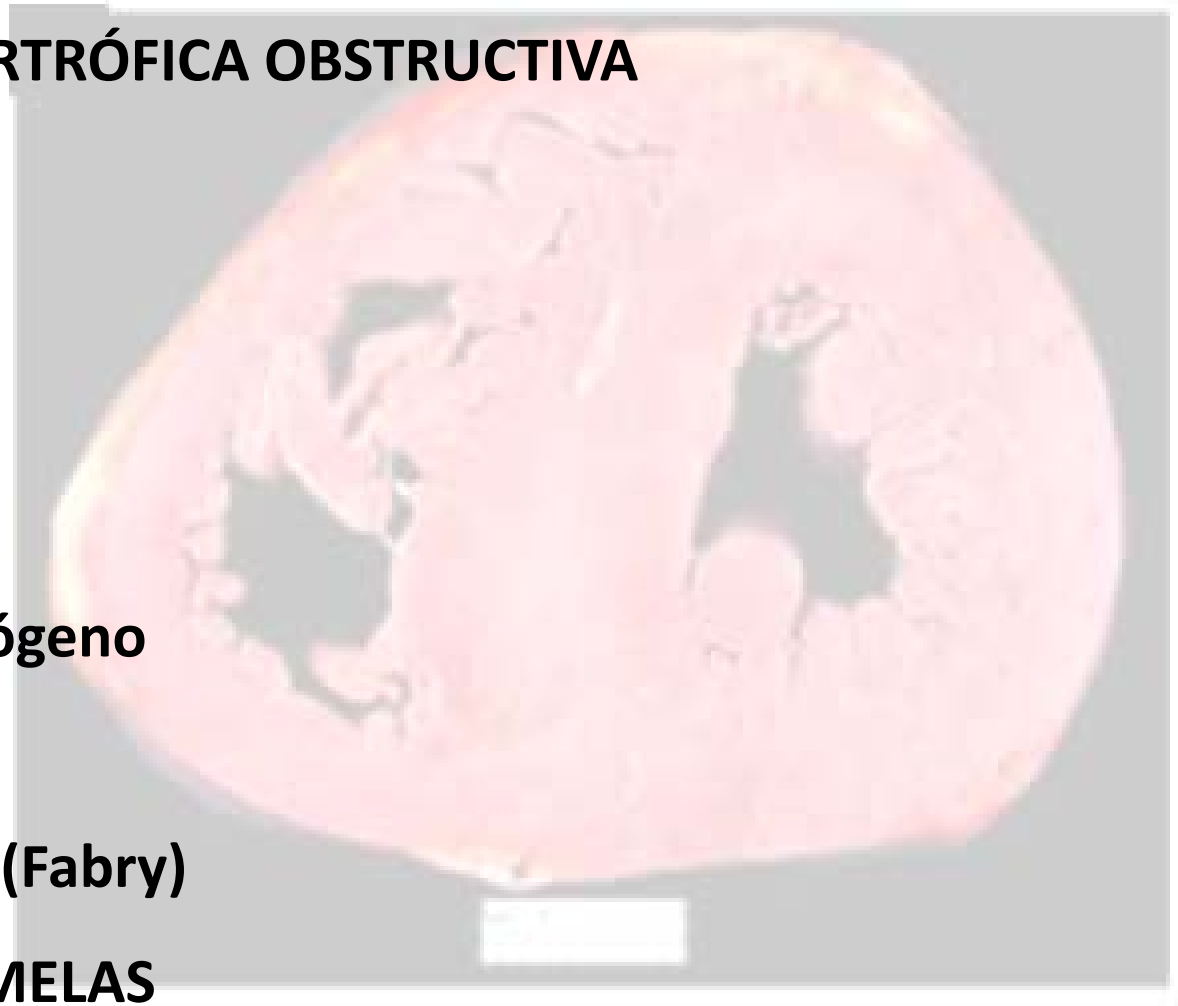
ÍNDICE



1- INTRODUCCIÓN:

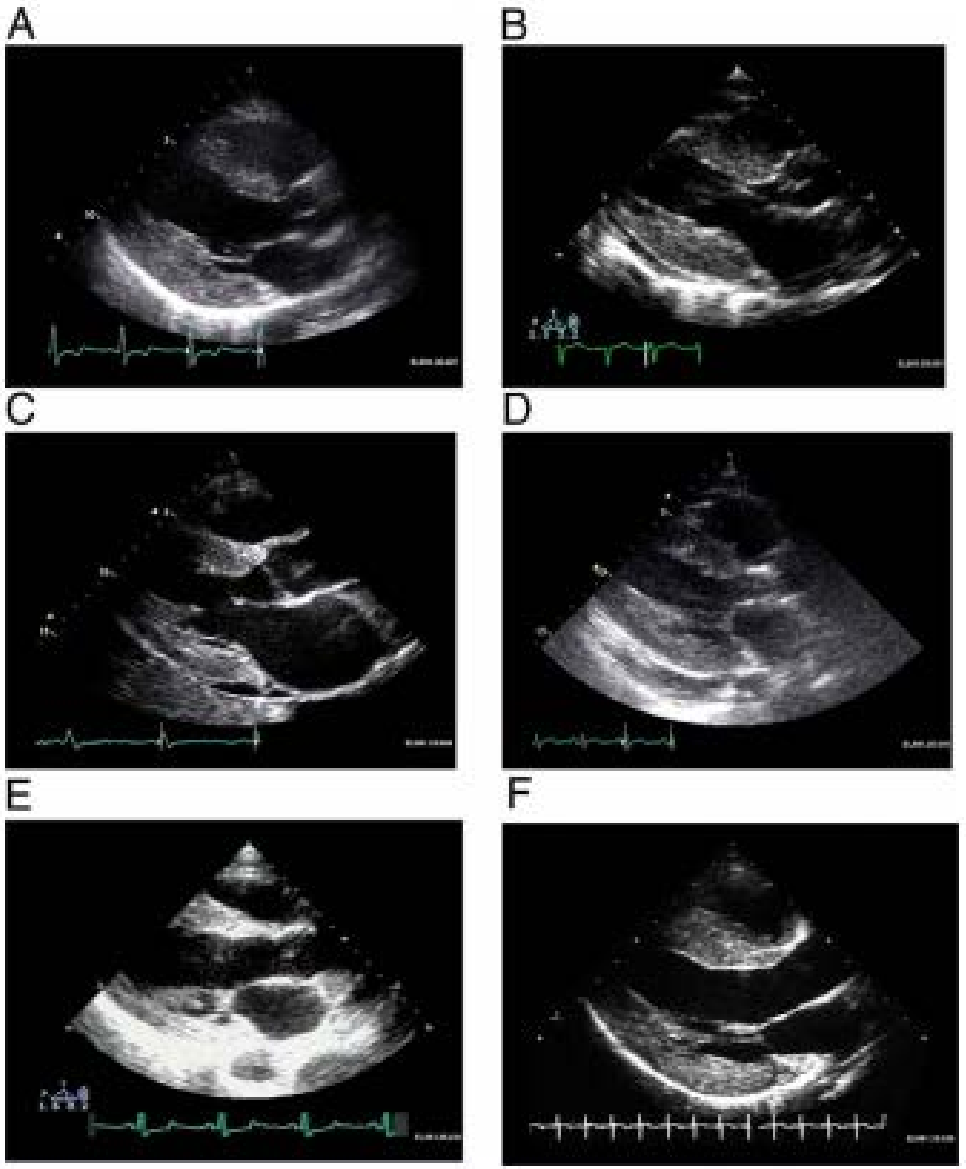
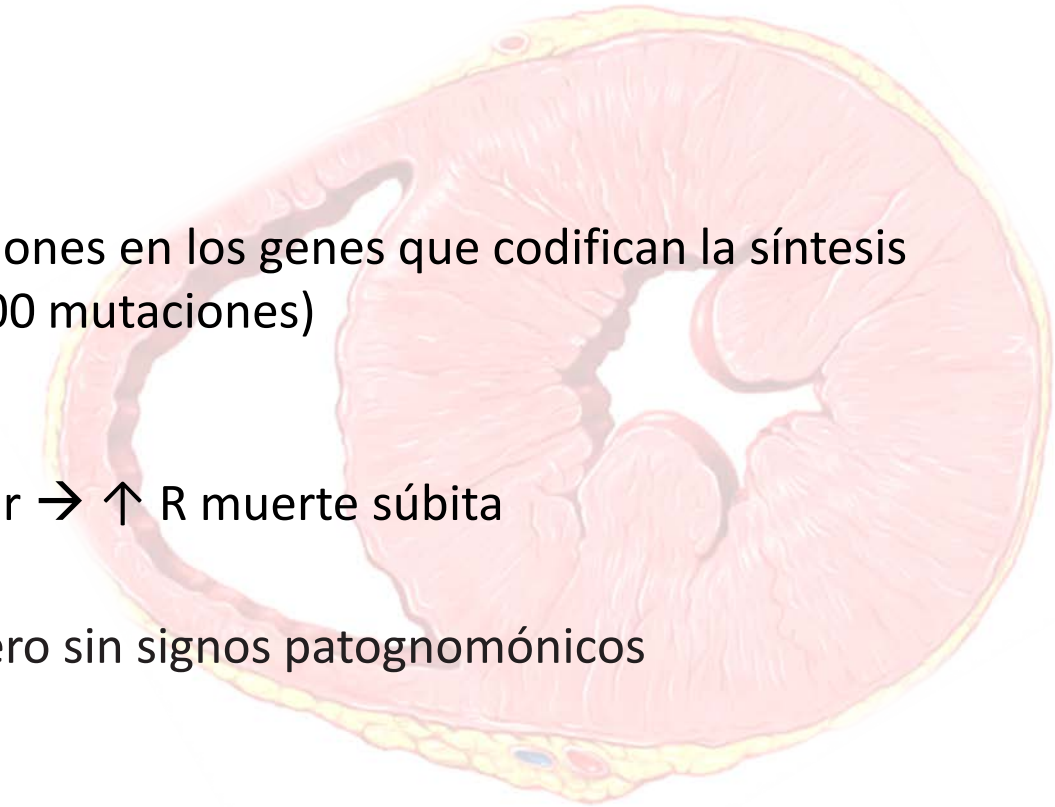


Figure 2 Conditions Presenting With Increased Left Ventricular Mass and Thick Ventricular Walls

(A) Hypertrophic nonobstructive cardiomyopathy, (B) hypertensive heart disease with secondary renal failure, (C) cardiac amyloid, (D) mucopolysaccharidosis, (E) cardiac oxalosis, and (F) Friedreich ataxia. See text for descriptions.

doi:10.1016/j.jacc.2009.12.040

MIOCARDIOPATÍA HIPERTRÓFICA



- Trastorno heterogéneo del músculo cardíaco → mutaciones en los genes que codifican la síntesis proteínas sarcoméricas del corazón (descritas > de 1.000 mutaciones)
- Prevalencia de 1/500.
- 50% de los casos HAD / 50% esporádica.
- MCH → ↑ masa muscular + desorganización miofibrilar → ↑ R muerte súbita

→ **ECG**: Anormal 75–90% de los pacientes pero sin signos patognomónicos

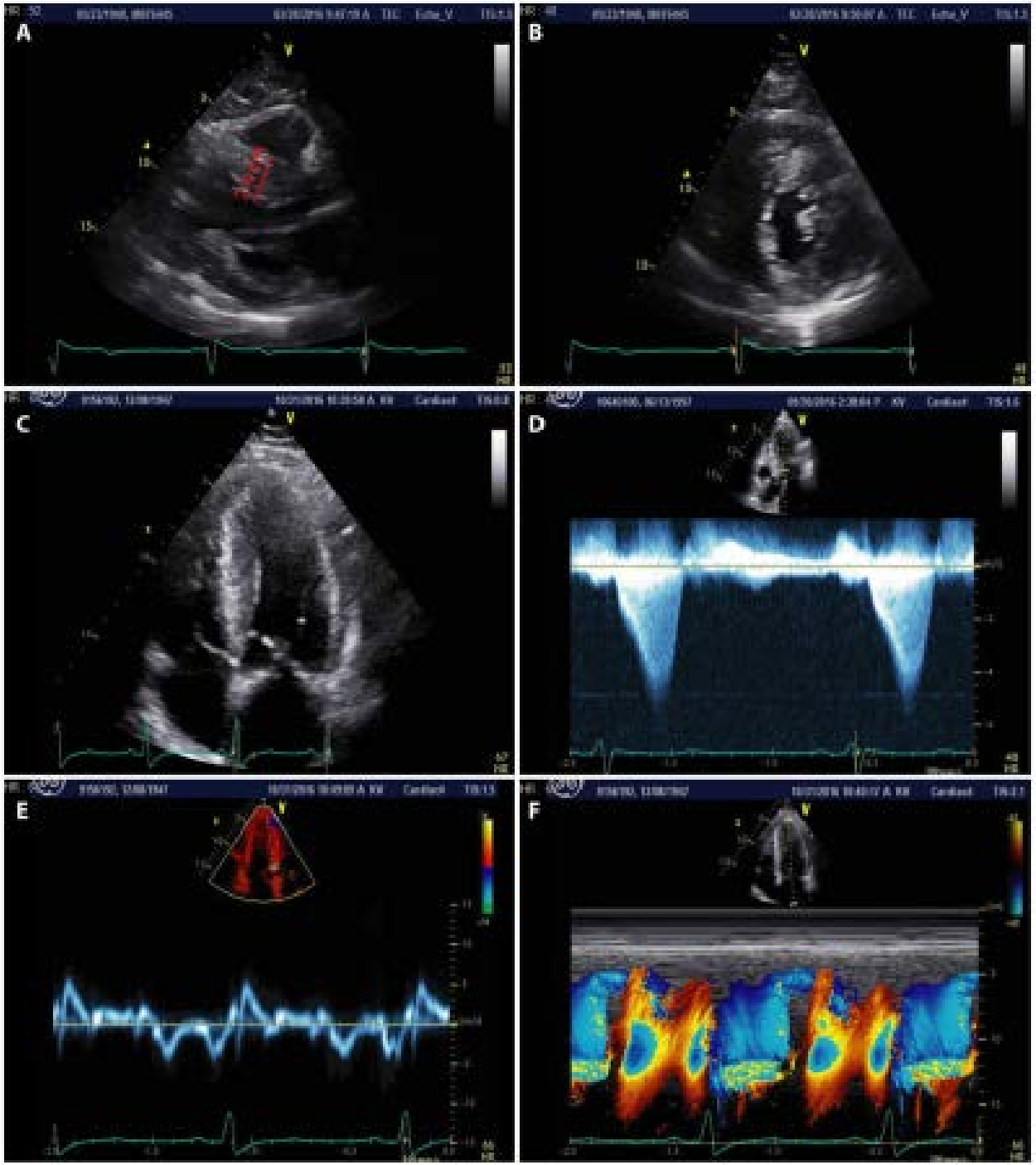
→ **Ecocardiografía:**

- ✓ ↑ grosor: medio de 20 mm
- ✓ ASIMÉTRICO: Septo anterior -- 7% apical – 10% hipertrofia concéntrica
- ✓ + disfunción diastólica

→ **RMN**:

- ✓ Identificar hipertrofia en apex
- ✓ Malformaciones asociadas: elengación valvas mitrales, músculos papilares anómalos, …
- ✓ RTG: 65%, septo

→ **Genética**



doi:10.1161/CIRCRESAHA.117.311059.

2- HVI FISIOLÓGICA: CORAZÓN DEL ATLETA

- Grosor pared VI **≤ 12-16 mm** → < 2% ENTRENAMIENTO **VIGOROSO**
- Tipo de ejercicio:
  - ✓ > Hipertrofia: **remo, ciclismo, esquí de fondo, carreras de fondo y natación**
  - ✓ Isométricos: levantamiento de peso, lucha libre… → No ↑ grosor miocárdico
- Mujeres: muy raro HVI > **11 mm** → Sospechar hipertrofia patológica
- Historia familiar
- ☹ **ECG Atletas** ≈ HVI patológica: Bradicardia, ↑ V, repolarización precoz, inversión onda T, ondas Q profundas…

- EcoTT: Atletas:
  - ✓ patrón **simétrico** de la hipertrofia
  - ✓ **DTDVI > 55 mm → atletas**; DTDVI < 45 mm → patológico
  - ✓ Patrón de llenado **NORMAL** en atletas

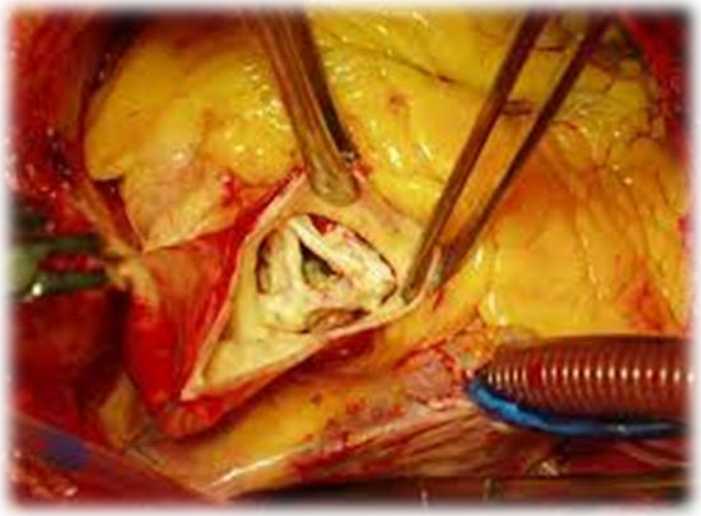
- RMN Atletas: Sin patrón de RTG

- Si persisten dudas:
  - ✓ Ergometría con VO2 max >110–120% del predicho → cambio fisiológico
  - ✓ Stop ejercicio físico → **↓ 2 mm en 3 meses → corazón de atleta**

3- HVI SECUNDARIA

→ **HTA**

Historia clínica
HVI < 15 mm
Concéntrica
Ausencia de dilatación de VI



→ **EAo**

Historia clínica
27% HVI asimétrica (septo basal-medio)

→ HVI INDUCIDA POR FÁRMACOS:

Restrictive Cardiomyopathy Secondary to Hydroxychloroquine Therapy

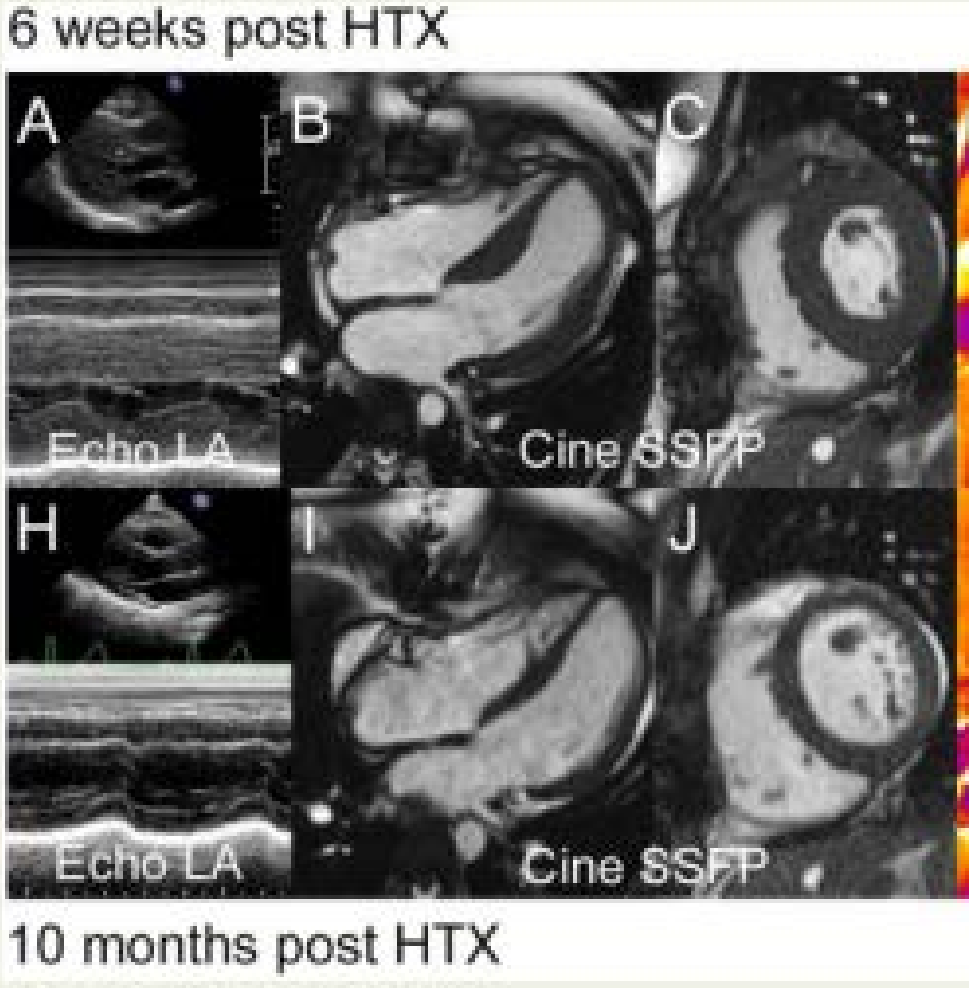
VINAYAK A. MANOHAR, MD, Resident; KEVIN G. MODER, MD, Staff Consultant, Division of Rheumatology, Department of Internal Me
WILLIAM D. EDWARDS, MD, Staff Consultant, Department of Laboratory Medicine and Pathology; KYLE W. KLARICH, MD, Staff Consultant, D
of Cardiovascular Diseases, Department of Internal Medicine, Mayo Clinic, Rochester, Minnesota, USA. Address reprint requests to Dr. K.W. Klaric
First Street SW, Rochester, MN 55902. J Rheumatol 2009;36:472–3; doi:10.3899/jrheum.080305

Impaired systolic and diastolic left ventricular function in children and adolescents with congenital adrenal hyperplasia receiving corticosteroid therapy

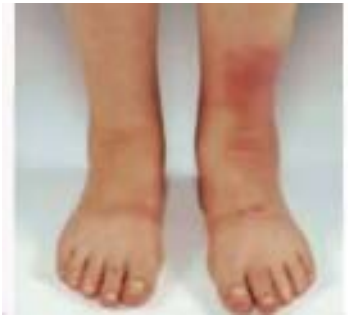
Tacrolimus-induced left ventricular hypertrophy: insights with cardiac magnetic resonance mapping techniques

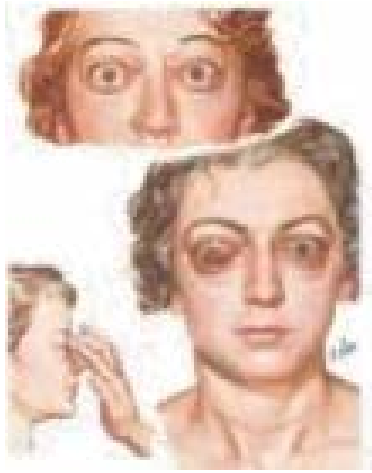
Miroslav Muršić[1,2], Zuckermann Andreas[3], Loewe Christian[2], Greil Sabine[4], and Beitzke Dietrich[2]*

[1]Department of Radiology, Clinical Hospital Centre Zagreb, Zagreb, Croatia; [2]Department of Biomedical Imaging and Image Guided Therapy, Medical University of Vienna, Währinger Gürtel 18-20, 1090 Vienna, Austria; [3]Department of Surgery, Medical University of Vienna, Vienna, Austria; and [4]Department of Pediatric Cardiology, Medical University Vienna, Vienna, Austria



→ HIPOTIROIDISMO:

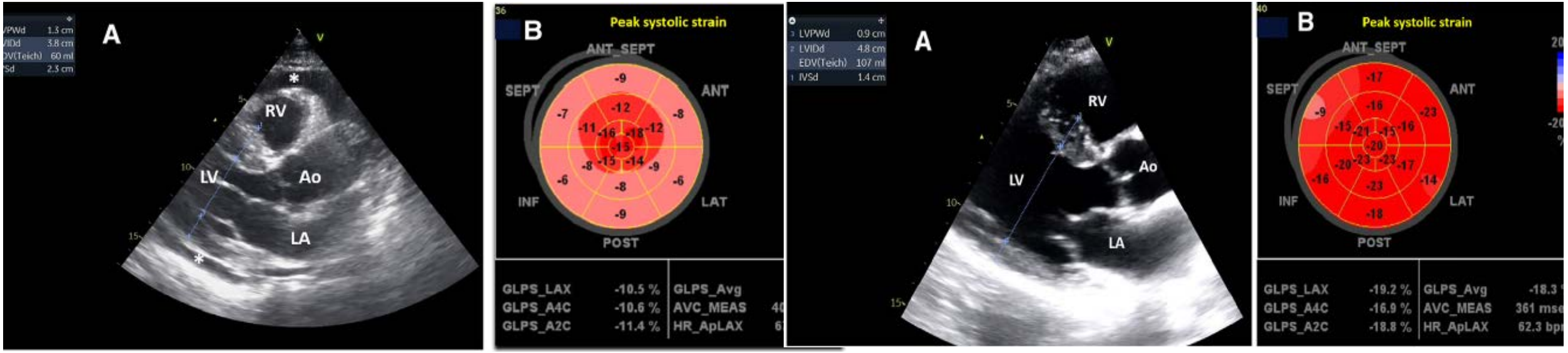




Hipotiroidismo grave: mixedema

- 4.6% de la población (0.3% manifiesta, 4.3% subclínico)
- ↑ prevalencia con la edad
- Afectación cardiaca: HTA, Bradicardia sinusal, ↑ QT, derrame pericárdico….
  - ✓ Raro: miocardiopatia hipotiroidea: dilatada > **hipertrofica (Asimétrica, septal) → Reversible (≈ 5 m tras tto)**

DOI: 10.1111/echo.15183



→ MCH TRANSITORIA EN LACTANTE: HIJOS DE MADRES DIABÉTICAS

- Neonatos de madres diabéticas: ↑ morbilidades (transitorias): hipoglucemia, hiperbilirrubinemia, hipoCa, hipoMg, policitemia, distrés respiratorio, **miocardiopatía**

- Miocardiopatía:
  - ✓ **hipertrofia** (¿hiperinsulienmia?)→ ± OTSVI
  - ✓ Transitoria → 6-12m
  - ✓ + en madres con peor control glucémico

Inborn errors of metabolism

Multiple congenital anomaly syndromes

Neuromuscular disorders

Mitochondrial disorders

AMILOIDOSIS

TABLE 5 Clinical Features in Patients With "HCM Phenocopies (Mimics)"

Typical Presentation Age	Systemic Features	Possible Etiology	Diagnostic Approach
Infants (0-12 mo) and toddlers	Dysmorphic features, failure to thrive, metabolic acidosis	■ RASopathies ■ Glycogen storage diseases, other metabolic or mitochondrial diseases ■ Infant of a mother with diabetes	■ Geneticist assessment ■ Newborn metabolic screening ■ Specific metabolic assays ■ Genetic testing
Early childhood	Delayed or abnormal cognitive development, visual or hearing impairment	■ RASopathies ■ Mitochondrial diseases	■ Biochemical screening ■ Genetic testing
School age and adolescence	Skeletal muscle weakness or movement disorder	■ Friedrich ataxia, Danon disease ■ Mitochondrial disease	■ Biochemical screening ■ Neuromuscular assessment ■ Genetic testing
Adulthood	Movement disorder, peripheral neuropathy, renal dysfunction	■ Anderson-Fabry disease, Friedrich ataxia, infiltrative disorders (e.g., amyloidosis), glycogen storage diseases	■ Biochemical screening ■ Neuromuscular assessment ■ Genetic testing

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4- MIOCARDIOPATÍAS INFILTRATIVAS (≈ MCH)

Errores innatos del metabolismo:
Enfermedades de depósito del glucógeno:
- Pompe
- Danon
- AMP cinasa (PRKAG2)
- Trastornos de la carnitina
- Enfermedades de depósito lisosomal
  - Anderson-Fabry

Amiloidosis
- ATTR familiar
- TTR silvestre (senil)
- AL

doi:10.1016/j.jacc.2009.12.040

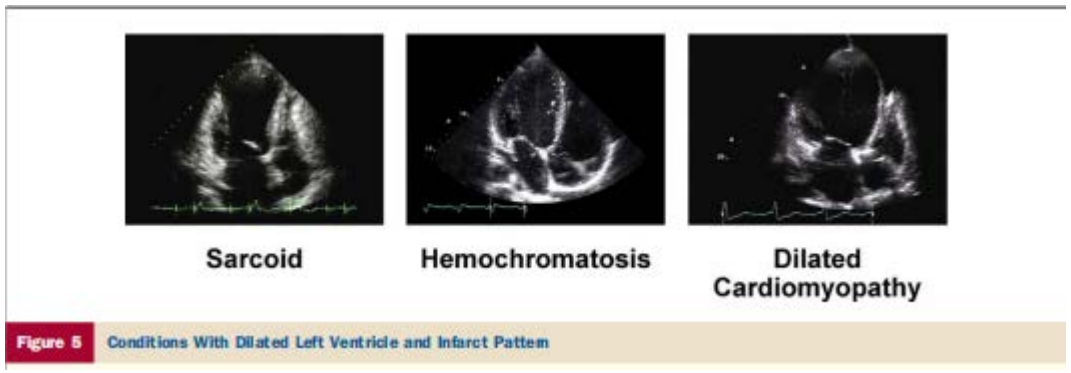


Figure 5 Conditions With Dilated Left Ventricle and Infarct Pattern

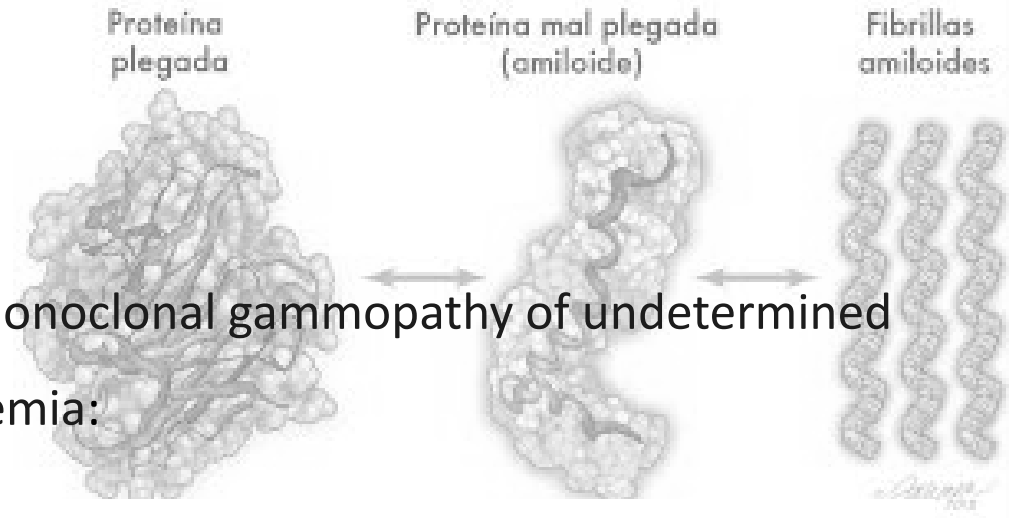
… Infiltrativas en general …

- Depósito de sustancias en paredes ventriculares → rígidas → ☹ relajación (**MC RESTRICTIVAS, DISFUNCIÓN DIASTÓLICA)**
- → ≈ MCH / ≈ MCD
- ↑ pared ≠ hipertrofia miocitos (ej: acumulo en intesticio) ≠ voltajes ↑ ECG

  SOSPECHA MC INFILTRATIVA: AUSENCIA DE VOLTAJES ↑ EN ECG (Amiloidosis, ataxia de Friedreich)

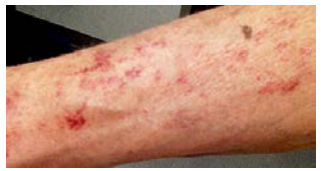
- Papel de **RMN** en diagnóstico: Distribución RTG
- Panel **genético** para varias miocardiopatías: ☹ si > 1 gen / penetrancia dependiente de edad /…

A) AMILOIDOSIS: TIPOS

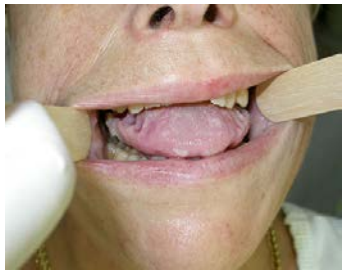


1- Amiloidosis por cadenas ligeras de inmunoglobulinas (AL); monoclonal gammopathy of undetermined significance, multiple myeloma, or Waldenström macroglobulinemia:

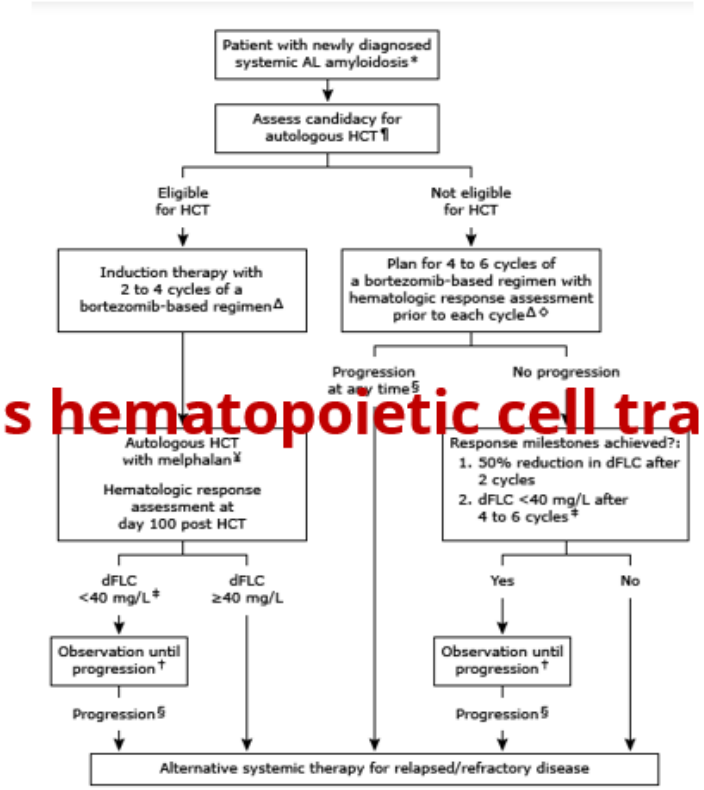
- **≥40** años
- Enfermedad multisistémica



+ Sdme Nefrótico
+ Neuropat periférica…



Autologous hematopoietic cell transplantation



https://static1.squarespace.com/static/5b44f08ac258b493a25098a3/t/5fad7f650e8bbf646ff5c9cf/1605205862155/Amyloid+Treatment+mSMART+2020+revision+October+2020.pdf (Accessed on October 10, 2022)

2- Amiloidosis ATTR (TTR, formerly known as prealbumin), a tetrameric protein synthesized by the liver that normally functions to transport thyroid hormone and retinol (vitamin A))

→ **Wild-type amyloidosis (wtATTR amyloidosis)** ≥70 años

→ **Hereditary amyloidosis (hATTR amyloidosis)**: HAD, penetrancia variable.

- 120 mutaciones conocidas.
- Edad de presentación: según mutación

Extremely Early Onset Transthyretin Familial Amyloid Polyneuropathy with a Leu55Pro Mutation: A Pediatric Case Report and Literature Review

Yun Jeong Lee [1], Jeeyoung Oh [2], Su-Kyeung Hwang [1], Eun Joo Lee [1], Dong Heon Yang [3], Yong-Jin Kim [4], Soonhak Kwon [1], Myung Chul Hyun [1]

17 años

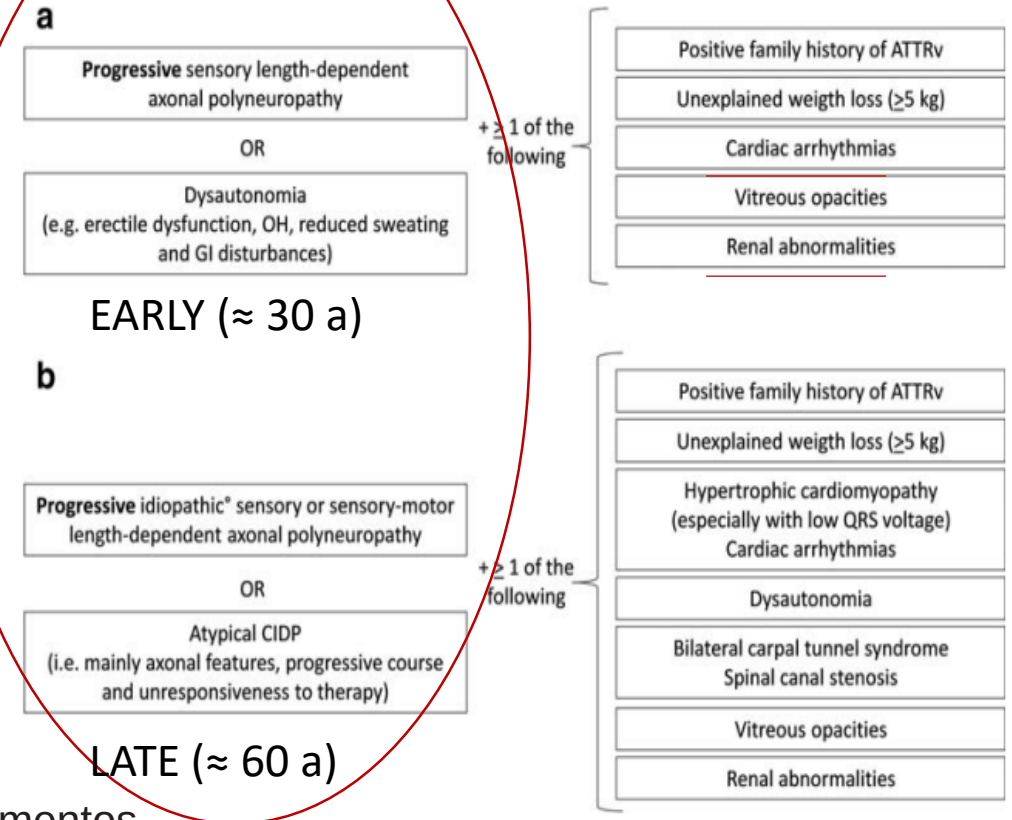
Anhidrosis, ortostatismo, náuseas, vómitos, diarrea…

+ HVI (**hermano Dx MCH**)

→ Tafamidis ☺

Fig. 1 Suspicion index for diagnosis of ATTRv amyloidosis with PN [adapted from Adams et al. 2019 [8]]. **a** In early-onset phenotype. **b** In late-onset phenotype. ATTRv, hereditary amyloidogenic transthyretin amyloidosis; CIDP, chronic inflammatory demyelinating polyradiculoneuropathy, GI gastrointestinal, OH orthostatic hypotension. Screening test for more common peripheral neuropathy negative

NEUROPATÍA (S, M, Autonómico)



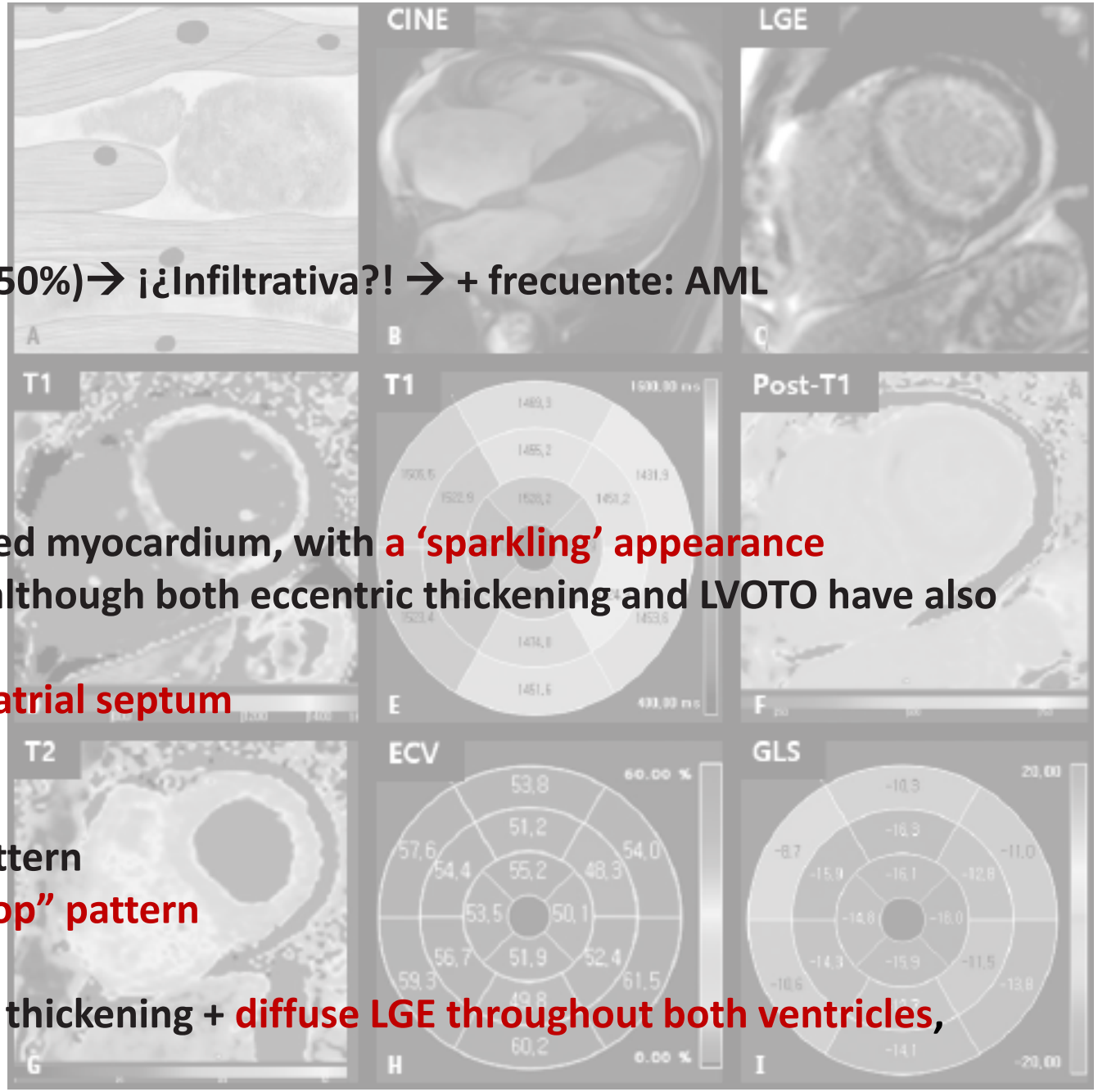
Rñ, ojos, articulaciones y ligamentos

A) AMILOIDOSIS: PPCC

- ECG:
  - ✓ Voltajes bajos en paciente con HVI (≈ 50%)→ ¡¿Infiltrativa?! → + frecuente: AML
  - ✓ Pseudoinfarction pattern
  - ✓ Conduction delays

- ETT:
  - ✓ Increased echogenicity of the thickened myocardium, with a 'sparkling' appearance
  - ✓ LV thickening is typically concentric, although both eccentric thickening and LVOTO have also been reported
  - ✓ Thickening of the RV, valves and interatrial septum
  - ✓ Enlarged atria
  - ✓ Pericardial effusion
  - ✓ Diastolic dysfunction → restrictive pattern
  - ✓ Strain assessment → "cherry on the top" pattern

- RMN: the demonstration of concentric LV thickening + diffuse LGE throughout both ventricles, particularly the subendocardium (↑ E)



A) AMILOIDOSIS: Dx

Left Ventricular Wall Thickness ≥ 12 mm

+ ≥1 of

- Heart failure in ≥ 65 years
- Aortic stenosis in ≥ 65 years
- Hypotension or normotensive if previously hypertensive
- Sensory involvement, autonomic dysfunction
- Peripheral polyneuropathy
- Proteinuria
- Skin bruising
- Bilateral carpal tunnel syndrome
- Ruptured biceps tendon
- Subendocardial/transmural LGE or increased ECV
- Reduced longitudinal strain with apical sparing
- Decreased QRS voltage to mass ratio
- Pseudo Q waves on ECG
- AV conduction disease
- Possible family history

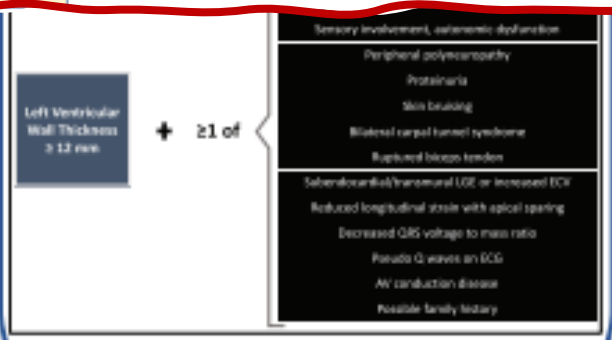
doi:10.1002/ejhf.2140

Cardiac amyloidosis

ESC Myocardial WG position paper

SUSPECT

Screen if



DIAGNOSIS

Diagnostic criteria

Invasive (all types)	Non-Invasive (only for ATTR)
Cardiac Biopsy positive for amyloid or Extracardiac Biopsy positive for amyloid + Echocardiographic/CMR criteria	Grade 2 or 3 cardiac uptake at diphosponate Scintigraphy + Negative serum free light chains & negative serum and urine immunofixation (SPIE & UPIE) + Echocardiographic/CMR criteria

Diagnostic algorithm

^{99m}Tc-DPD/PYP/HMDP Scintigraphy with SPECT & Haematologic tests (serum free-light chain quantification & serum and urine immunofixation)

Diagnosis made or proceed to **CMR and/or biopsy** according to results

TREATMENT

Cardiac complications and comorbidities

- Heart Failure
- Thromboembolism
- Atrial fibrillation
- Conduction disorders
- Ventricular arrhythmias
- Aortic stenosis

Disease modifying treatment

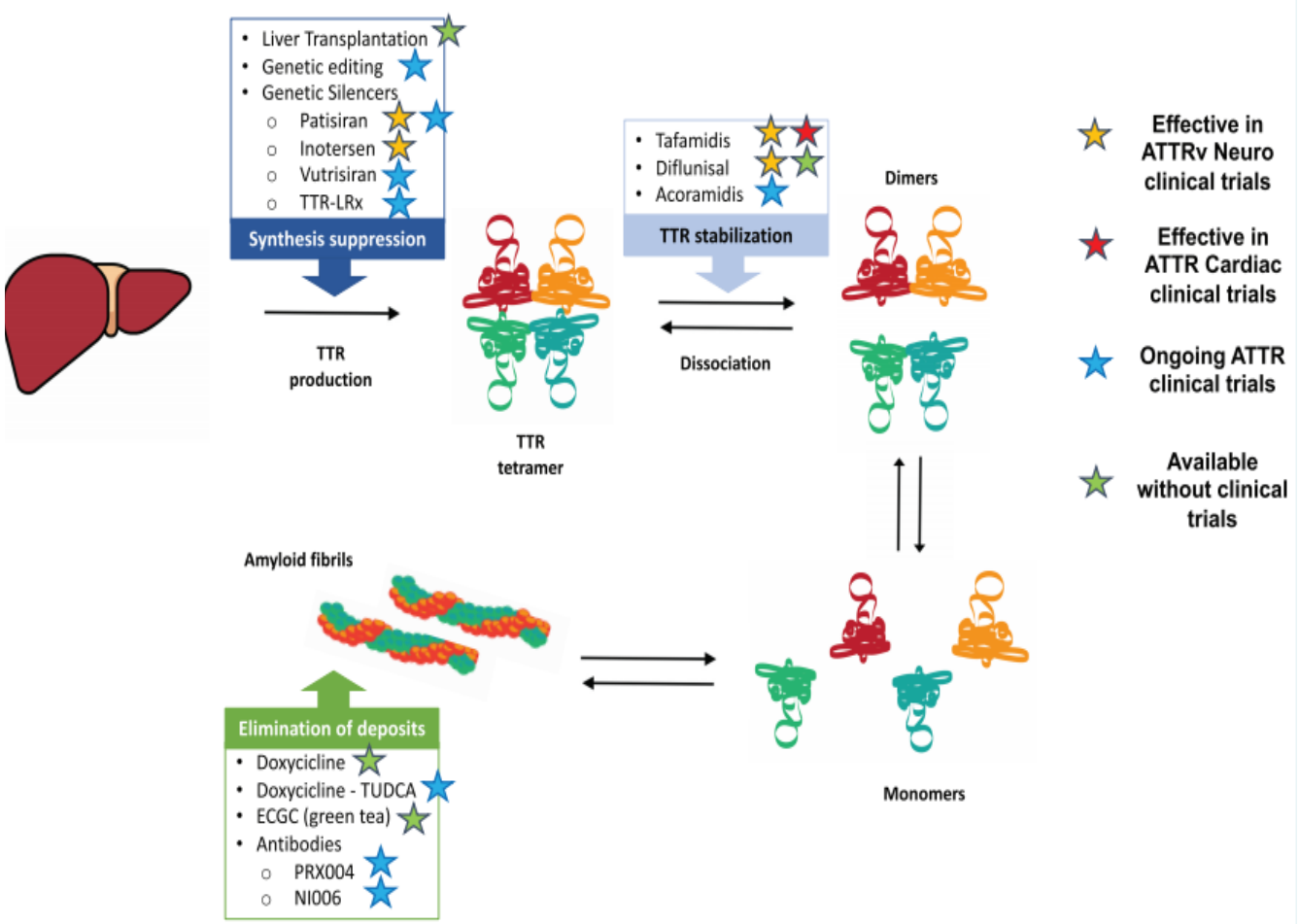
- **ATTR**: genetic silencers, stabilizers and removers.
- **AL**: chemotherapy and ASCT.
- **AA**: anti-inflammatory, anti-infective and immunosuppressive drugs.

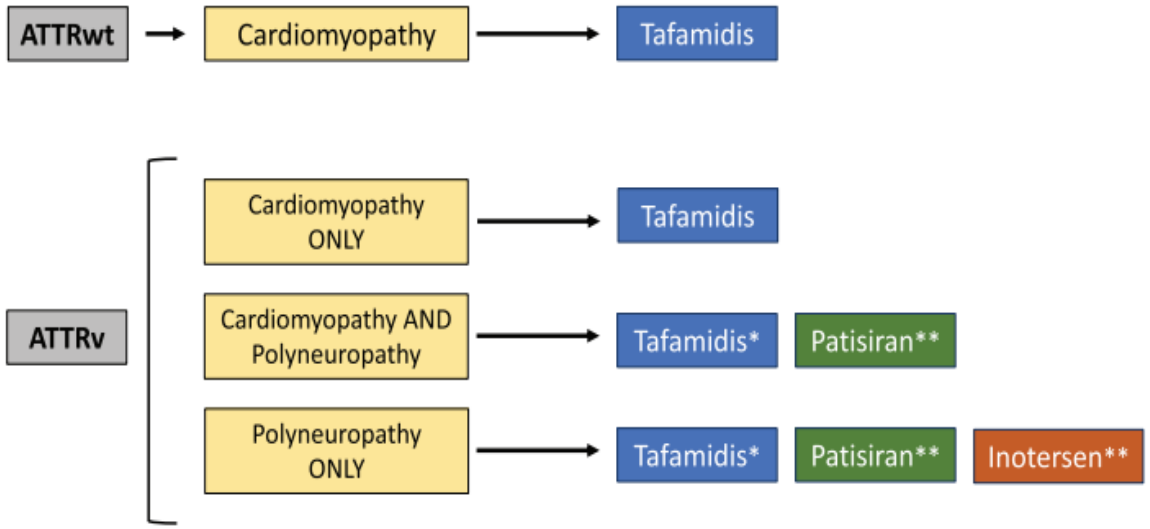
Diagnosis of Cardiac Amyloidosis

Invasive (all types)	Non-Invasive (only for ATTR)
Cardiac Biopsy positive for amyloid or Extracardiac Biopsy positive for amyloid + Echocardiographic/CMR criteria	Grade 2 or 3 cardiac uptake at diphosponate Scintigraphy + Negative serum free light chains & negative serum and urine immunofixation (SPIE & UPIE) + Echocardiographic/CMR criteria

doi:10.1002/ejhf.2140

A) AMILOIDOSIS: Tto





* Polyneuropathy Stage 1
** Polyneuropathy Stage 1 & 2

doi:10.1002/ejhf.2140

B) ENFERMEDADES DEL DEPÓSITO DE GLUCÓGENO:

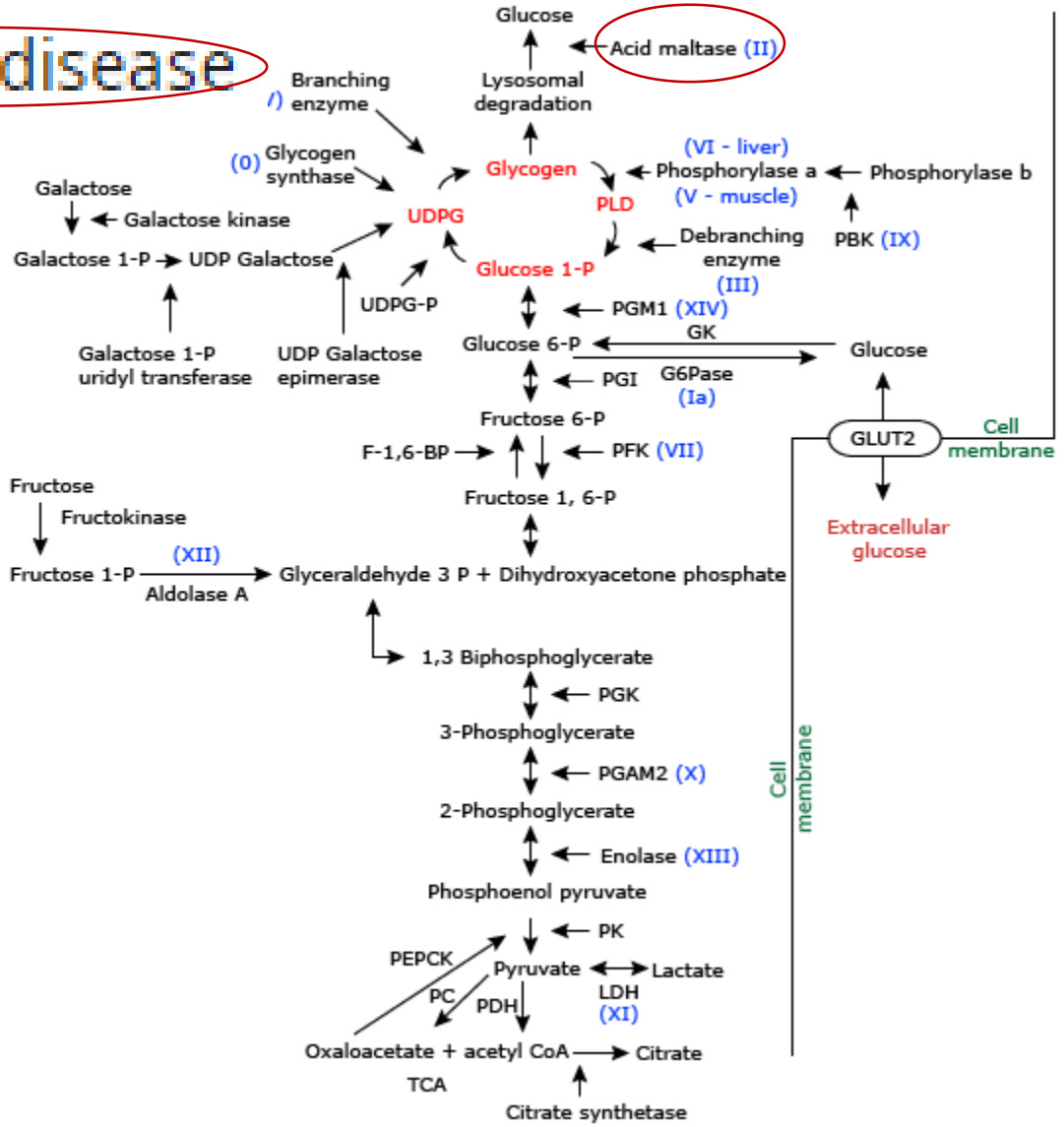
Type II: Acid maltase deficiency or Pompe disease

- 1/40.000
- HAR, > 600 variantes

→ Acúmulo glucógeno en lisosomas y citoplasma → destrucción tisular

- 2 formas:
  - → E**arly onset** (forma clásica, ausencia enzima):
    - ✓ 1os **meses** vida
    - ✓ HIPERTROFIA BIVENTRICULAR, IC
    - ✓ Extracardiaco: debilidad muscular, hipotonía, distrés respiratorio
    - ✓ Dx: prueba del talón (actividad enzimática de la GAA). Muestra sanguínea.
    - ✓ **Tto: Reemplazo enzimático con alglucosidasa alfa (MYOZIME, iv c/15d).**
    - ✓ Px: ☺

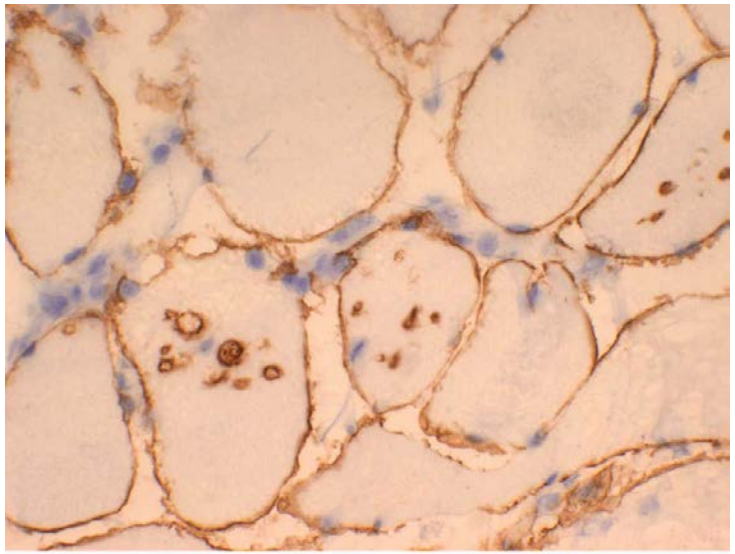
  →**Late-onset** (↓ enzima): adultos, SIN afectación cardiaca (miopatía).



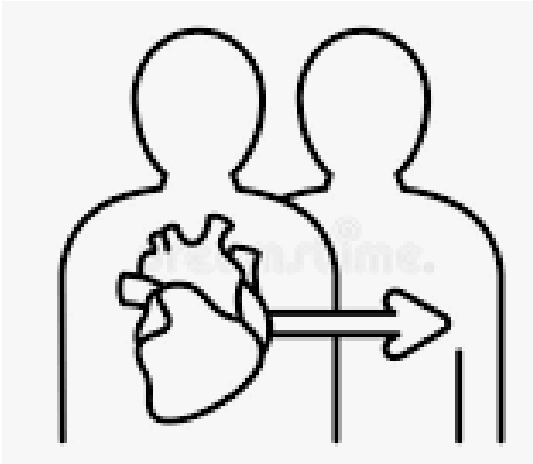
Danon disease, lysosomal GSD with normal acid maltase (IIb)

- Déficit de proteína LAMP2 (¿? Función)
- HAD ligada al X
- Miocardiopatía (Hipertrófica >> dilatada)
- Extracardiaco: Miopatía esquelética, Alteraciones oftalmológicas, discapacidad intelectual, trastornos psiquiátricos
- Dx:
  - ✓ biopsia muscular: VACUOLAS INTRACITOPLASMÁTICAS con glucógeno
  - ✓ Genética: mutación gen *LAMP2*

- ~~TTO ESPECÍFICO~~

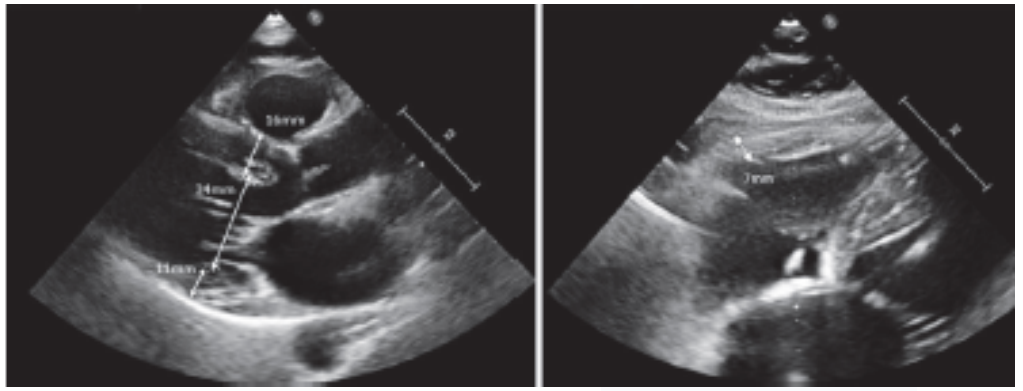


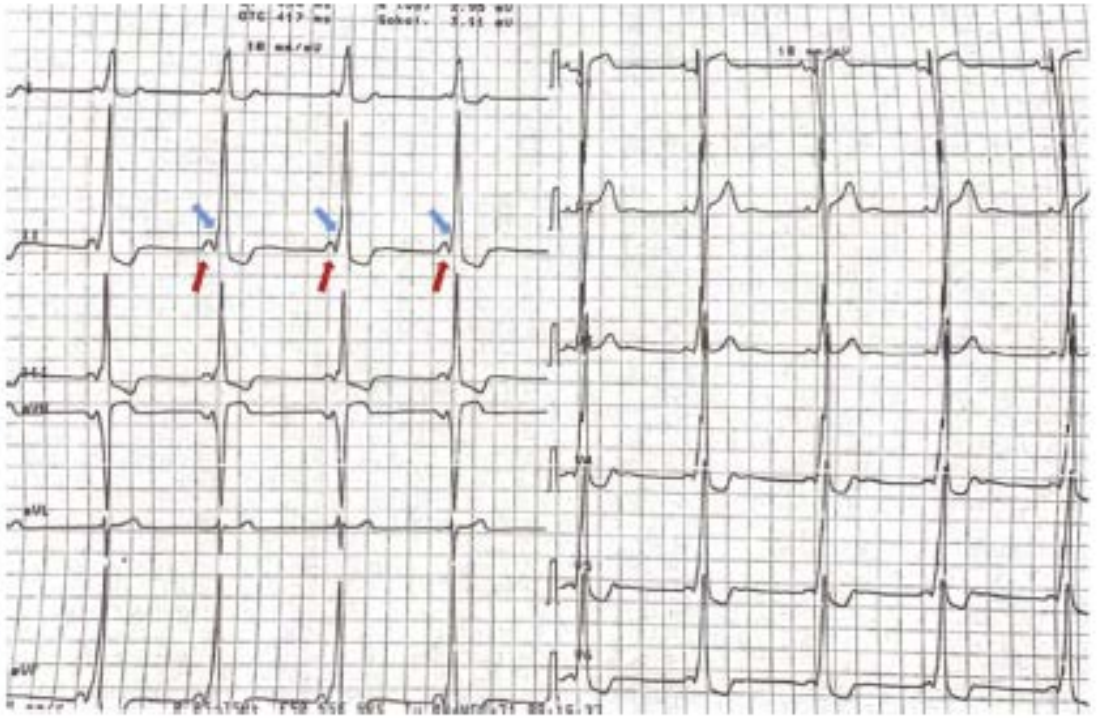
Neurologia. 2017;32:331–2

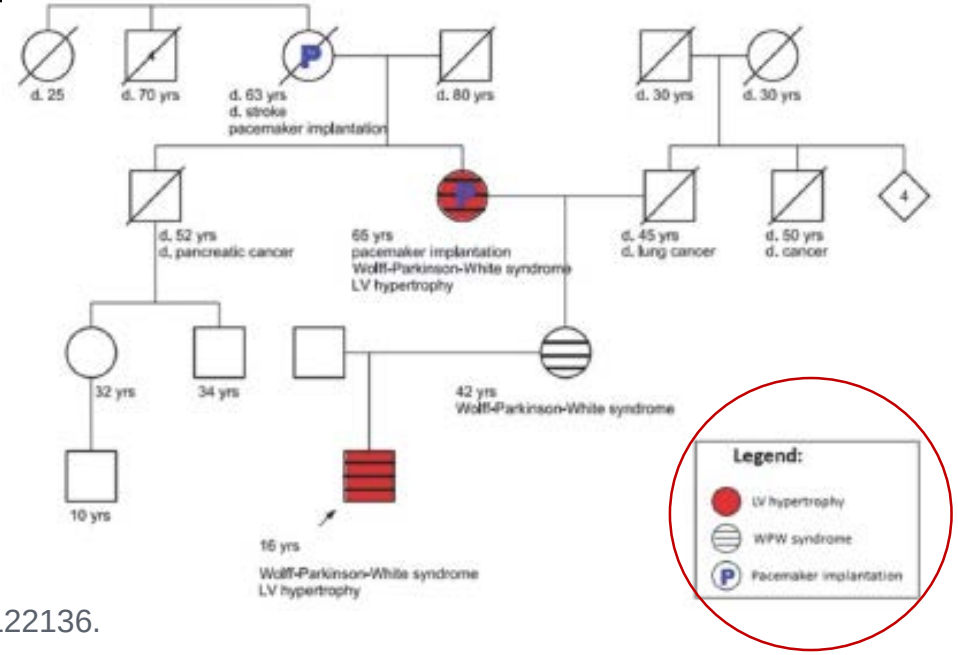


C) AMP CINASA (PRKAG2, PS):

- HAD. Mutaciones gen PRKAG2 → cambios estructurales de enzima (AMPK) que modula la **captación de glucosa → absorción deficiente de glúcidos en los miocitos → Depósito**
- Prevalencia: 0.23–1% de los pacientes con sospecha de MCH*
- ***"Early-onset":*** < 30 a
- **↓PR (70%) + Hipertrofia BIV + degeneración progresiva del sistema de conducción (≈ 30 a)**
- **+ TSV en jóvenes (≈ 40 a FLA/ FA) → Ictus**
- **50% HTA (jóvenes)**







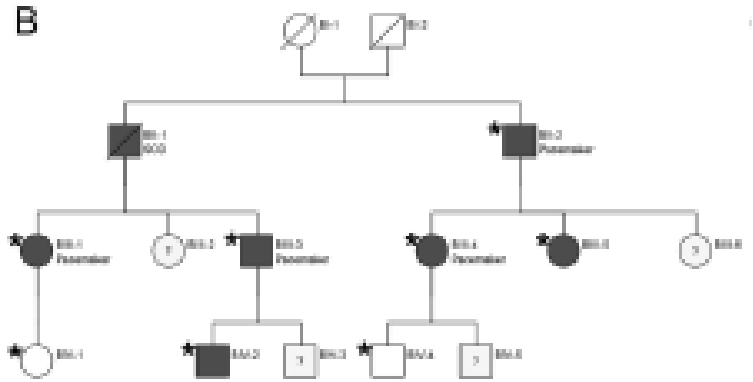
**

Fenotipos distintos en una misma familia

doi: 10.3390/life12122136.

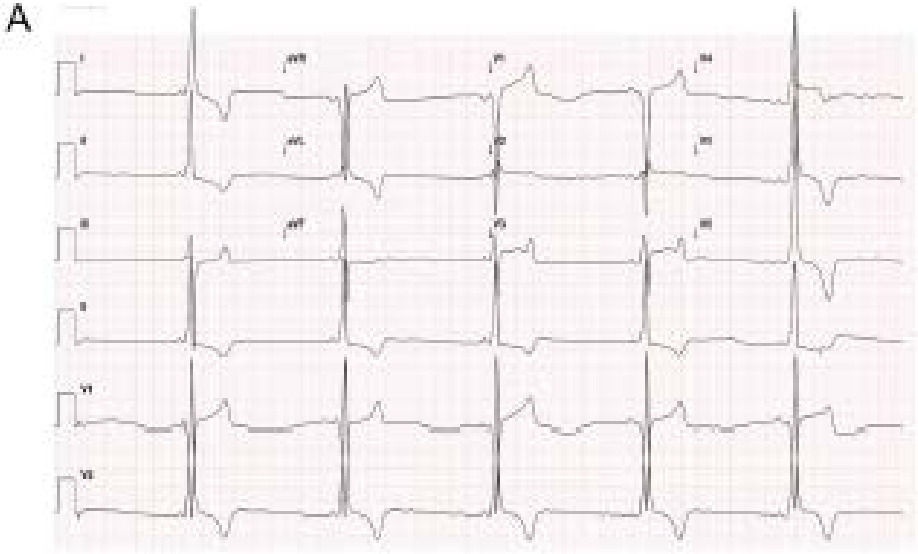
→ ESTUDIO GENÉTICO: Confirma Dx y precide severidad (Genotyping)

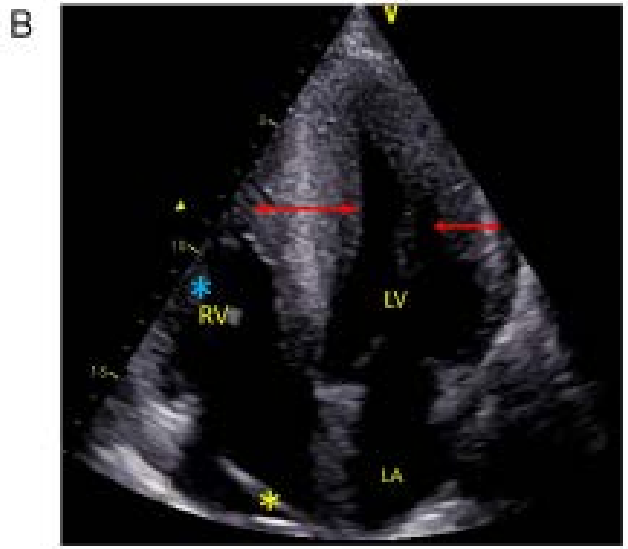
- ✓ c.1592G>A (Arg531Gln) → HVI agresiva (meses de vida)
- ✓ c.905G>A → + preexcitación
- ✓ c.1463A>T → Síncope por BAV Avanzado e implante de MCP



→ ¡! MONITORIZACIÓN Y SEGUIMIENTO (Holter): BAV, FA

→ SIN TTO ESPECÍFICO (¡! Dx diferencial)



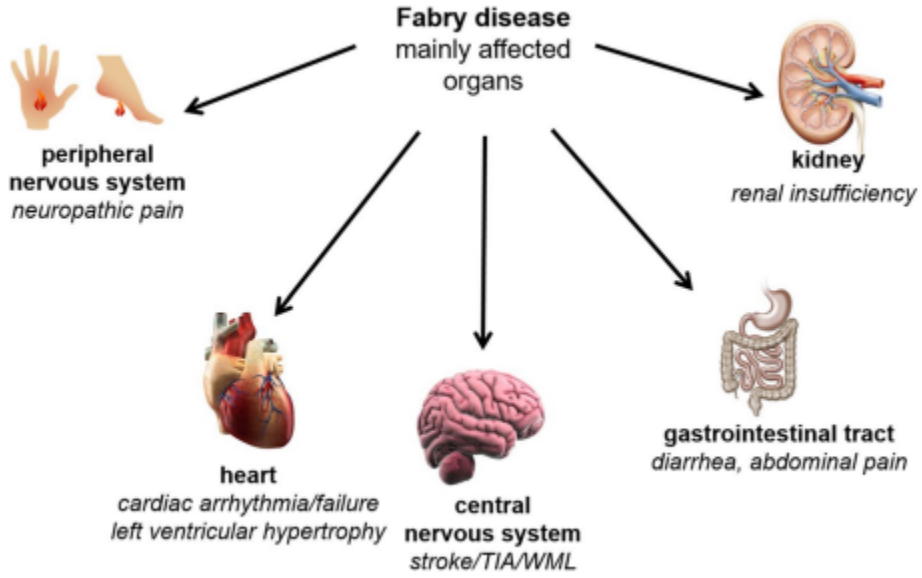


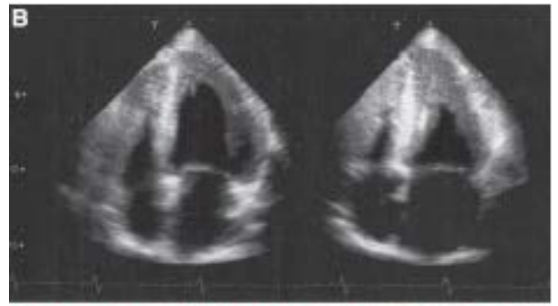
1- Sospechar e identificar PS
2- Establecer estratificación del R
3- Monitorización estrecha

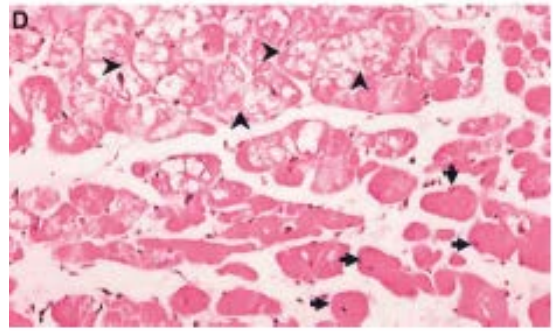
doi: 10.1038/s41598-020-77124-9.

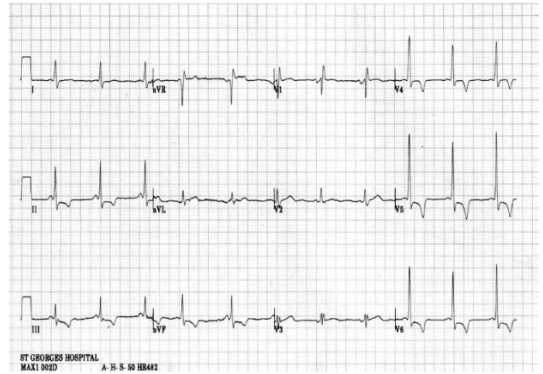
D) ENFERMEDADES POR DEPÓSITO LISOSOMAL: E. FABRY

- 6% de "**LATE-ONSET**" MCH (Varones)
- **Deficiencia de αGalactosidasa** por mutaciones gen **cromosoma X** (region Xq22.1) → Error innato del metabolismo → **depósito intracelular (lisosomal) de glicoesfingolípidos (vacuolas)** en diversas células → enfermedad multisistémica
- Espectro variable de clínica: grave (hombres) --- asintomático (mujeres)









doi: 10.1007/s40265-021-01486-1.

Clinical manifestations of Fabry disease

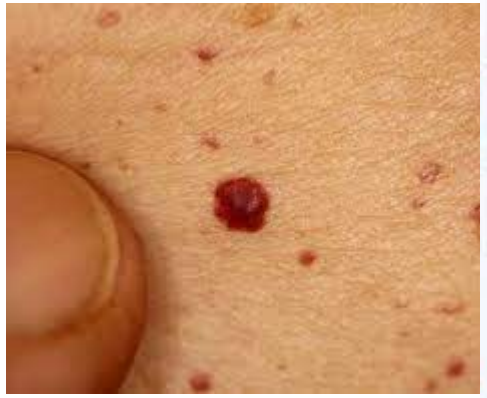
Childhood
Acroparesthesia, may be severe
Telangiectasias on ears, conjunctiva
Hypohidrosis, poor exercise and heat tolerance
Nausea, diarrhea, and abdominal pain
Raynaud phenomenon
Ophthalmologic abnormalities (cornea verticillata)
Early adulthood
Extensive angiokeratomas, telangiectasias
Albuminuria, hematuria, oval fat bodies in urine
Nausea, diarrhea, and abdominal pain
Fever, heat collapse, anhidrosis
Proteinuria
Cornea verticillata, conjunctival vessel tortuosity, and lymphedema
30 to 40 years of age
Cardiac disease: Left ventricular hypertrophy, conduction and rhythm abnormalities, valvular disease, small coronary vessel disease
Kidney function impairment usually with proteinuria
Ischemic cerebrovascular stroke or TIAs
Progressive length-dependent small fiber neuropathy: Acroparesthesia, loss of cold and warm perception
Nausea, diarrhea, and abdominal pain

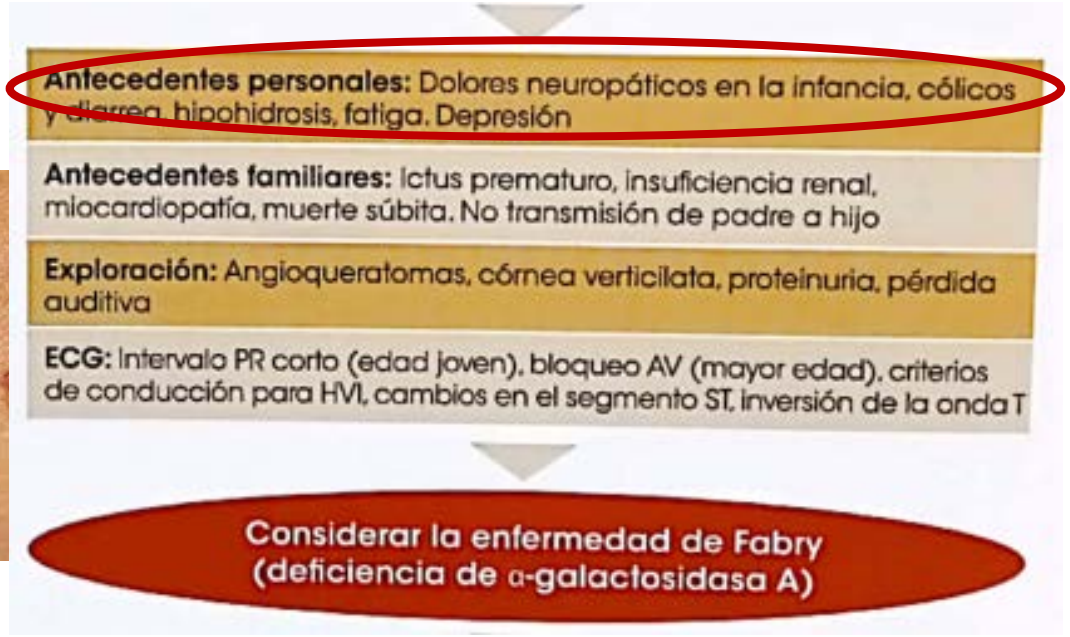
TIAs: transient ischemic attacks.

Adapted from: Cho ME, Kopp JB. Fabry disease in the era of enzyme replacement therapy: a renal perspective. Pediatr Nephrol 2004; 19:583.

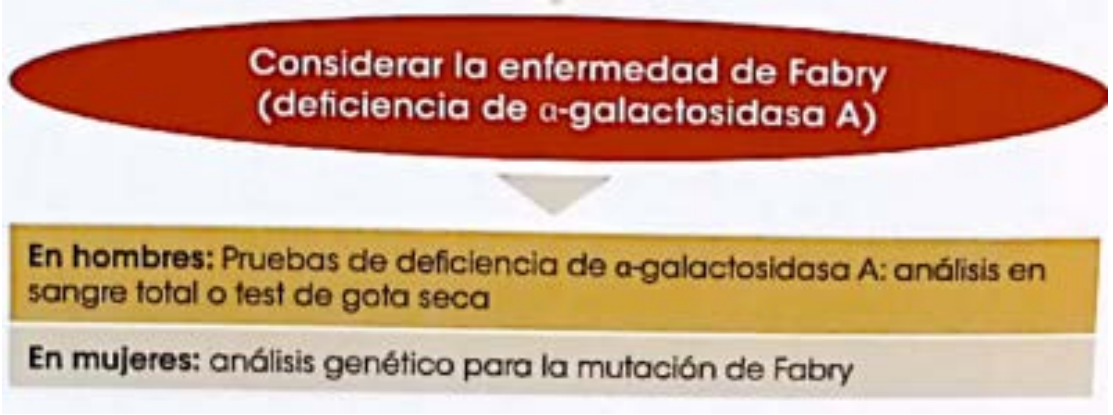
UpToDate®

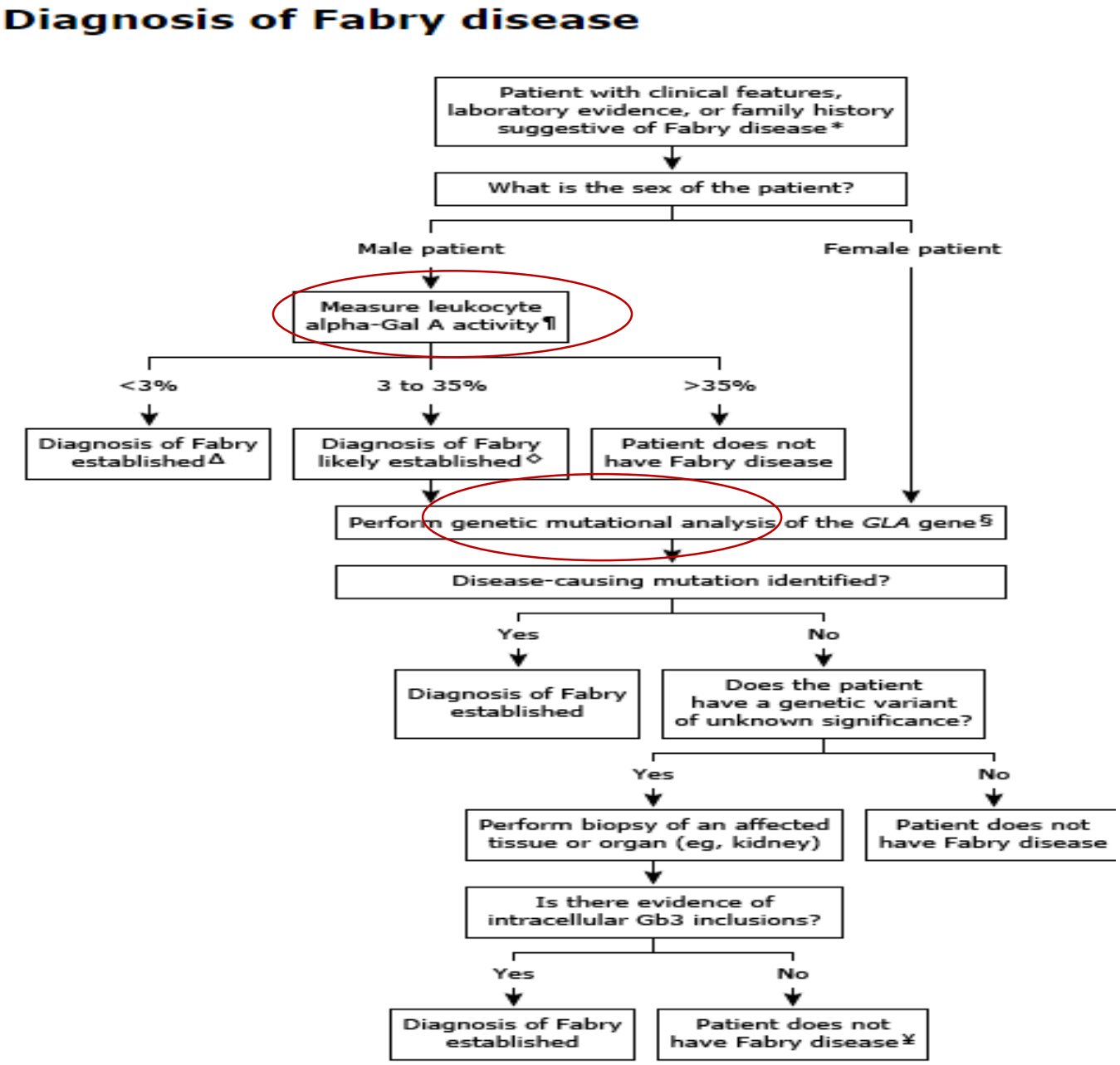
angioqueratomas





D) E. FABRY (Dx)


Considerar la enfermedad de Fabry (deficiencia de α-galactosidasa A)
En hombres: Pruebas de deficiencia de α-galactosidasa A: análisis en sangre total o test de gota seca
En mujeres: análisis genético para la mutación de Fabry


Diagnosis of Fabry disease
Patient with clinical features, laboratory evidence, or family history suggestive of Fabry disease*
What is the sex of the patient?
Male patient
Female patient
Measure leukocyte alpha-Gal A activity¶
<3%
3 to 35%
>35%
Diagnosis of Fabry established△
Diagnosis of Fabry likely established◇
Patient does not have Fabry disease
Perform genetic mutational analysis of the GLA gene§
Disease-causing mutation identified?
Yes
No
Diagnosis of Fabry established
Does the patient have a genetic variant of unknown significance?
Yes
No
Perform biopsy of an affected tissue or organ (eg, kidney)
Patient does not have Fabry disease
Is there evidence of intracellular Gb3 inclusions?
Yes
No
Diagnosis of Fabry established
Patient does not have Fabry disease¥

D) E. FABRY (Tto)

- ✓ Fabrazyme (agalsidasa beta)

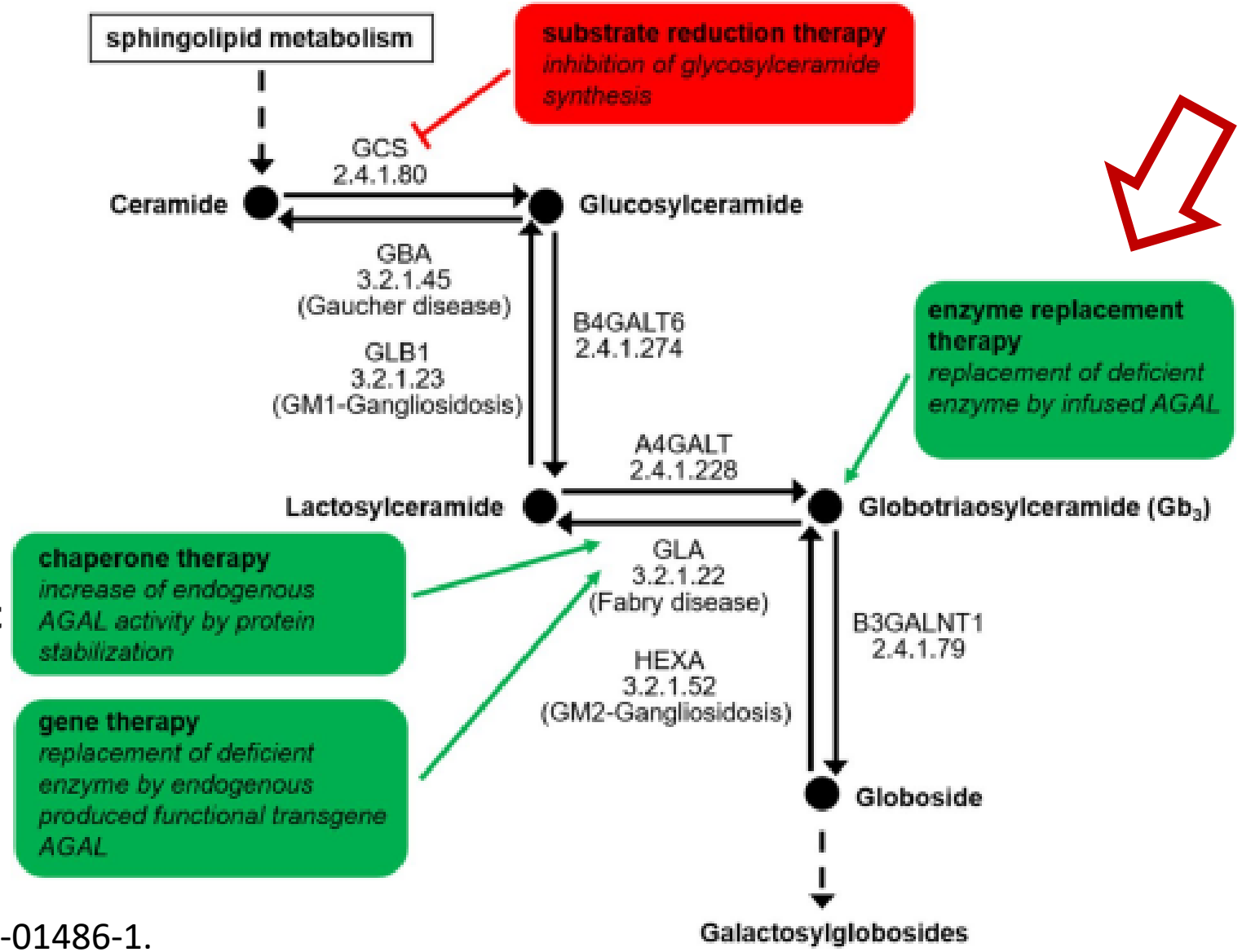
  1 mg/kg c/15d iv

- ✓ Replagal (agalsidasa alfa)

  0.2 mg/kg c/15 d iv

→ long-term ERT or migalastat treatment can **reduce left ventricular wall thickness**

Migalastat



doi: 10.1007/s40265-021-01486-1.

Table 1 Conditions Presenting With Increased LV Mass and Thick Ventricular Walls

Condition	Age at Presentation	History and Clinical Presentation	Echocardiography	ECG Profile	CMR LGE	Biopsy
Cardiac amyloid	>30 yrs	Heart failure symptoms, nephrotic syndrome, idiopathic peripheral neuropathy, unexplained hepatomegaly	Symmetrical increase in LV and RV wall thickness, dilated LA and RA, granular appearance of myocardium, pericardial effusion, decreased EF in advanced cases	Decreased or normal QRS complex voltage, pseudoinfarction in inferolateral leads	Global, diffuse, pronounced in subendocardium; RV and LV walls	Myocyte atrophy, amyloid replaces normal cardiac tissue
Fabry disease	Male: 11 ± 7 yrs; female: 23 ± 16 yrs	Neuropathic pain, impaired sweating, skin rashes	Symmetrical increase in LV and RV wall thickness, normal EF	Increased or normal QRS complex voltage, short or prolonged PR interval	Focal, midwall, inferolateral wall	Enlarged myocytes with clusters of concentric glycolipid (myelinoid bodies) within lysosomes
Danon disease	<20 yrs	Heart failure, skeletal myopathy, mental retardation	Very thick LV (20–60 mm), RV may or may not be thick, decreased EF	Increased or normal QRS complex voltage, short PR interval (delta wave)	Subendocardial, does not correspond to perfusion territory	Sarcoplasmic vacuolization, focal storage of PAS-positive material, myofibrillar disarray
Friedreich ataxia	25 yrs (range 2–51 yrs)	Gait abnormality	Increase in LV septal and posterior wall thickness, normal EF	Normal QRS complex voltage, ventricular tachycardia		Nonspecific
Cardiac oxalosis	>20 yrs	Juvenile urolithiasis and nephrocalcinosis	Symmetrical increase in LV and RV wall thickness; patchy, echodense speckled reflection; normal EF	Increased or normal QRS complex voltage, complete heart block	Increased myocardium attenuation on CT	Intra- and extracellular deposition of oxalate crystals without concomitant inflammation and necrosis
Mucopolysaccharidoses	1–24 yrs (median, 10 yrs)	Variable depending on subtype, coarse facial features, delayed mental development, skeletal deformities, corneal clouding, hepatosplenomegaly	Asymmetrical septal hypertrophy, mitral and/or aortic valve stenosis or insufficiency, normal EF	Increased or decreased QRS complex voltage, malignant arrhythmia		Swollen myocytes with clear cytoplasm due to accumulation of mucopolysaccharides within lysosomes
Differential diagnosis						
Hypertrophic cardiomyopathy	17–18 yrs	Maybe asymptomatic, dyspnea, angina, syncope, sudden death	Asymmetrical hypertrophy, small LV cavity, LVOT obstruction, normal EF	Increased QRS complex voltage, pseudo–delta wave, giant T-wave inversion	Patchy, midwall, junctions of the ventricular septum and RV	Myocyte hypertrophy, myofibrillar disarray, and interstitial fibrosis
Hypertensive heart disease	Adults	History of hypertension	Symmetrical increase in LV wall thickness, mild LV dilation, normal EF	Increased QRS complex, nonspecific ST-T-wave changes	No pattern, predominantly subendocardial	Enlarged myocytes with enlarged or replicated nuclei

doi:10.1016/j.jacc.2009.12.040

5- OTRAS CAUSAS DE HVI

Inborn errors of metabolism
Glycogen storage diseases:
Pompe disease (glycogen storage disease type II)
Forbes disease (glycogen storage disease type III, also known as Cori disease)
Phosphorylase kinase deficiency (glycogen storage disease type IX)
Carnitine deficiency:
Carnitine palmitoyltransferase type II deficiency
Carnitine-acylcarnitine translocase deficiency
Mucopolysaccharidoses:
Hurler syndrome (mucopolysaccharidosis type I)
Hunter syndrome (mucopolysaccharidosis type II)
Morquio syndrome
Scheie syndrome
Other lysosomal diseases:
Danon disease
Fucosidosis
I-cell disease
Fabry disease
Mannosidosis
Organic acidurias:
Methylmalonic aciduria
Barth syndrome (3-methylglutaconic aciduria, type II)
Glycosylation disorders (eg, phosphomannomutase 2 deficiency)
Congenital generalized lipodystrophy

Multiple congenital anomaly syndromes
Noonan syndrome
LEOPARD syndrome
Beckwith-Wiedemann syndrome
Cardiofaciocutaneous syndrome
Rubinstein-Taybi syndrome
Costello syndrome

Neuromuscular disorders
Friedreich ataxia
Myotonic dystrophy
Minicore (multicore) myopathy

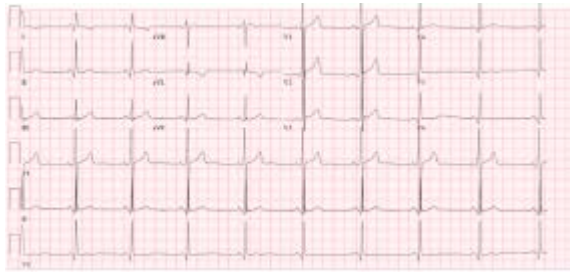
Mitochondrial disorders
MELAS syndrome
Leigh syndrome
Complex I deficiency
Sengers syndrome
Defects of beta-oxidation enzymes:
Very long chain acyl-CoA dehydrogenase deficiency
Long chain 3-hydroxyacyl-CoA dehydrogenase deficiency
Multiple acyl-COA dehydrogenase deficiency
Combined respiratory chain deficiencies

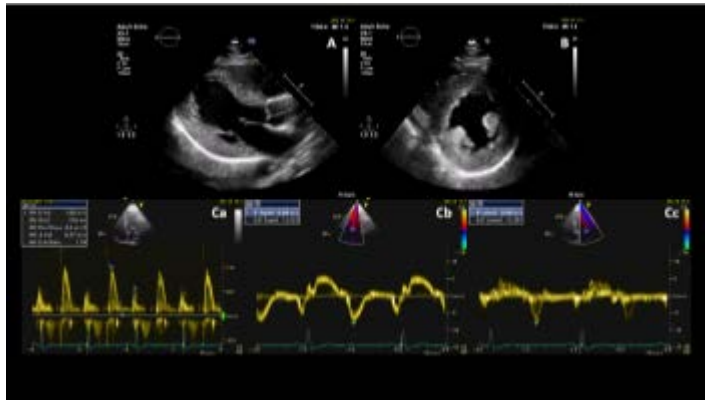
Interesting Images

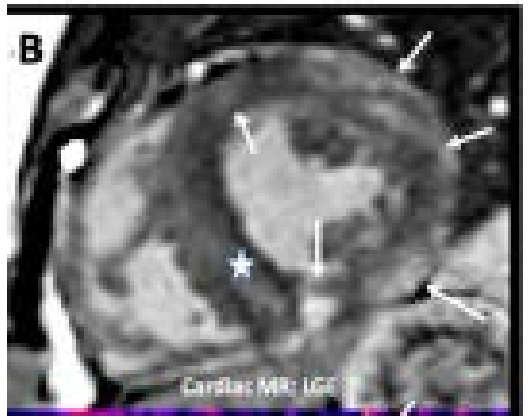
Unraveling an Unusual Phenocopy of Hypertrophic Cardiomyopathy: MELAS Syndrome

MELAS síndrome = mitochondrial encephalopathy with lactic acidosis and stroke-like episodes

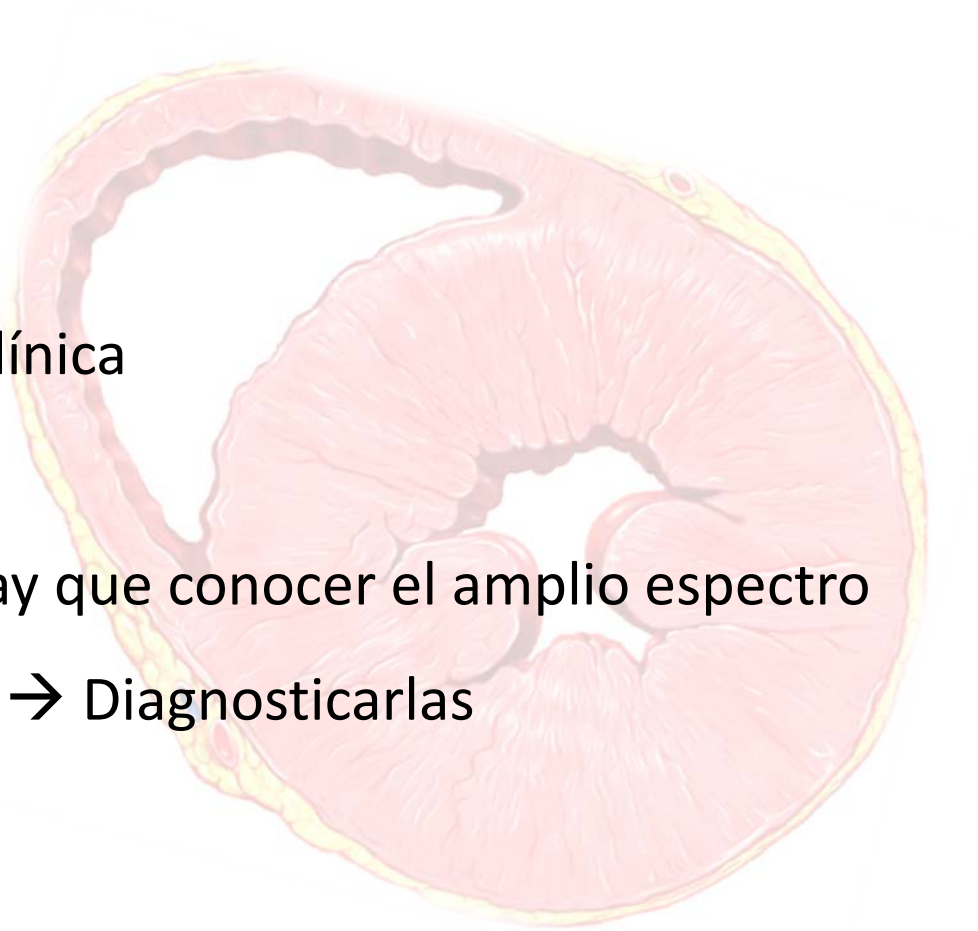
- **Miopatía** metabólica por afectación de DNA mitocondrial (herencia materna)
- Edad de inicio /grado de afectación variable: **epilepsia**, **DM**, **acidosis láctica**, debilidad muscular, **retraso cognitivo**, … + MCH + taquiarritmias, preexcitación
- RMN: Fibrosis intesticial difusa → RTG + distribución NO isquémica (difusa, subepicárdica…)
- SIN tto específico







TAKE HOME MESSAGES:



1. HV es un hallazgo frecuente en la práctica clínica
2. Reto diagnóstico establecer causa
3. Frecuente: 2ª (HTA, valvulopatía,…), pero hay que conocer el amplio espectro de FENOCOPIAS DE MCH para sospecharlas → Diagnosticarlas
4. Importancia de la **edad de presentación**
5. **Red flags** en cada fenocopia
6. Fenocopias con **tratamiento** establecido: **Amiloidosis, E. pompe, E. Fabry**

MUCHAS GRACIAS ☺

Phenocopy Conditions for Hypertrophic Cardiomyopathy

Phenotype	Gene	Protein	Phenotypic clue
AMPK mediated Glycogen storage	*PRKAG2*	Protein Kinase A, γ subunit	Normal or reduced left ventricular systolic function, pre-excitation pattern
Pompe disease	*GAA*	α-1,4-glucosidase (acid maltase)	Autosomal recessive, multi-organ disease, Pre-excitation pattern
Anderson-Fabry disease	*GLA*	α-galactosidase A	X-linked, multi-system also involving skin, kidney and peripheral nerves
Danon disease	*LAMP2*	Lysosome-associated membrane protein 2	X-linked dominant, Proximal muscle weakness, intellectual disability, short PR on ECG, elevated CK levels
Amyloidosis	*TTR*	Transthyretin	Low QRS voltage, other organ involvement, Subendothelial LGE
Kearns-Sayre syndrome	*mtDNA*	Mitochondrial protein	Multi-system disease
Friedreich ataxia	*FRDA*	Frataxin	Autosomal recessive, neurodegeneration
Myotonic dystrophy	*DMPK*	Myotonin Protein kinase	Myotonia, muscular dystrophy, cataract, frontal baldness
	ZNF9	Zinc Finger Factor 9	
Noonan/LEOPARD syndromes (Rasopathies)	*PTPN11*	Protein tyrosine phosphatase, nonreceptor type 11	Congenital heart defects, Lentigines, Café-au-lait spots
	SOS1,SOS2	Son of Sevenless	
	RAF1	Murine leukemia viral oncogene homolog 1	
	KRAS	Kirsten rat sarcoma virus homolog	
	Others (*A2ML1, BRAF, CBL, MAP2K1, MAP2K2, NRAS, RIT1, RRAS, SHOC2*)		
Neimann-Pick disease	*NPC1*	Neimann-Pick	Autosomal recessive neuro-degenerative disease
Refsum disease	*PAHX (PHYH)*	Phytanoyl-CoA hydroxylase	Retinitis pigmentosa, peripheral neuropathy, and ataxia
Deafness	*MYO6*	Unconventional myosin 6	Autosomal dominant deafness

Abbreviations: ECG: Electrocardiogram; CK: Creatine kinase; LGE: late gadolinium enhancement

Circ Res. 2017 September 15; 121(7): 749–770.
doi:10.1161/CIRCRESAHA.117.311059.

Table 2 Conditions With Dilated LV and Infarct Pattern

Condition	Age at Presentation	History	Echocardiography	ECG	CMR LGE	Cardiac Biopsy
Sarcoidosis	Young adults	Congestive heart failure	Variable wall thickness, focal or global hypokinesis, LV aneurysm	Infrahisian block, atypical infarction pattern	Patchy, basal and lateral LV walls	Noncaseating, multinucleated giant cell granuloma surrounded by band of dense collagen fibers
Wegener disease	Young adults	Chronic upper and lower respiratory tract infections	Regional hypokinesis, pericardial effusion, mild MR, LV systolic dysfunction	Atrial fibrillation, atrioventricular block, atypical infarction pattern	Diffuse, midwall	Vasculitis with necrotizing granulomatous inflammation
Hemochromatosis	Hereditary hemochromatosis: >30 yrs in men, older in women; secondary hemochromatosis: any age	Hereditary hemochromatosis: liver function abnormalities, weakness and lethargy, skin hyperpigmentation, diabetes mellitus, arthralgia, impotence in men; secondary hemochromatosis: hemolytic anemia, multiple blood transfusions	Dilated LV with global systolic dysfunction	Supraventricular arrhythmia, ventricular conduction abnormality is rare		Iron deposits within the myocyte
Differential diagnoses						
Ischemic cardiomyopathy	Adult	Coronary artery disease, congestive heart failure	Dilated LV, regional hypokinesis corresponding to perfusion territory, decreased systolic function	Multiform premature ventricular complexes, nonsustained ventricular tachycardia	Subendocardial, different degrees of transmural extension, corresponds to perfusion territory	
Idiopathic dilated cardiomyopathy	Adult	Congestive heart failure, no known cardiovascular disease	Dilated LV with global systolic dysfunction	Atrial fibrillation	No LGE, or if present, midwall and patchy	

doi:10.1016/j.jacc.2009.12.040

Figure 5 Conditions With Dilated Left Ventricle and Infarct Pattern