Hospital Universitario Ramón y Cajal

Enfermedades Musculares en la Infancia y Adolescencia(XIV)

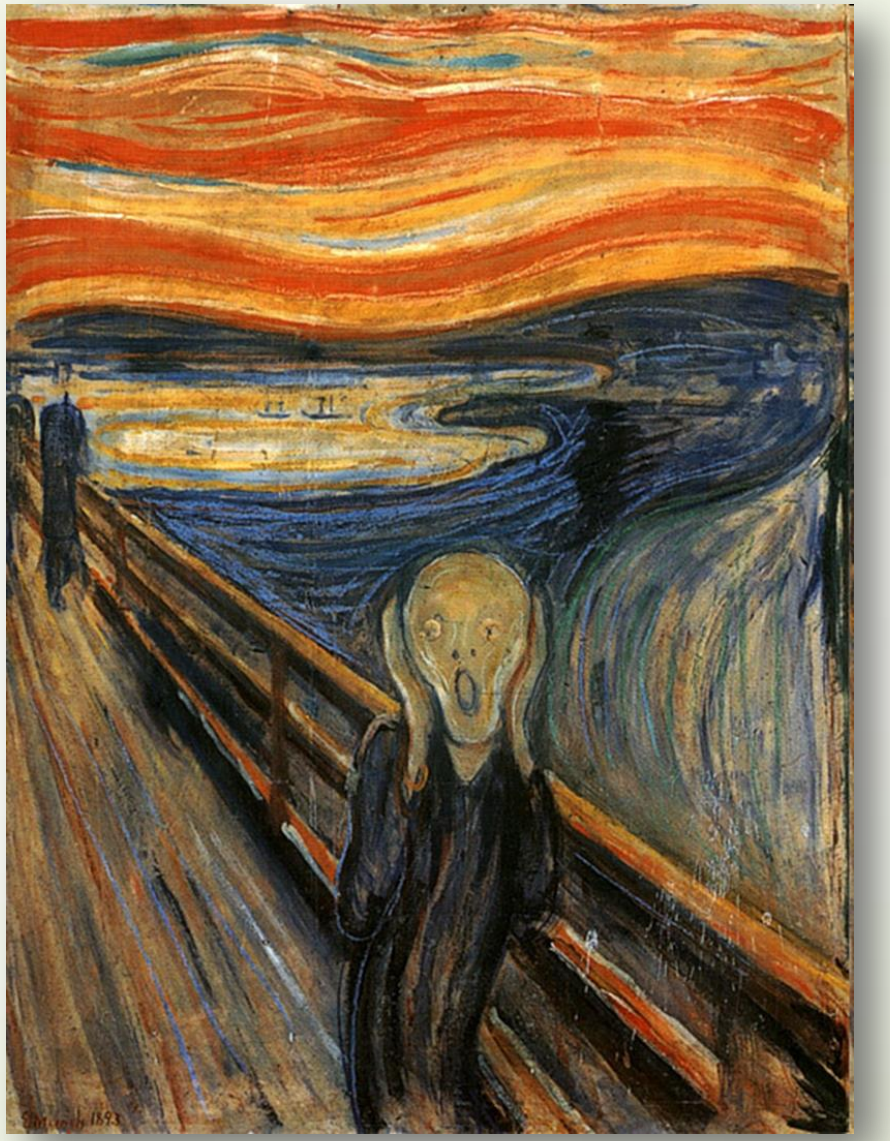
30 y 31 de Marzo de 2017

Terapia enzimática en la enfermedad de Fabry. Casos clínicos.

Dr. F.J. Aguirre Rodríguez

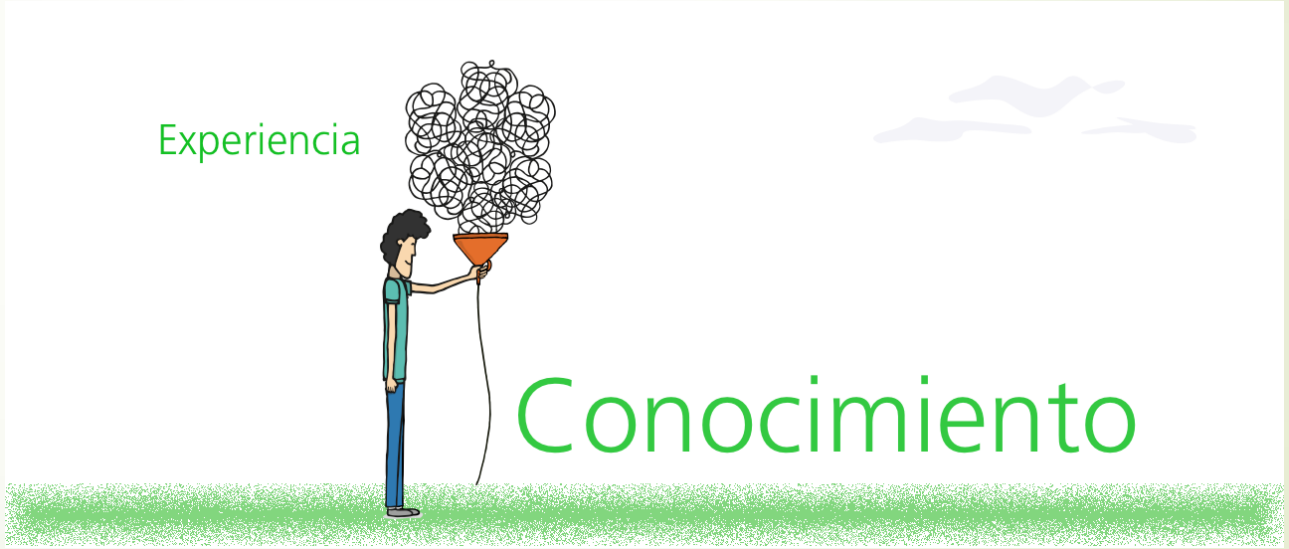
Neuropediatra
Hospital Torrecardenas
Almería

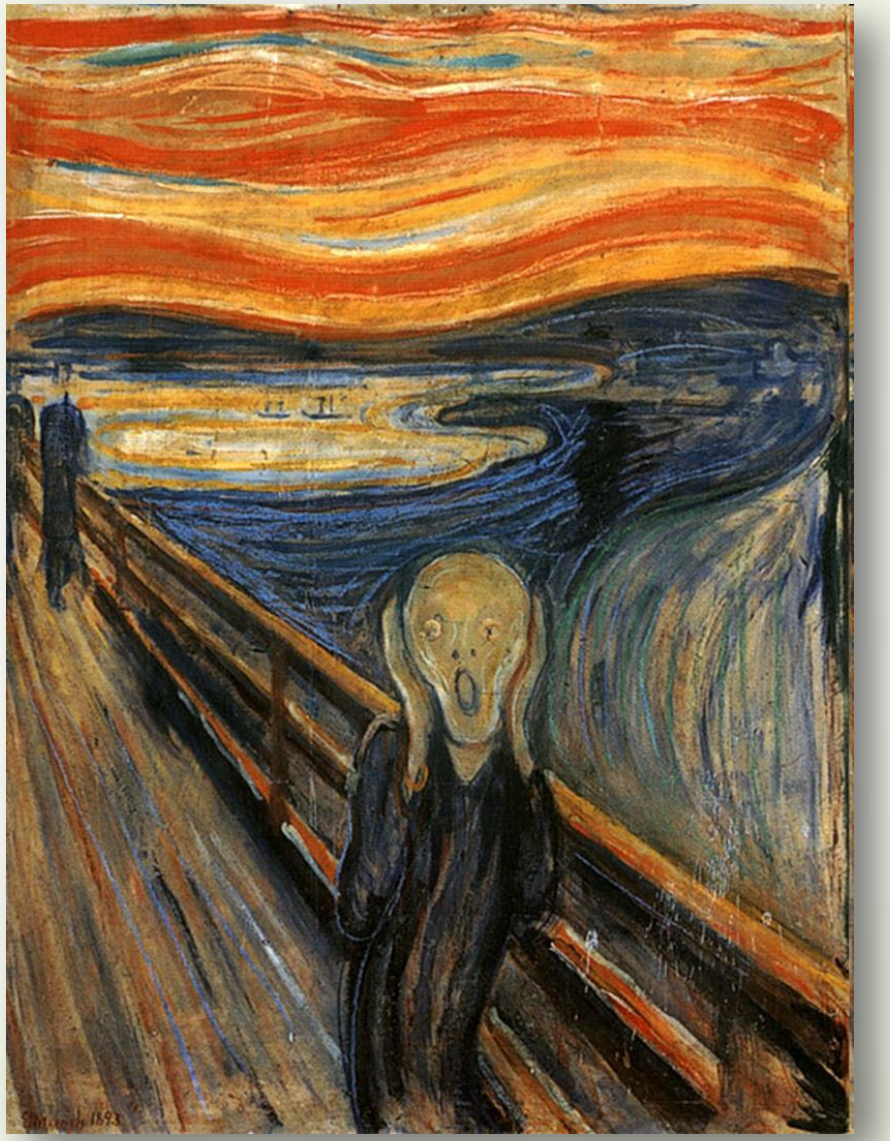
Muchas
Gracias...



ENFERMEDAD DE FABRY

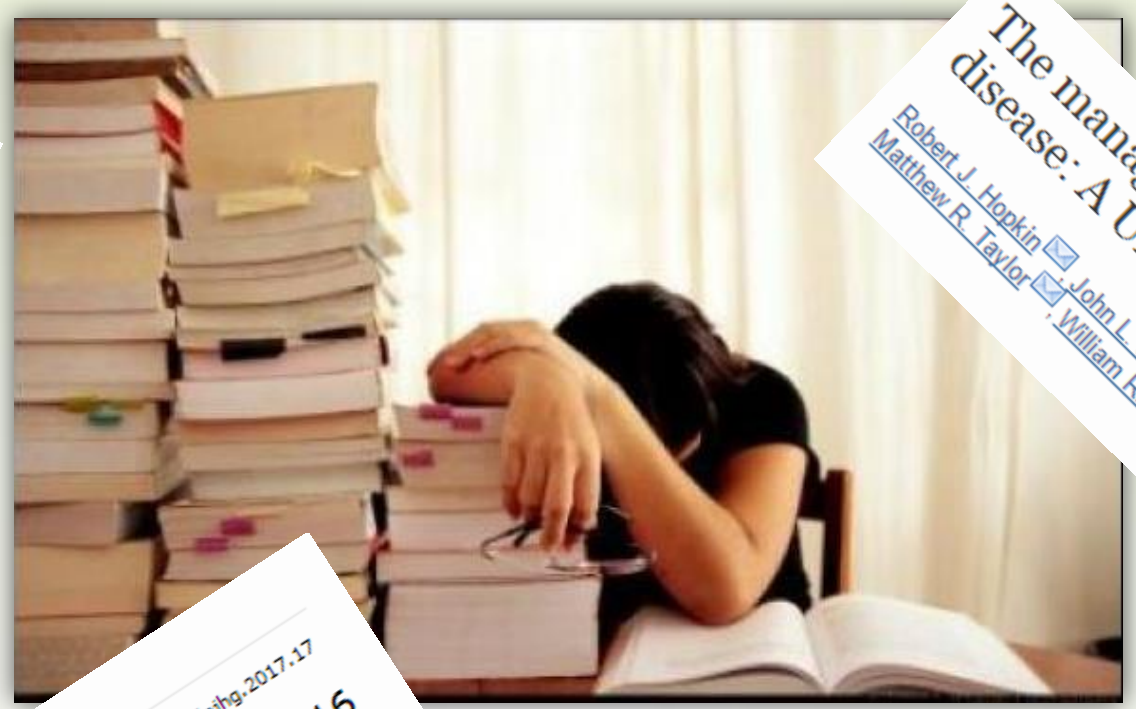
- 1 CASO





Fabry disease diagnostic guideline

Tamás Constantin, Éva Rákóczi, Andrea Ponyi, Csaba Ambrus, Krisztina Kádár, Ildikó Vastagh, Angéla Dajnoki, Beáta Tóth, Gergely Bokréta, Veronika Müller, Mária Katona, Márta Csikós, Orsolya Fiedler, Rita Szechey, Edit Varga, Gábor Rudas, Attila Kertész, Sándor Molnár, Sarolta Kárpáti, Viktor Nagy, Pál Magyar, Mohamed Mahdi, Krisztina Németh, Dániel Bereczki, Miklós Garami, Melinda Erdős, László Maródi, György Fekete



The management and treatment of children with Fabry disease: A United States-based perspective

Robert J. Hopkin, John L. Jefferies, Dawn A. Laney, Victoria H. Lawson, Michael Mauer, Matthew R. Taylor, William R. Wilcox, on behalf of the Fabry Pediatric Expert Panel

Clinical Utility Gene Card Update

European Journal of Human Genetics advance online publication 22 March 2017; doi: 10.1038/ejhg.2017.17

Clinical utility gene card for: Fabry disease – update 2016

Andreas Gal[1], Michael Beck[2], Wolfgang Höppner[1] and Dominique P Germain[3]

Fabry-betegség

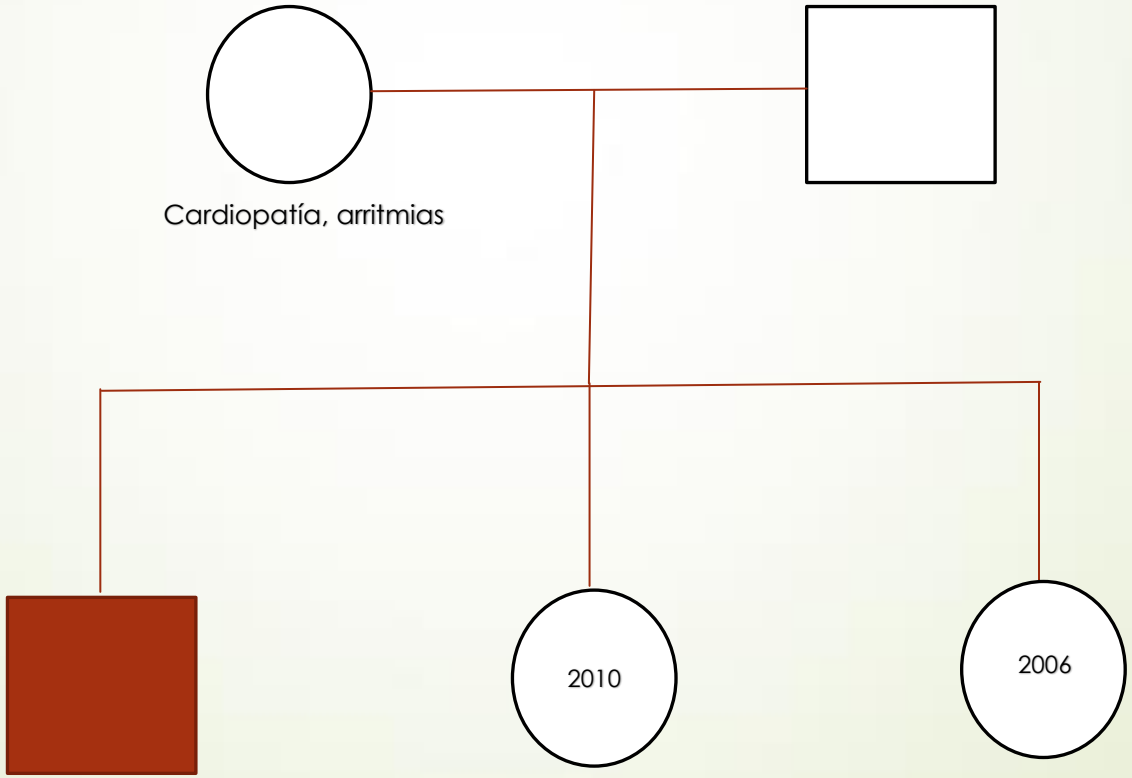
Diagnosztikai útmutató

ORIGINAL RESEARCH

An open-label clinical trial of agalsidase alfa enzyme replacement therapy in children with Fabry disease who are naïve to enzyme replacement therapy

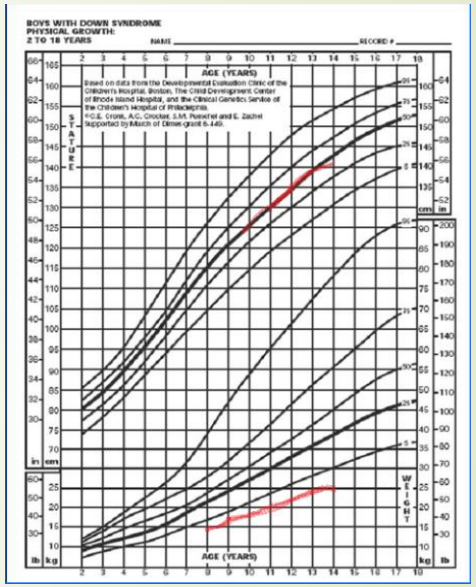
CASO CLINICO

- Varón de 14 años ascendencia argelina. Nacido año 2001 España



CASO CLINICO

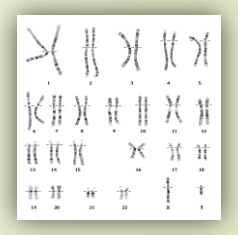
- DIGESTIVO: (2004) 3 años de edad bajo peso y escasa ganancia ponderal
- Traumatología: (2006) 5 años dolor en pies, sobre todo cambio estacional y calor.
- Nutrición: (2012) 11 años por desnutrición moderada
- Endocrinología (2014): 13 años , baja talla
- Reumatología (2014): 13 años dolor tb en manos
- Neuropediatría (2015): 14 años, se establece el diagnostico

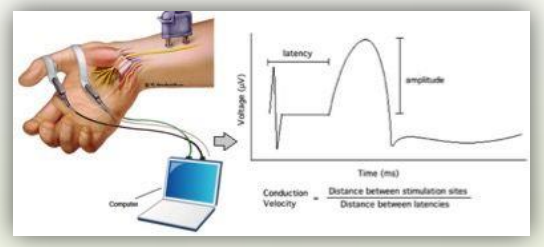


6 especialistas y 11 años

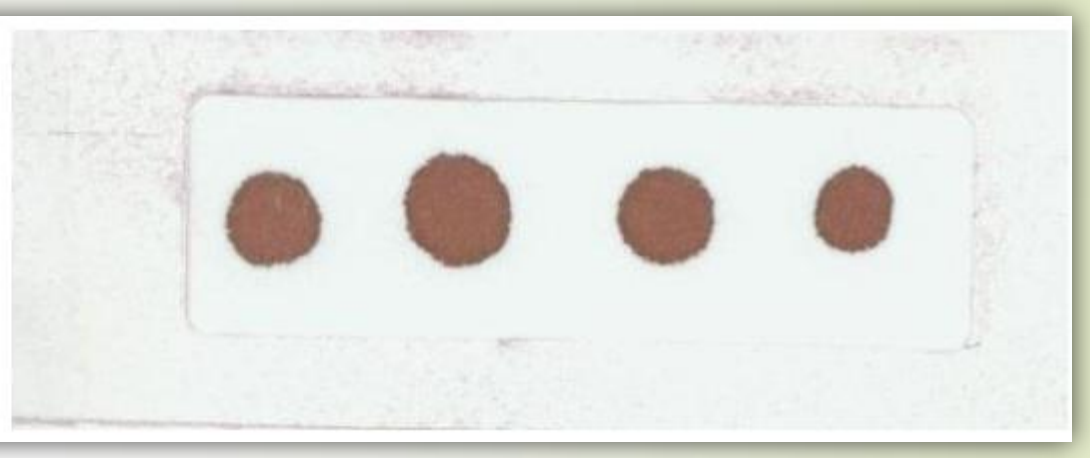
PRUEBAS COMPLEMENTARIAS

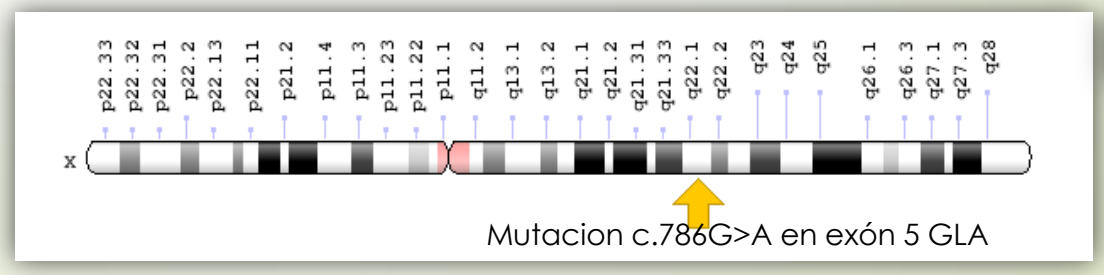
- Hemograma, Bioquimica,VSG,CPK
- TSH,T4, serie osea, IGFBP3, Vit D, Metabolismo fosofocalcico
- LDH,Igs, serologías víricas, Brucella
- ANAs,Anti CCP,ANCA, Factor reumatoideo,
- AEM,AGA, ATGT, Calprotectina, Elastasa pancreática,Capilaroscopia ungueal
- Cariotipo.
- Ecocardiografia, Ecog. Abdomianles, Rm columna, Rm cerebral
- EMG, ENG





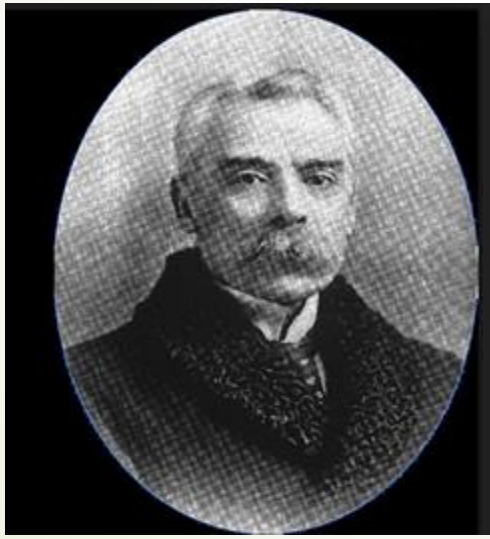
PRUEBAS COMPLEMENTARIAS

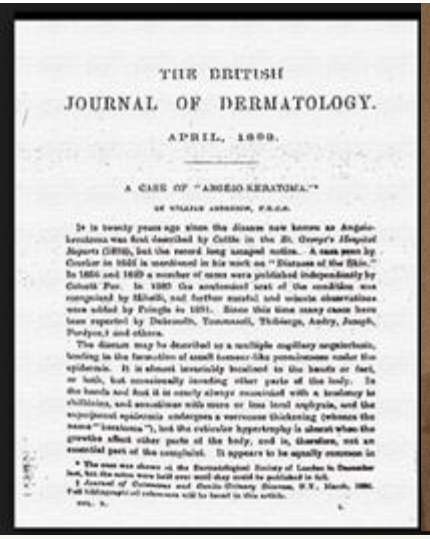




Cytogenetic Location: Xq22.1,

Enfermedad de Fabry





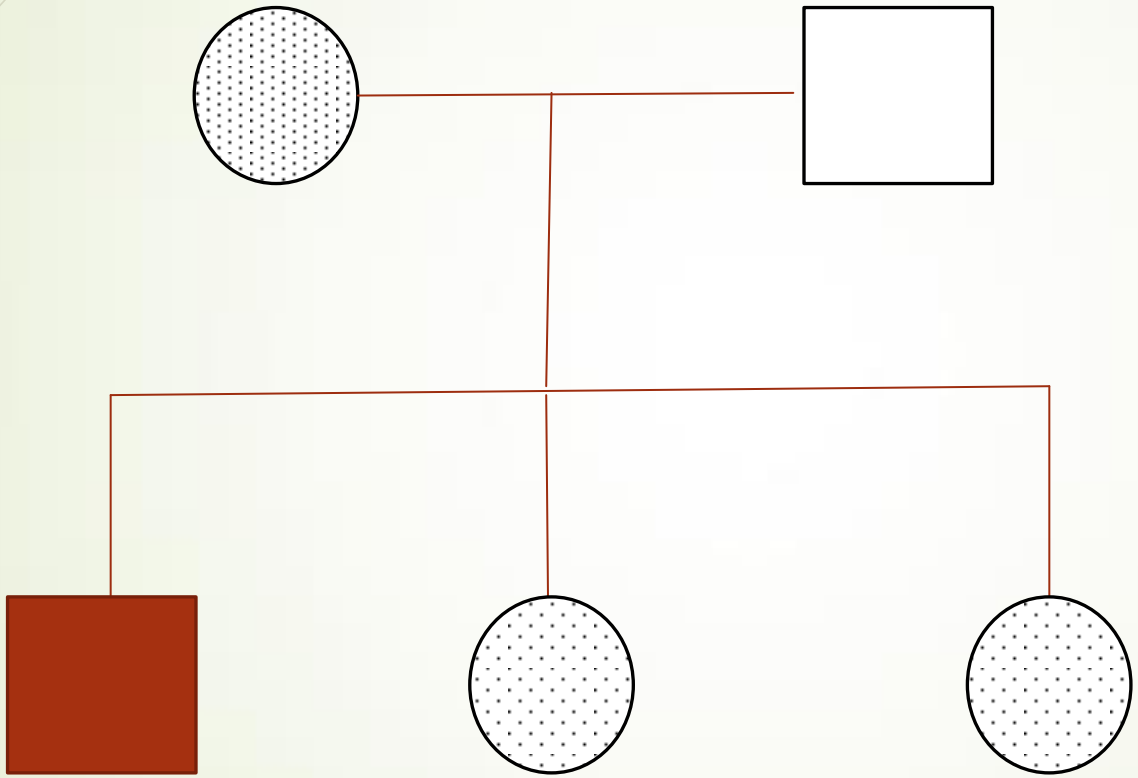
THE BRITISH

JOURNAL OF DERMATOLOGY.

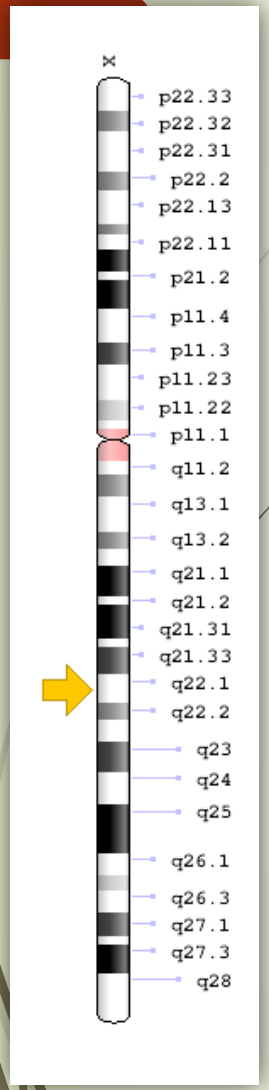
APRIL, 1898.

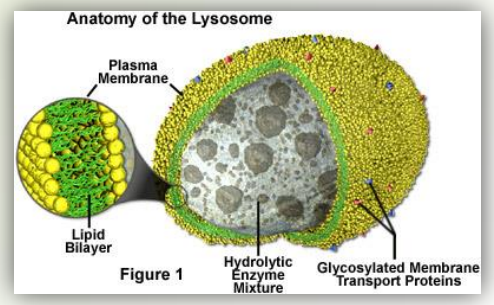
A CASE OF "ANGIO-KERATOMA."*

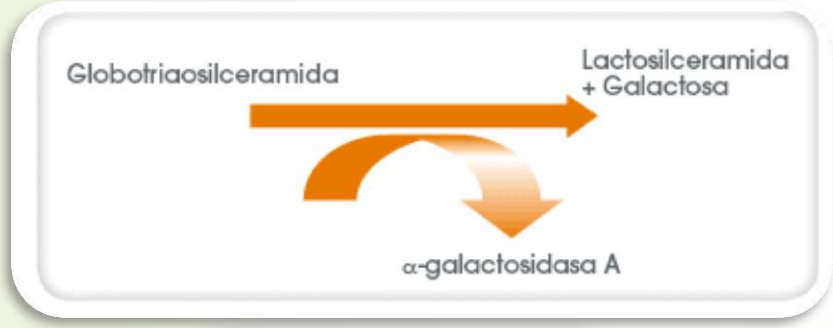
Familia Larby

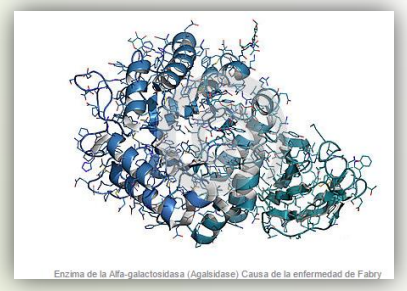


Enfermedad de Fabry

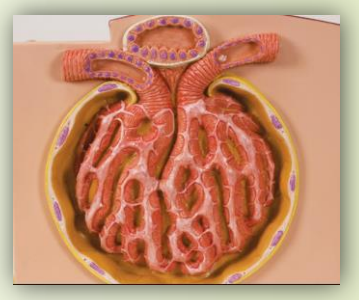




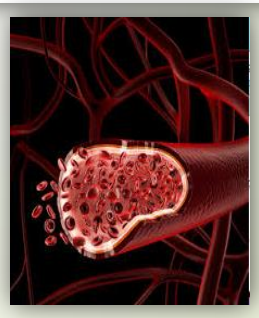




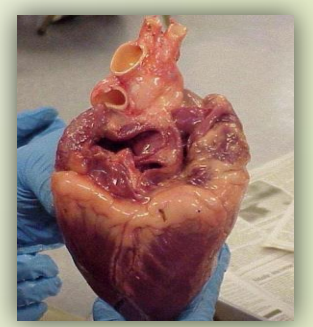
Neuronas de ggnglios raquídeos post,SNA,tronco y corteza cerebral



Podocitos,c.endoteliales glomerulares, tubulares y mesnagiales

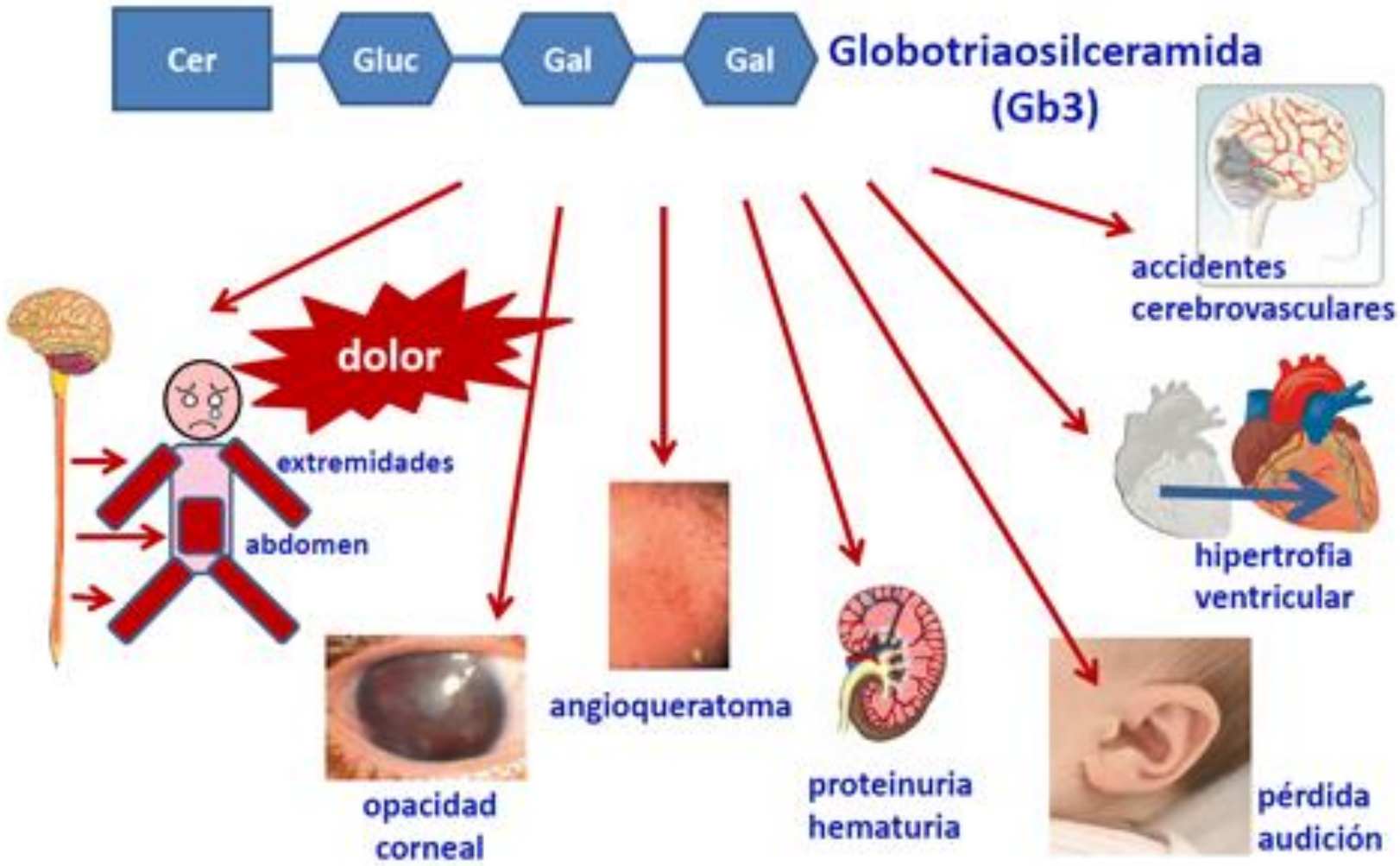


C endoteliales,pericitos y c musciulares lisas vasculares



Miocardiocitos y fibroblastos valvulares

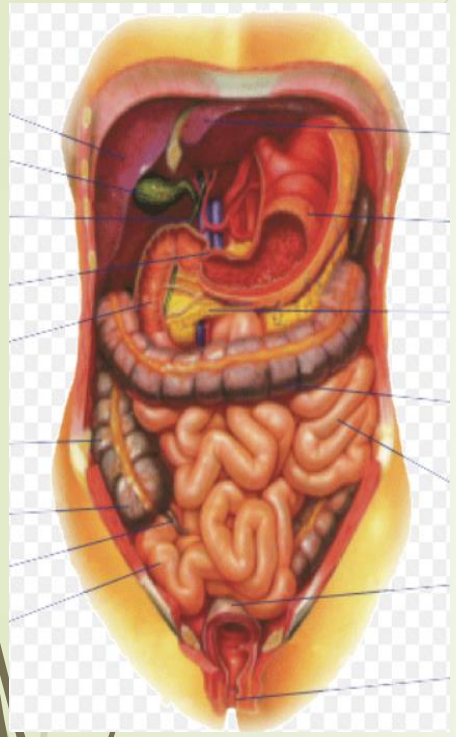
Manifestaciones clínicas de la enf. Fabry



Enfermedad de Fabry

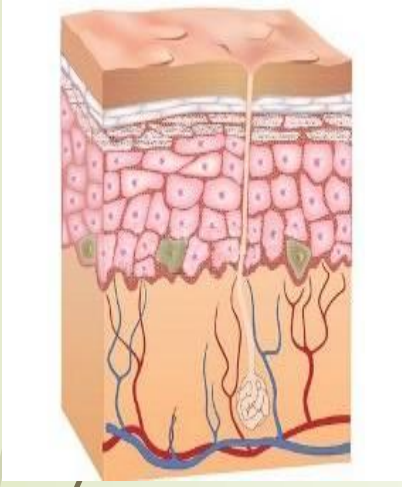
- **Dolor neuropático** (punzante, quemante y constante)
- Crisis de dolor (Crisis Fabry) manos y pies irradia intenso minutos o semanas
- Acroparestesias
- Hipohidrosis. (termorregulación)

Enfermedad de Fabry



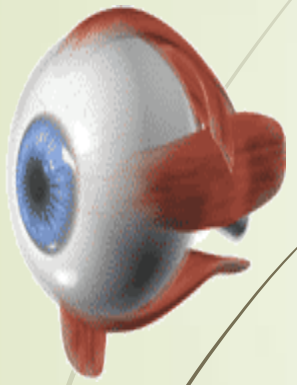
- **Dolor abdominal** colico
- **Alt habito intestinal**
- Nauseas, vomitos y distención abdominal
- Anorexia
- Perdida de peso

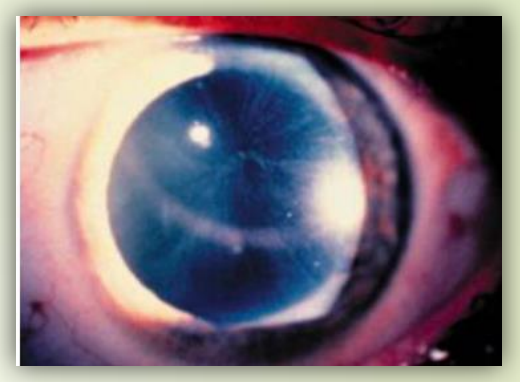
Enfermedad de Fabry



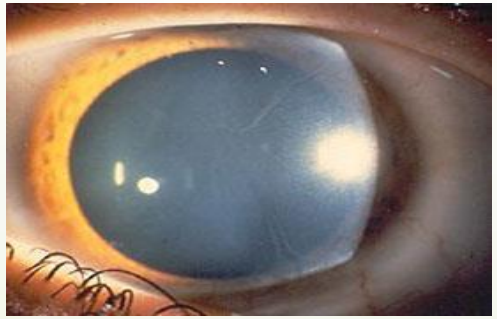
- **Angioqueratomas**
- teleangiectasias

Enfermedad de Fabry





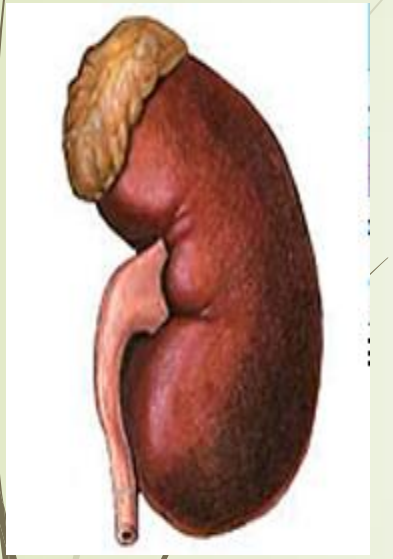
- **Cornea verticillata** (40% < 18 años)
- Tortuosidad venosa conjuntival
- Catartas subcapsulares posteriores



Enfermedad de Fabry

- Vértigos recurrentes
- Hipoacusia neurosensorial
- acufenos

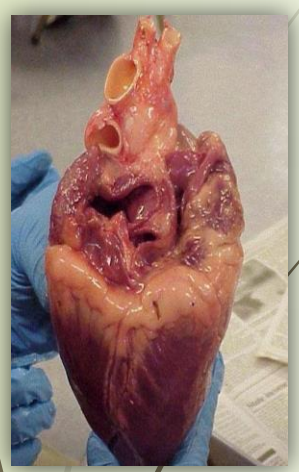
Enfermedad de Fabry



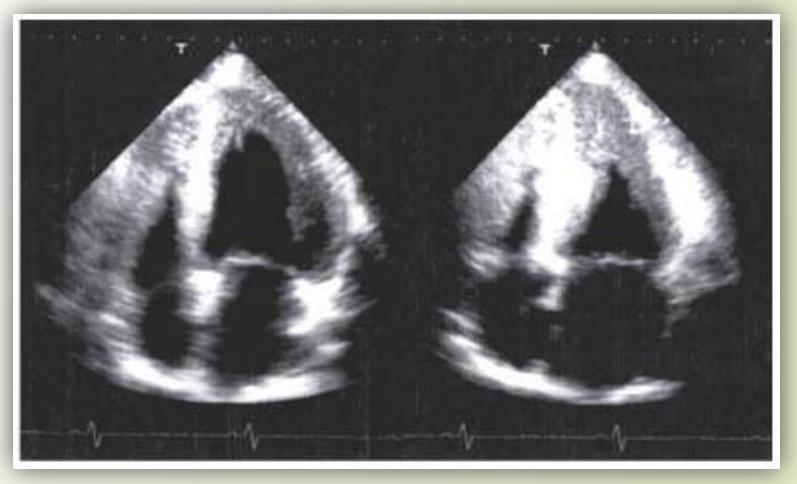
- Microalbuminura. Proteinuria
- Disminución capacidad concentración de la orina
- Fenomeno hiperfiltracion glomerular
- Hematuria
- Proteinuria glomerular o tubular
- IRC (25-50 años)

Quistes parapielicos

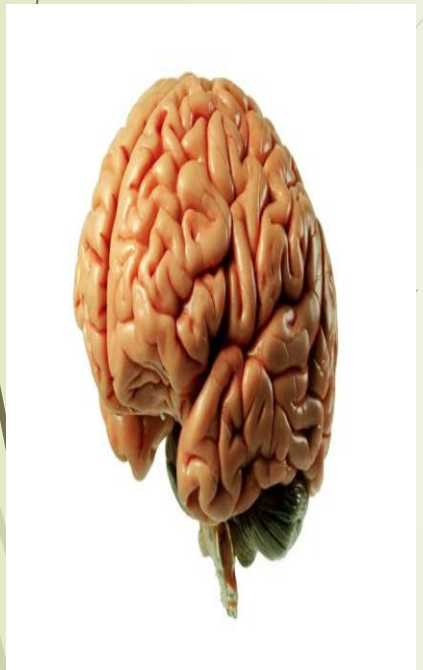
Enfermedad de Fabry



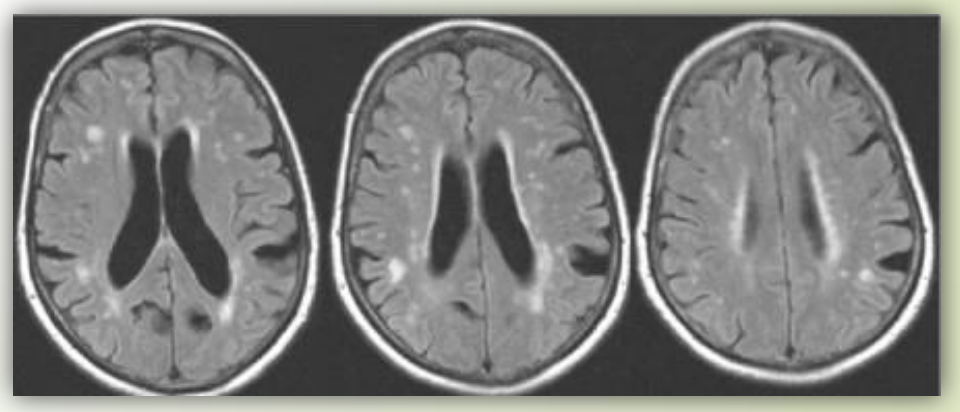
- Intervalo PR corto,bloqueo AV,anomalías ST y T
- **Miocardiopatia hipertrófica** **(septo y pared posteriorVI)**
- Arritmias cardiacas
- Anomalias valvulares
- Oclusion coronaria
- IAM



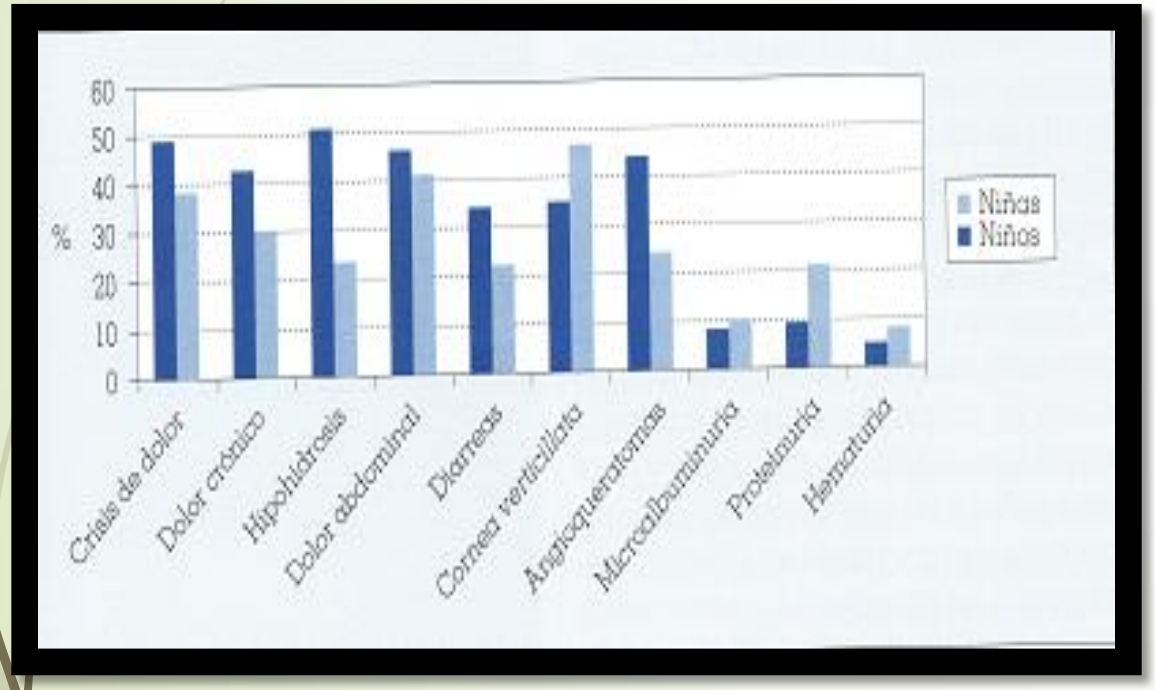
Enfermedad de Fabry

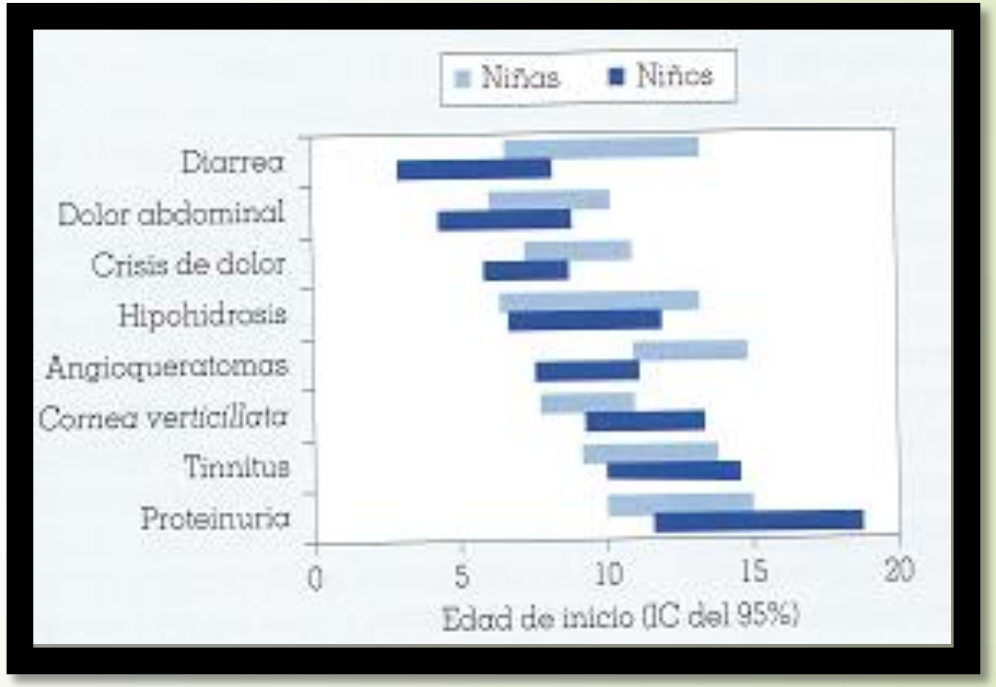


- **Accidentes Cerebro Vasculares precoces**
- Accidentes Isquémicos Transitorios
- Lesiones de sustancia blanca



Enfermedad de Fabry pediátrica



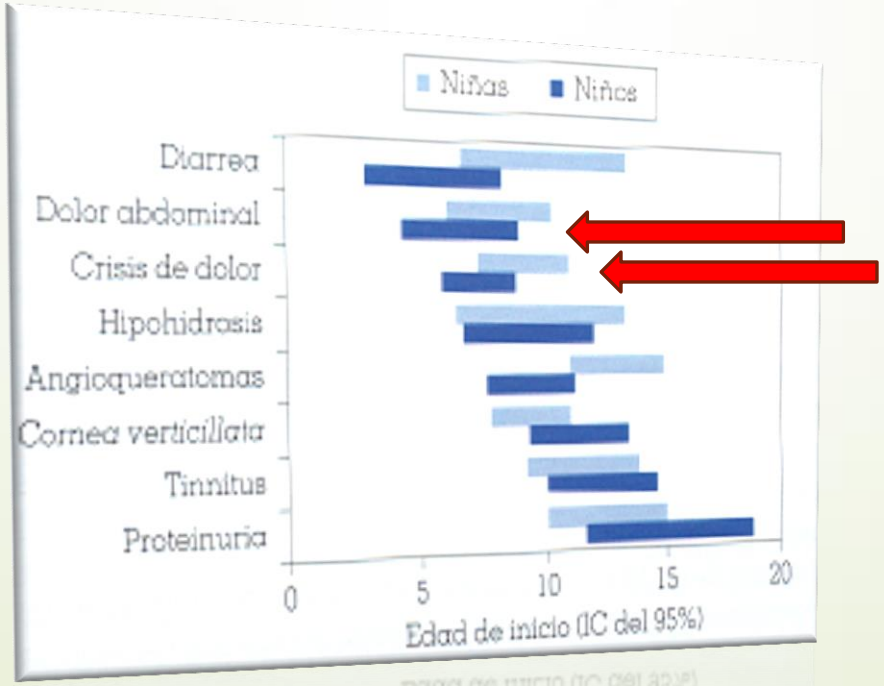


CASO CLINICO

- Síntoma guía: Dolor EE.

<<Refiere dolor que se inicia a los 4-5 años y desde entonces persiste en episodios recidivantes de dolor agudo, calambres de predominio en pies. No mejoraban con AINES y aparecían brotes mas fuertes sobre todo tras ejercicio o en verano que le impedían andar durante 1 semana o mas>>

- Dolor abdominal, Perdida de peso y Anorexia desde los 3 años



Tengo
un
Fabry

“No se diagnostica lo que no se conoce o aquello en lo que no se piensa, que casi siempre es por conocerse poco y se diagnostica con dificultad aquello que se ha visto en contadas ocasiones”

(M. A. Moreno)

TRATAMIENTO

Eur J Pediatr (2009) 168:1355–1363
DOI 10.1007/s00431-009-0937-9

ORIGINAL PAPER

Fabry disease in children and the effects of enzyme replacement treatment

Guillem Pintos-Morell · Michael Beck

REVIEW

Effects of enzyme replacement therapy in Fabry disease—A comprehensive review of the medical literature

Olivier Lidove, MD[1], Michael L. West, MD[2], Guillem Pintos-Morell, MD[3], Ricardo Reisin, MD[4], Kathy Nicholls, MD[5], Luis E. Figuera, MD[6], Rossella Parini, MD[7], Luiz R. Carvalho, MD[8], Christoph Kampmann, MD[9], Gregory M. Pastores, MD[10], and Atul Mehta, MD[11]

early initiation of enzyme replacement therapy to determine the optimal time to start treatment to prevent irreversible organ damage. The value of adjunctive and supportive therapies should also be rigorously analyzed. ***Genet Med* 2010:12(11):668–679.**

Key Words: *antibodies, clinical efficacy, enzyme therapy, Fabry disease, symptomatic therapy, tolerance*

CLINICAL GENETICS An International Journal of Genetics, Molecular and Personalized Medicine

Explore this journal >

Fabry disease in children and response to enzyme replacement therapy: results from the Fabry Outcome Survey

U Ramaswami ✉, R Parini, G Pintos-Morell, G Kalkum, C Kampmann, M Beck, on behalf of the FOS Investigators

First published: 25 April 2011 Full publication history

View issue TOC
Volume 81, Issue 5
May 2012
Pages 485–490

Shire	Genzyme
0.2 mg/kg	1.0 mg/kg
human cell line	Chinese hámster ovary cells

TRATAMIENTO

*significativa

enzyme replacement therapy

- Mejoría * de los síntomas digestivos tras 12 meses tratamiento
- Mejoría* del dolor tras 2 años de Tto
- Mejoría * de la calidad de vida de los pacientes
- Estabiliza la hipoacusia
- Reducción de la masa y tamaño del VI
- Mejoría * de la función cardiaca
- Estabilización de función renal o descenso de tasa de deterioro en pacientes con reducción de la misma leve /moderada

TRATAMIENTO

Terapia Enzimática de Reemplazo

Shire	Genzyme
0.2 mg/kg	1.0 mg/kg
human cell line	Chinese hámster ovary cells

Published:
25 July 2016

Authors:
El Dib R, Gomaa H, Carvalho R, Camargo SE, Bazan R, Barretti P, Barreto FC

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Treatment for Anderson-Fabry disease

Authors' conclusions:

Trials comparing enzyme replacement therapy to placebo show significant improvement with enzyme replacement therapy in regard to microvascular endothelial deposits of globotriaosylceramide and in pain-related quality of life. There is, however, no evidence identifying if the alfa or beta form is superior or the optimal dose or frequency of enzyme replacement therapy. With regards to safety, adverse events (i.e., rigors, fever) were more significant in the agalsidase beta as compared to placebo. The long-term influence of enzyme replacement therapy on risk of morbidity and mortality related to Anderson-Fabry disease remains to be established. This review highlights the need for continued research into the use of enzyme replacement therapy for Anderson-Fabry disease.

1. Mejoría depósitos endoteliales microvasculares Gb3
2. Mejoría del dolor
3. No hay, sin embargo, ninguna evidencia que identifique si la forma alfa o beta es superior

CASO CLINICO

- 1 mg/kg de peso corporal, administrada una vez cada 2 semanas por perfusión intravenosa.(port a cath)
- Tratamiento del dolor
  - Gabapentina 300-300-300
  - Fentanilo parches 25 mg /72 h
  - Lidocacina parche 700mg nocturno
  - Capsaicina crema /6h
  - Sulfato de morfina 2,5 mg oral si crisis (rescate)

Figura 3. Escala visual análoga.

Dolor basal 4
Crisis 9-10

CASO CLINICO

- Cuadro ansioso depresivo con ideas de suicidio por dolor
- 5-10 crisis mes EVA 9

- Tratamiento del dolor
  - Gabapentina 300-300-300
  - Meatadona 5mg 1-0-1
  - Lidocacina parche 700mg nocturno
  - Capsaicina crema /6h
  - Clorazepato dipotasico 5mg-5mg-5mg
  - Rescate morfina oral 55 si EVA 4 o mayor

Figura 3. Escala visual análoga.

CASO CLINICO

- Mejoría a los 6 meses de TER
- EVA 0 basal EVA 4 crisis aisladas
- Tratamiento del dolor
  - Gabapentina 300-300-300
  - Meatadona 5mg 1-0-1
  - Rescate morfina oral 55 si EVA 4 o mayor

Figura 3. Escala visual análoga.

CASO CLINICO

- Continua mejoría
- EVA 0 basal no crisis en 3 meses

- Tratamiento del dolor
  - Gabapentina 300-0-300
  - Meatadona 5 mg 1/2-0-1/2

Figura 3. Escala visual análoga.

CONCLUSION

11 AÑOS DE DOLOR

Si estamos dispuestos a oírle, con frecuencia el paciente nos dará el diagnóstico (Lewis)

Gracias