SEMINARIO PATOLOGÍA ULTRAESTRUCTURAL: CASO SANTIAGO DE COMPOSTELA

J. Forteza Vila (USC Santiago) y C. Valbuena (FMUP, UID-Nefrología Oporto)

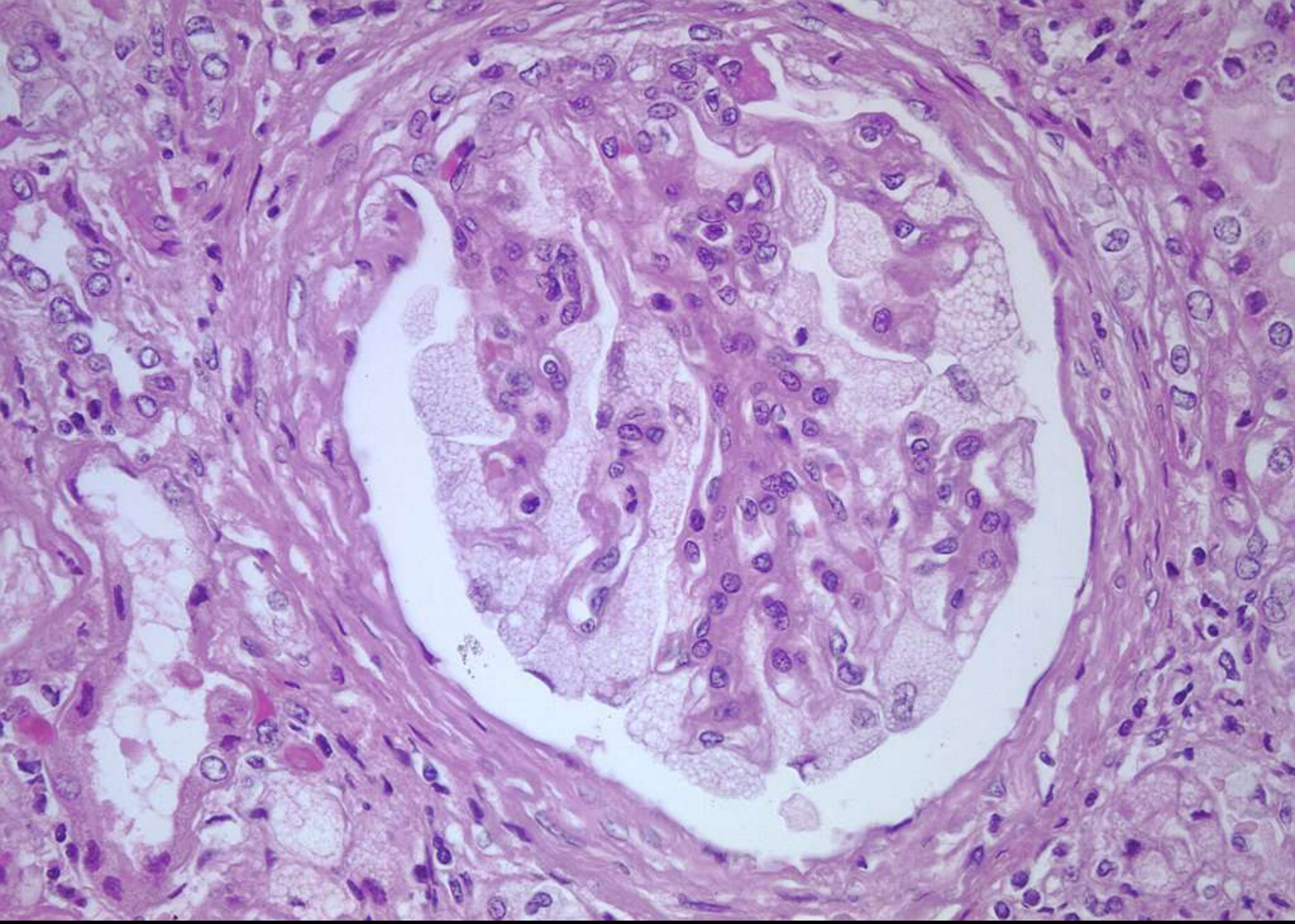
XXV Congreso de la Sociedad Española de Anatomía Patológica y División Española de la International Academy of Pathology.

18 mayo 2011 - Zaragoza

DATOS CLÍNICOS

- Varón de 58 años con angioqueratomas en párpado superior, proteinuria en rango de síndrome nefrótico, insuficiencia renal crónica. Miocardiopatía.

Caso Consulta procedente del servicio de Anatomía Patológica del Hospital Santa María Madre, Diputación Provincial de Orense (1992).



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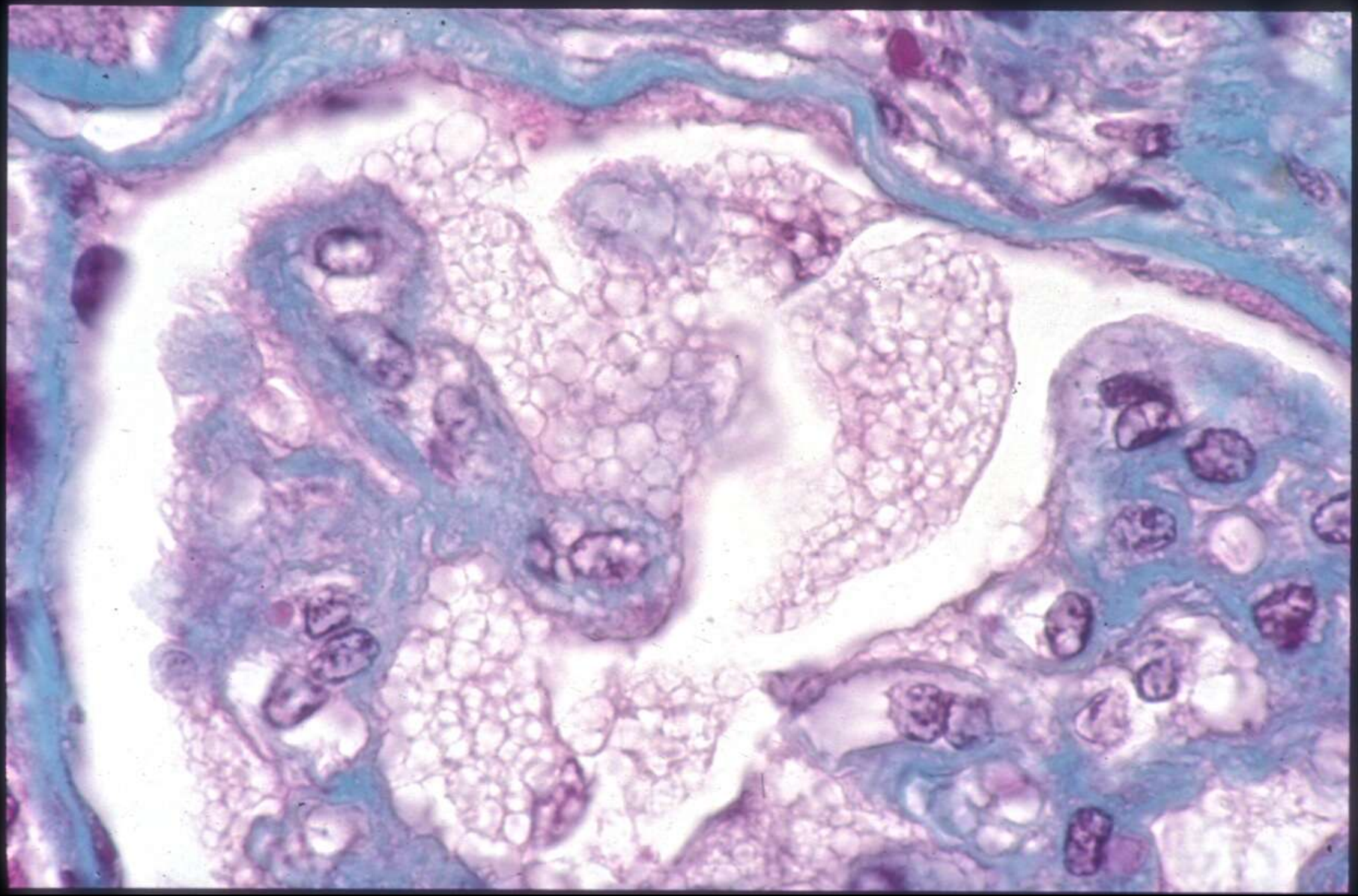

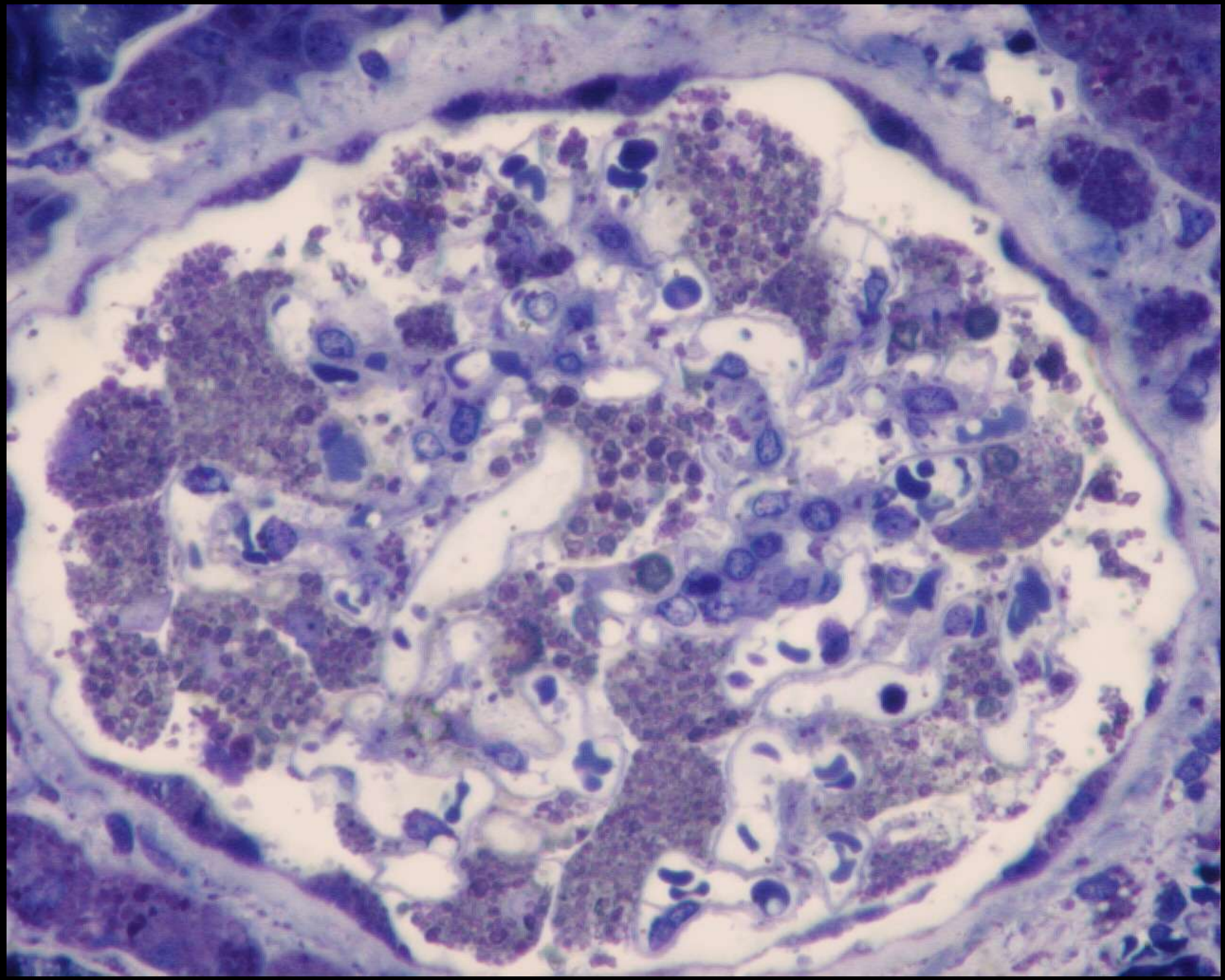

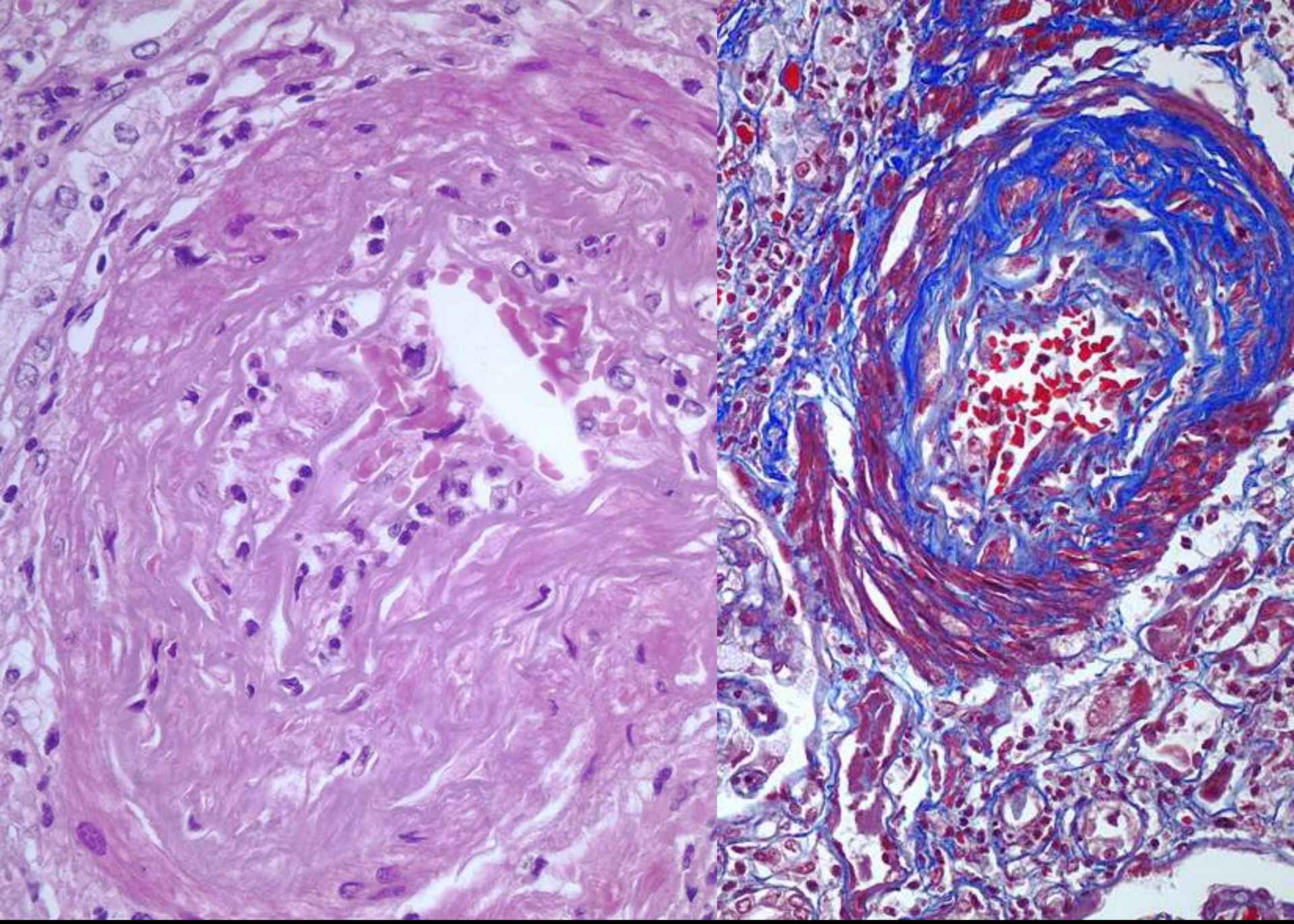

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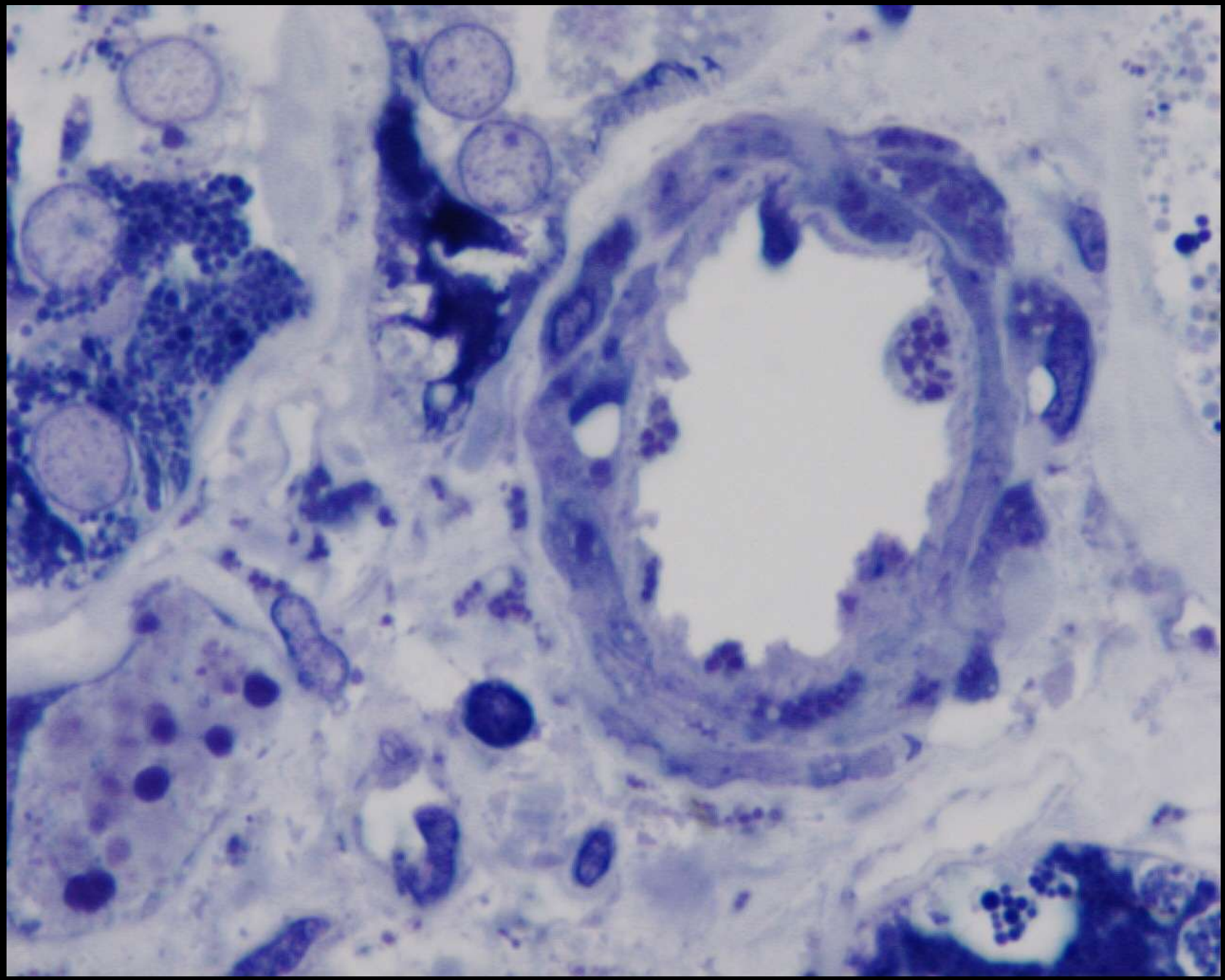
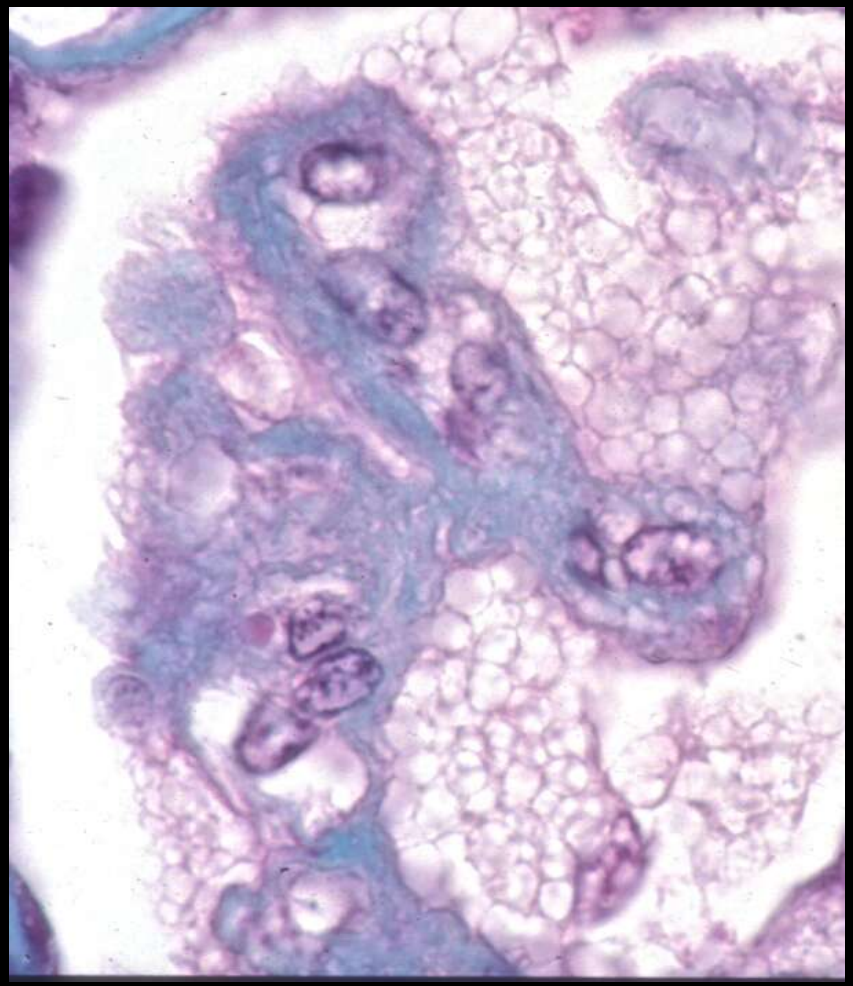
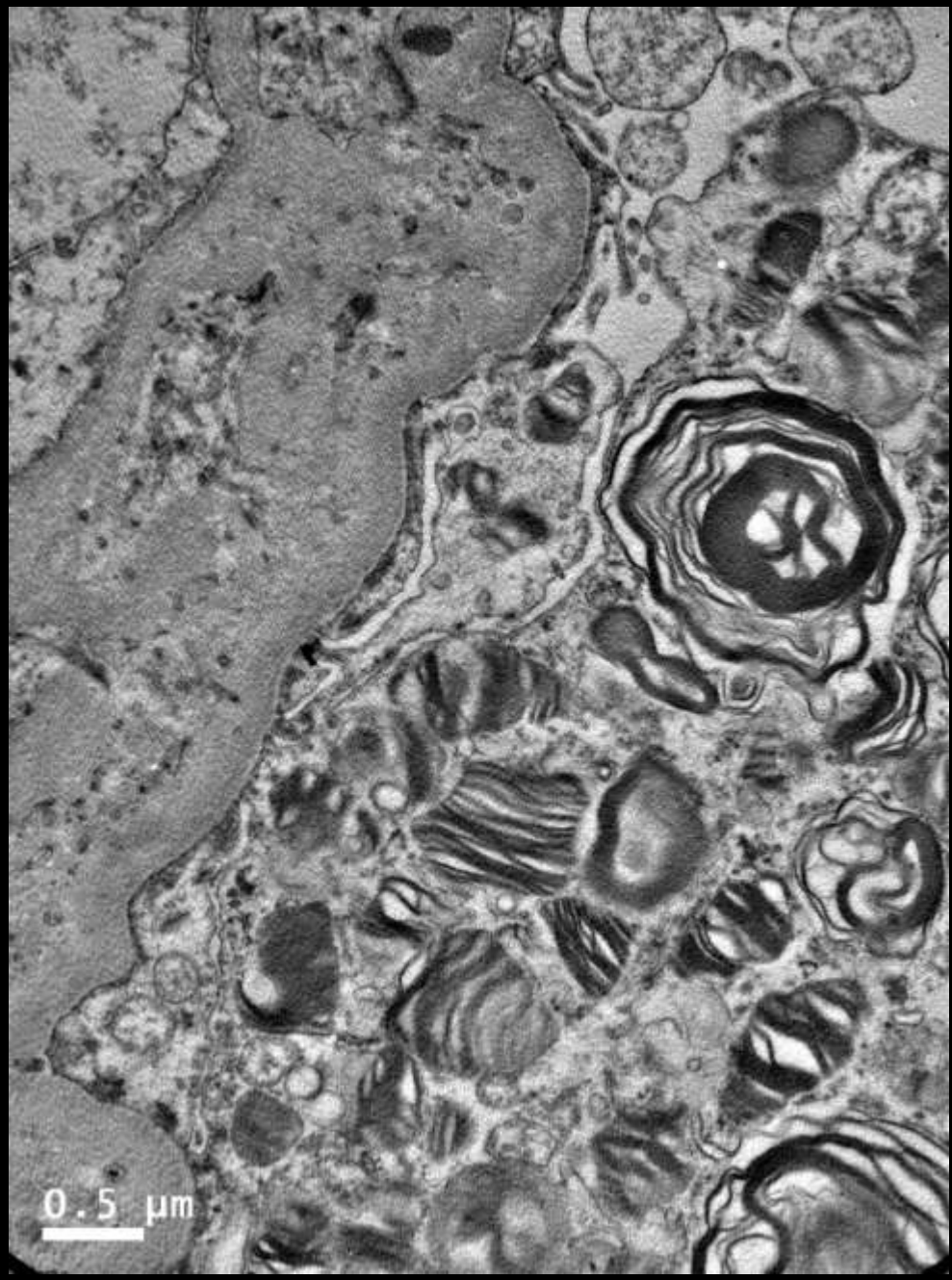
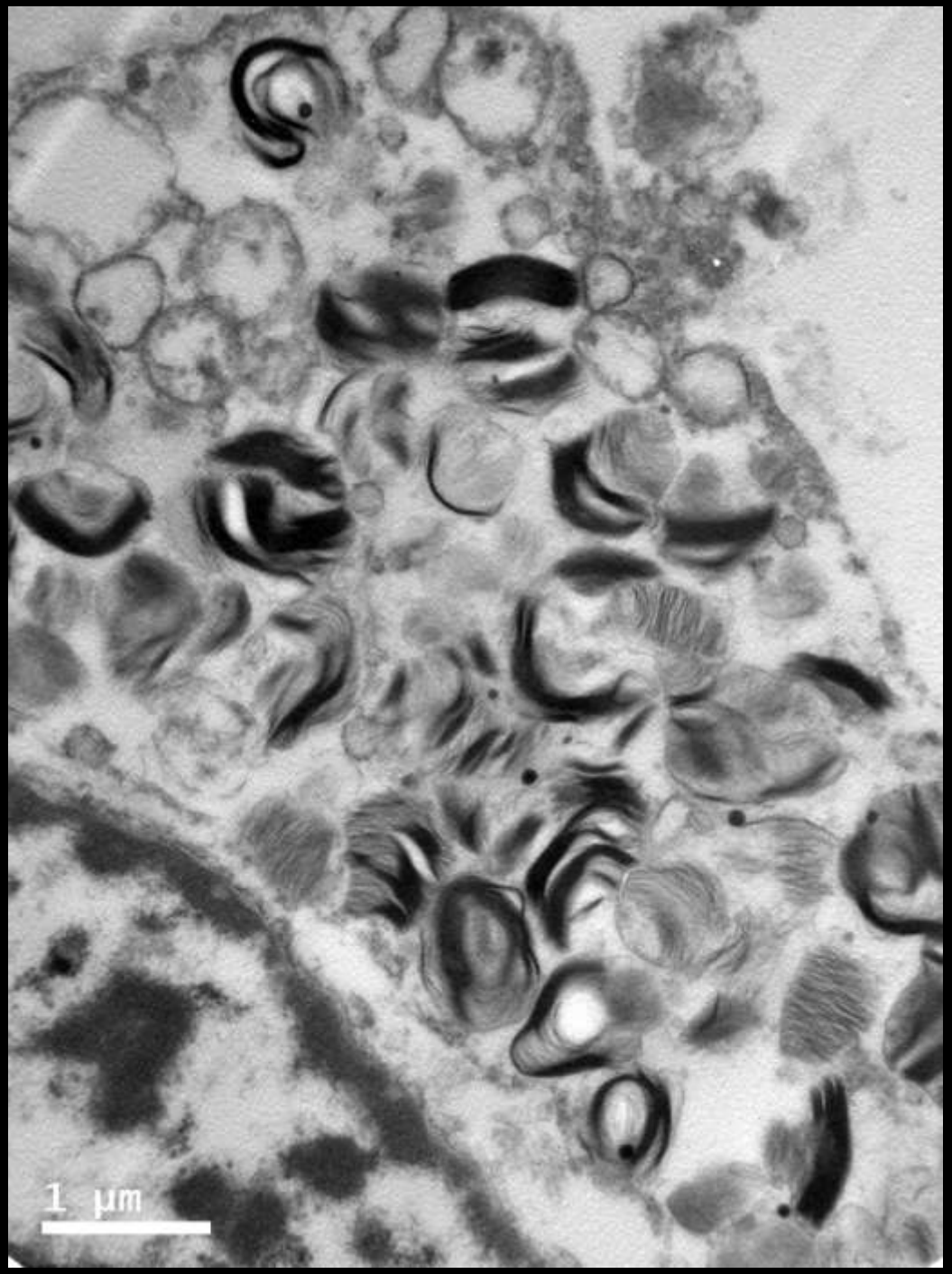
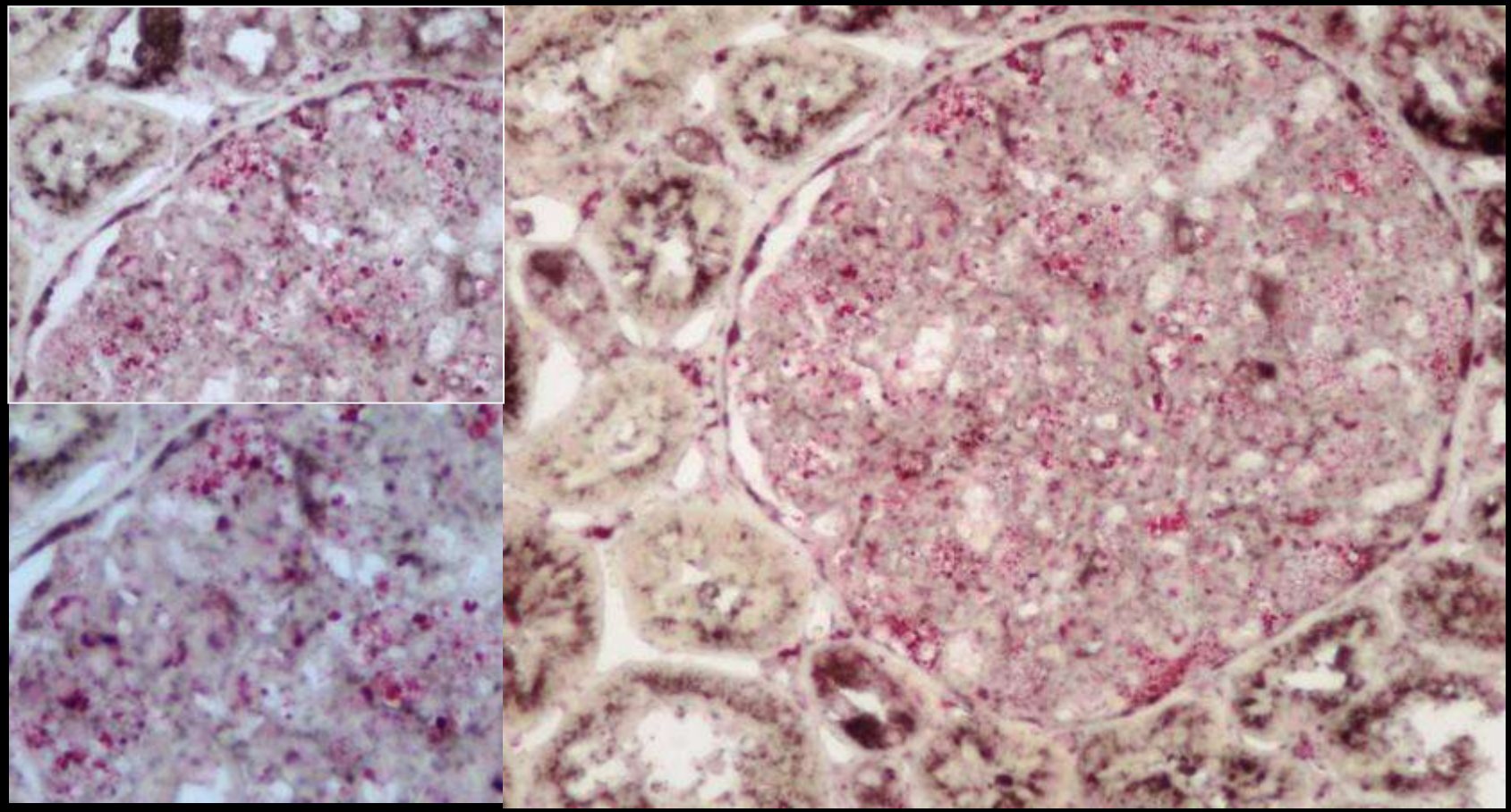





0.5 µm

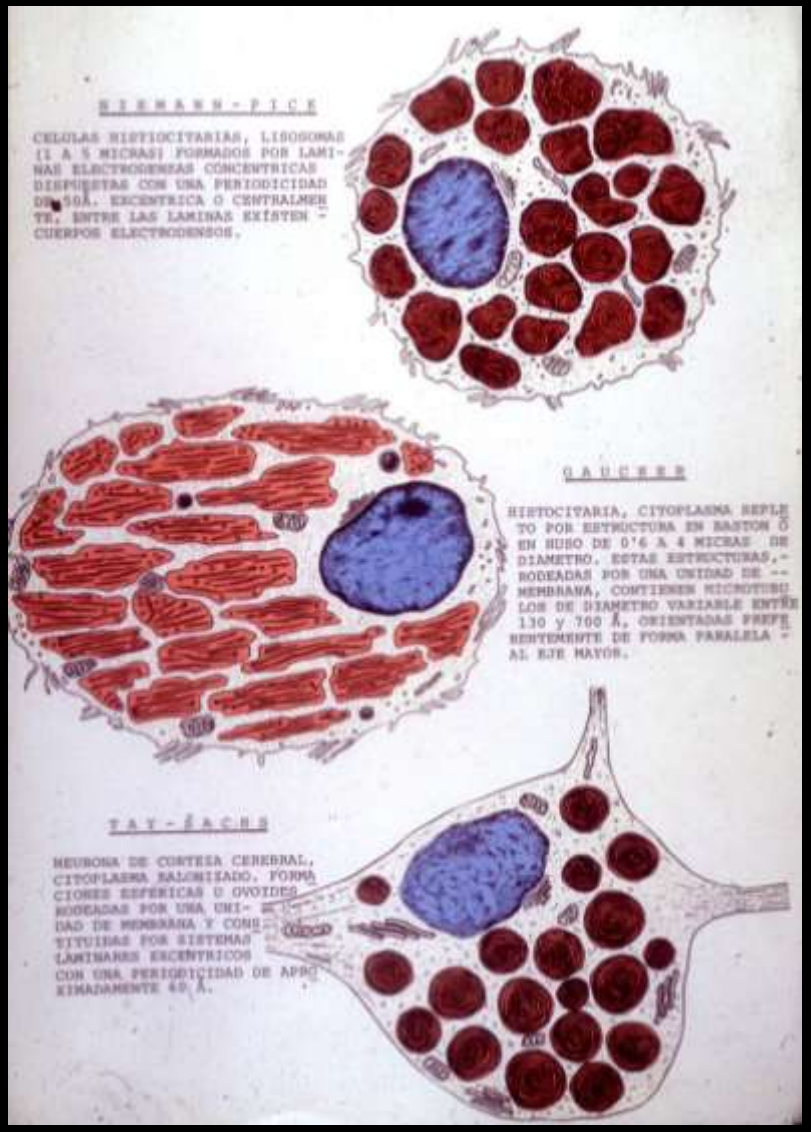

1 µm



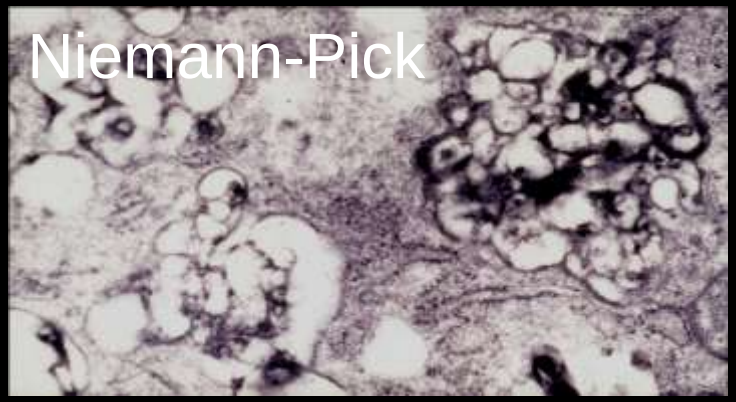
Gb3

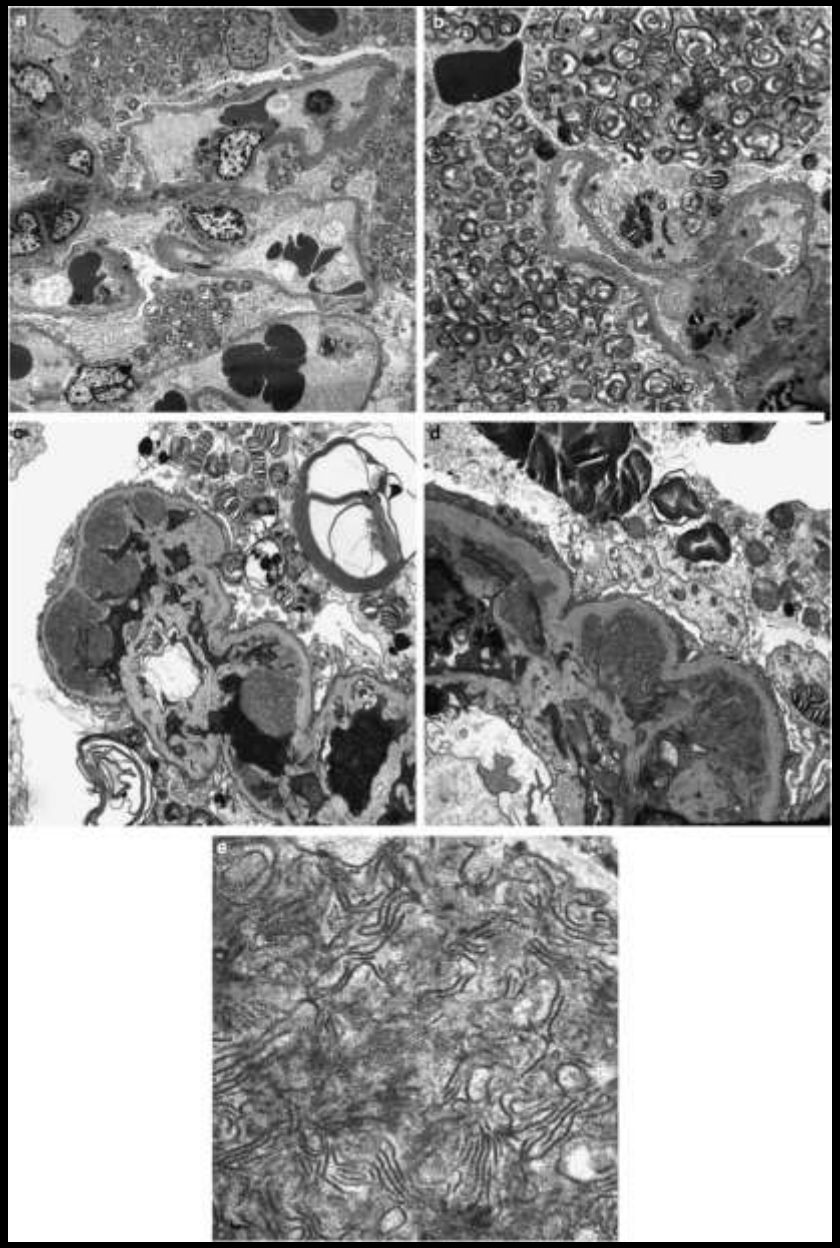
Diagnóstico:
Enfermedad de Fabry

Diagnóstico diferencial ultraestructural



Esquema Dr. Félix Contreras





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www.modernpathology.org

Fabry disease: a morphologic study of 11 cases

Edgar G Fischer, Michael J Moore and Donna J Lager

Department of Laboratory Medicine and Pathology, Mayo Foundation, Rochester, MN, USA

Figure 2 Electron microscopic changes in Fabry disease. (**a**, **b**) Myelin-like inclusions in podocyte cytoplasm (**a** ×1800; **b** ×4200). (**c–e**) Subendothelial deposits composed of membrane-like material associated with glomerular basement membrane duplications (**c** ×4200; **d** ×7400; **e** ×24 500).

“KEY POINTS” PARA EL DIAGNÓSTICO

1. La microscopía electrónica es importante para el diagnóstico de las enfermedades de depósito.

2. Cuando se diagnostique una enfermedad de Fabry debe de valorarse la cronicidad de la lesión.

3. Es especialmente importante la valoración de los “semifinos” para la localización y semicuantificación de los depósitos.

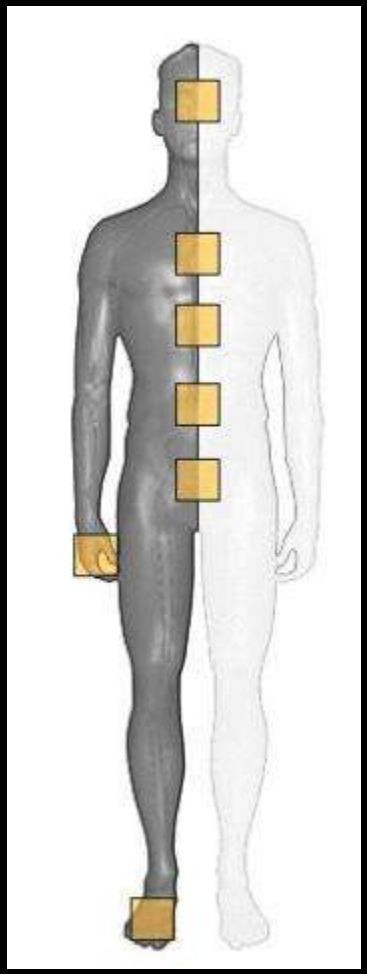
4. Existe un anticuerpo, el anti-Gb3 o CD77, que permite el diagnóstico de la enfermedad de Fabry en cortes de parafina

Enfermedad de Fabry

(*Fenotipo Clásico*)

La acumulación multisistémica de GSL neutros, principalemte Globotriaosilceramida (Gb3), es la base patogénica de los síntomas clínicos en varones homozigotos y hembras heterozigotas

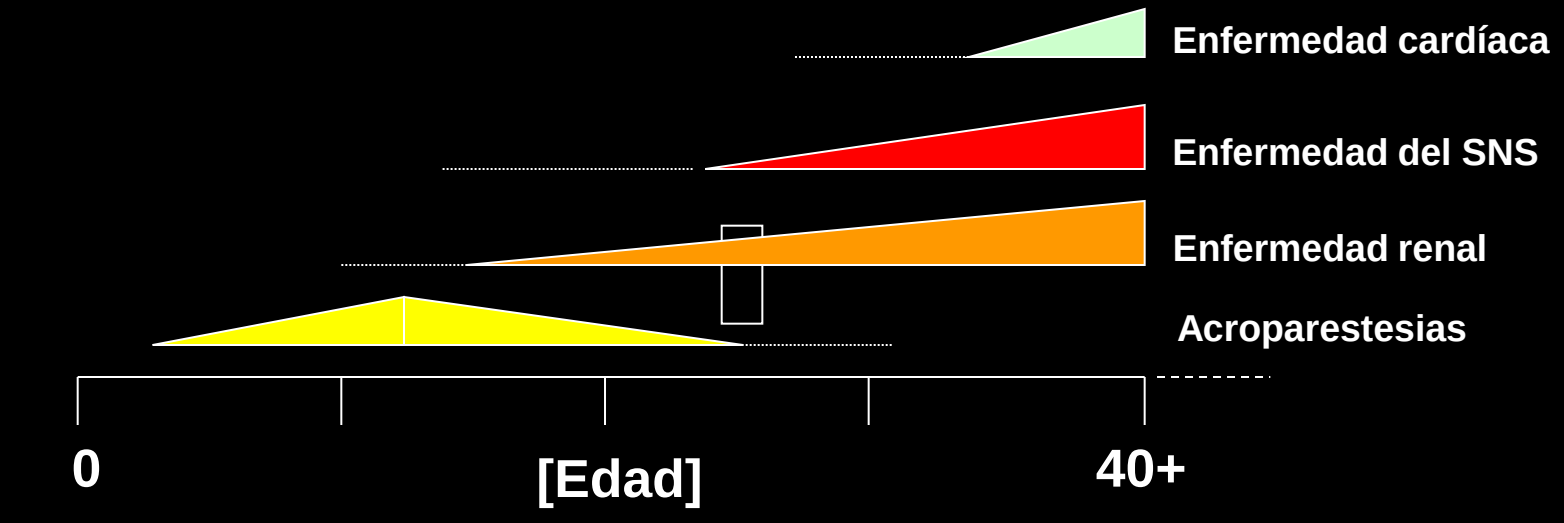
- **Acidente cerebro-vascular isquémico precoz**
- **Hipertrofia ventricular izquierda**
- **Hipo-hidrosis**
- **Insuficiencia renal progressiva**
- **Angioqueratomas**
- **Acroparestesias**



- **Acroparestesias**

Enfermedad de Fabry

(Formas *clínicas)*



No diagnosticada

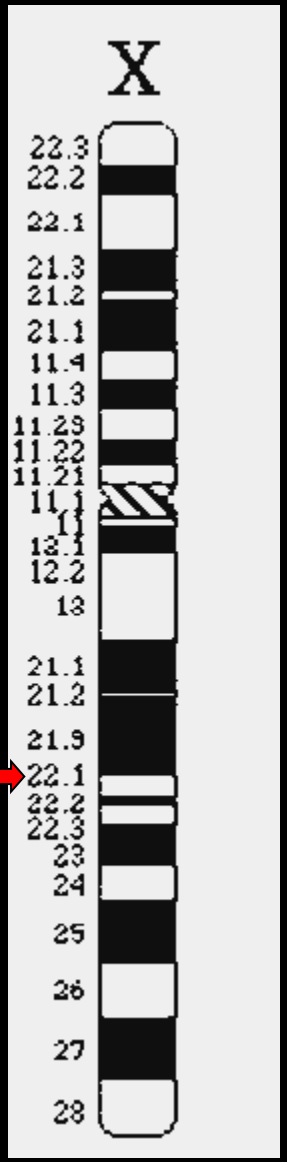
diagnosticada - no grave

diagnosticada - grave

Enfermedad de Fabry

(*Alteración metabólica*)

- Mutación en el gen de la α-galactosidasa A (*GLA*) localizado en q22.1 del cromosoma X.
- Herencia ligada al cromosoma X.
- Frecuencia estimada en 1:117.000 nacidos vivos.
- Causa el mal funcionamiento de la hidrolasa lisosomal α-galactosidasa A (alfa-gal o GLA), responsable del catabolismo de los glicoesfingolípidos (GSL) neutros.
- Terapéutica de reposición enzimática con α-Gal A recombinante humana (rhαgalA) desde 2001.



MODELO ANIMAL DE LA ENFERMEDAD

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Virchows Arch
DOI 10.1007/s00428-011-1051-8

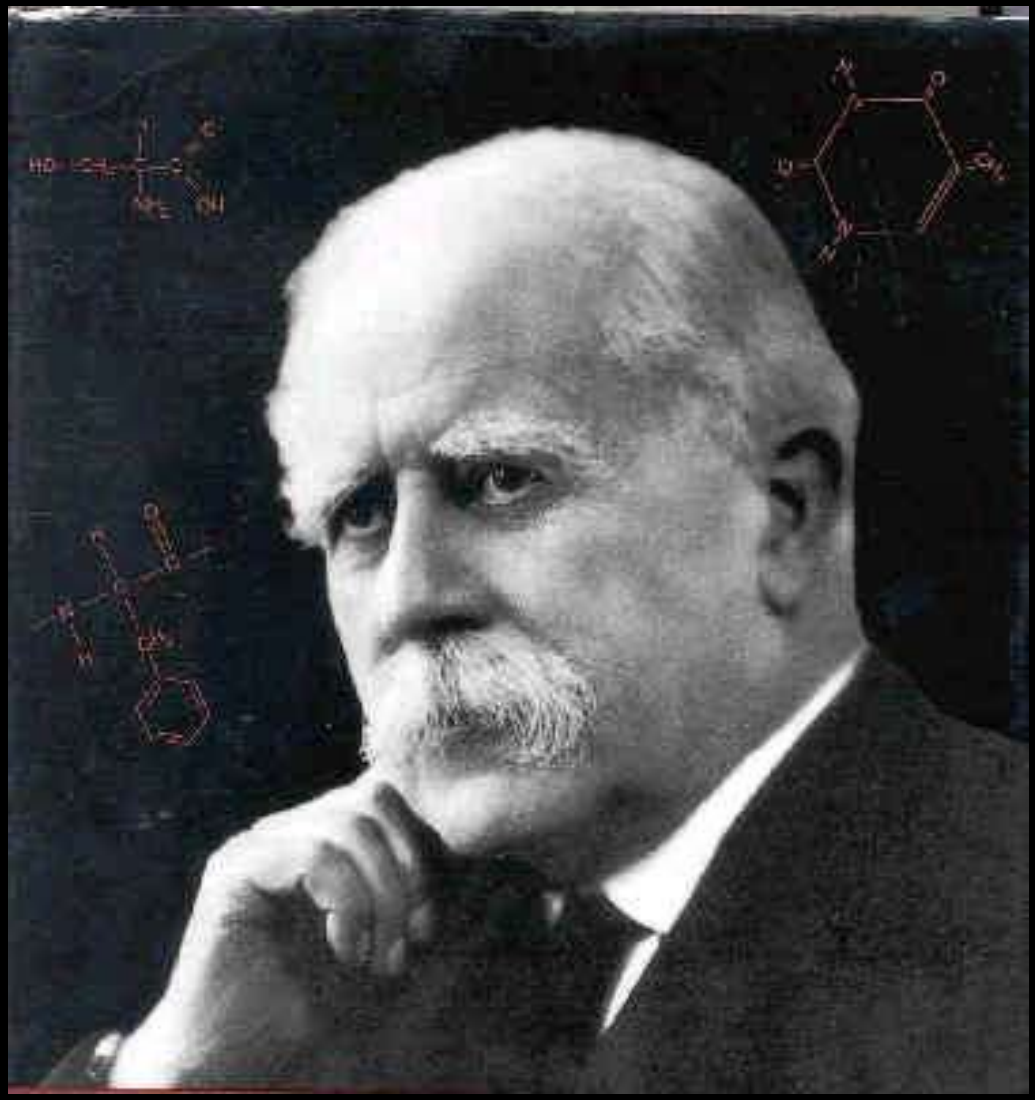
ORIGINAL ARTICLE

Kidney histologic alterations in α-Galactosidase-deficient mice

Carmen Valbuena · João Paulo Oliveira · Fátima Carneiro · Sandra Relvas · Mariana Ganhão · M. Clara Sá-Miranda · Lorena G. Rodrigues

Received: 25 August 2010 / Revised: 18 January 2011 / Accepted: 22 January 2011

Abstract Fabry disease is a rare X-linked disorder caused by mutations in the α-galactosidase gene (*GLA*), the resultant deficiency of lysosomal α-galactosidase enzyme activity leading to systemic accumulation of globotriaosylceramide and other glycosphingolipids. *GLA* knockout mice ("Fabry mice") were generated as an animal model for Fabry disease but, as they do not manifest progressive chronic kidney disease (CKD), their relevance as a model for human Fabry nephropathy is uncertain. We evaluated the histological alterations in the kidneys of Fabry mice at different ages, as contrasted to those observed in wild-type mice. Furthermore, we compared the renal histological alterations of Fabry mice to the kidney pathology reported in patients with Fabry disease at comparable age ranges and across different CKD stages, using a scoring system that has been developed for Fabry nephropathy. Fabry mice are phenotypically different from wild-type mice, displaying progressive age-related accumulation of glycosphingolipids in all types of renal cells. There were no statistically significant differences between Fabry mice and Fabry patients in the prevalence of glycosphingolipid storage per renal cell type with the exceptions of mesangial (higher in humans) and proximal tubular cells (higher in mice). However, Fabry mice lack the nonspecific histological glomerulosclerotic and interstitial fibrotic renal lesions that best correlate with progressive CKD in Fabry patients, and do not develop large podocyte inclusions. We postulate that the elucidation of the mechanisms underlying these species differences, may contribute important clues to a better understanding of the pathogenesis of Fabry nephropathy.



Archibald Edward *Garrod 1957 – 1936*

ERRORES CONGÉNITOS DEL METABOLISMO