

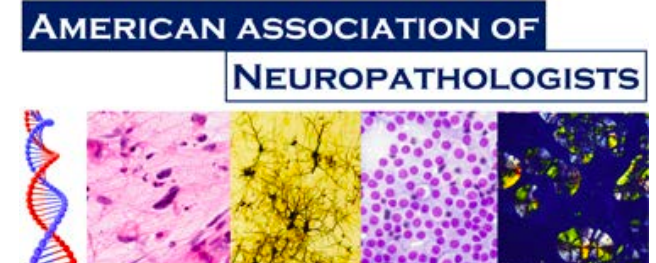
Case 2021-6

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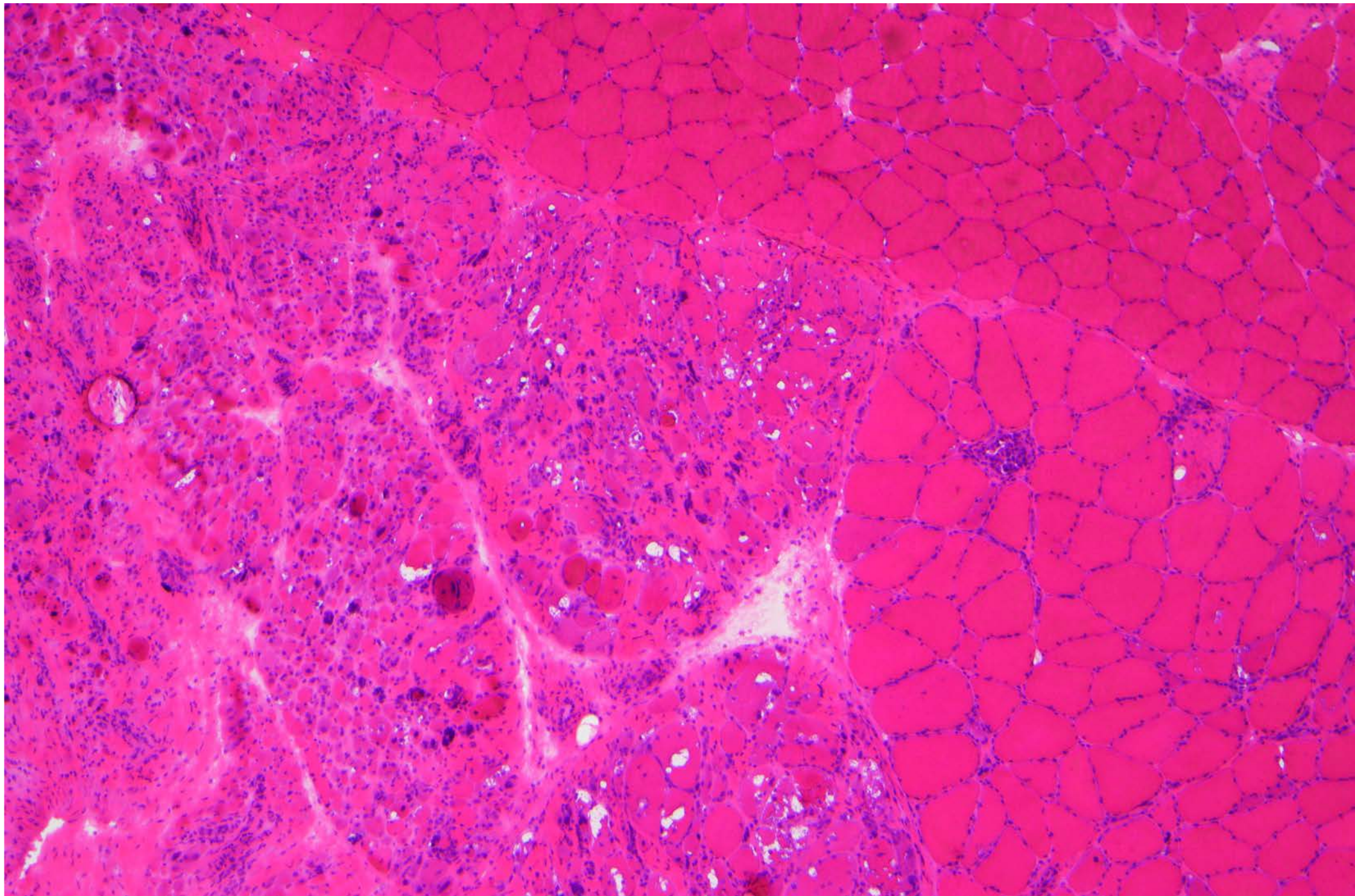
Disclosure

- We have no financial relationships to disclose

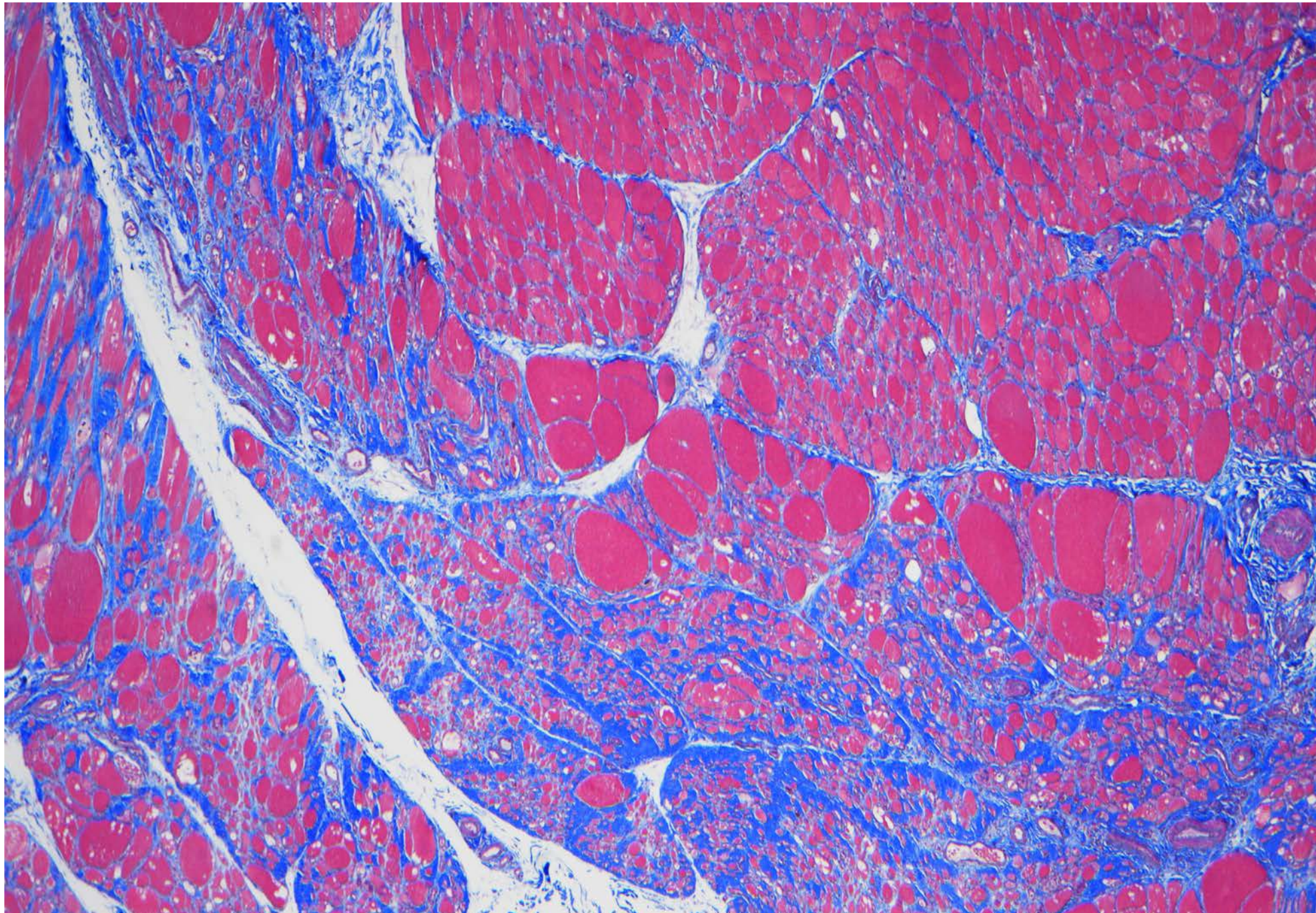
Clinical history

- 37 y/o man
- History of end stage renal disease s/p two renal transplants
- Distal hand weakness and atrophy
- Dysphagia, balance problems, and poor vision
- EMG shows myopathy in hand and forearm muscles
- A biopsy of extensor carpi radialis longus (ECRL) is performed

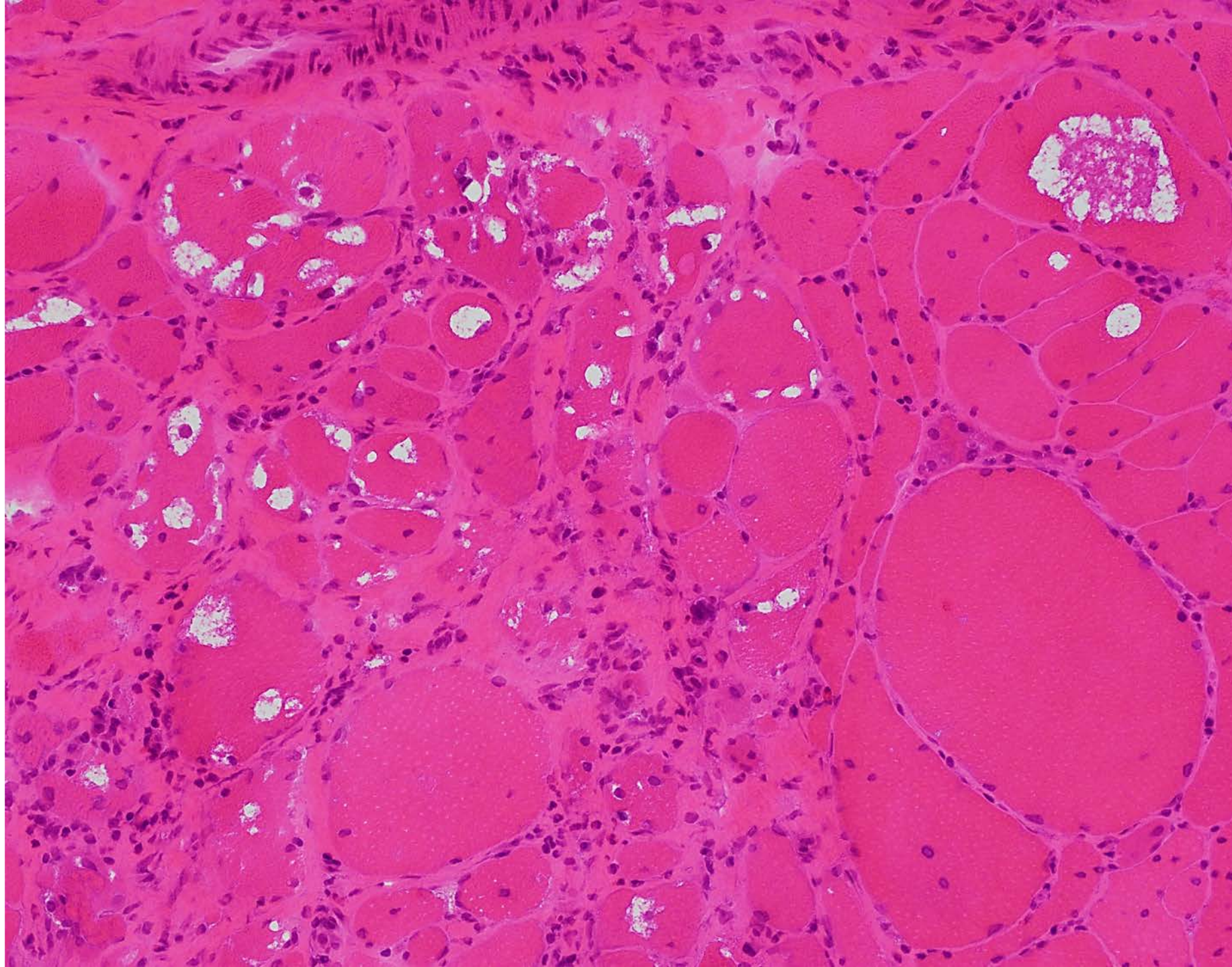
H&E



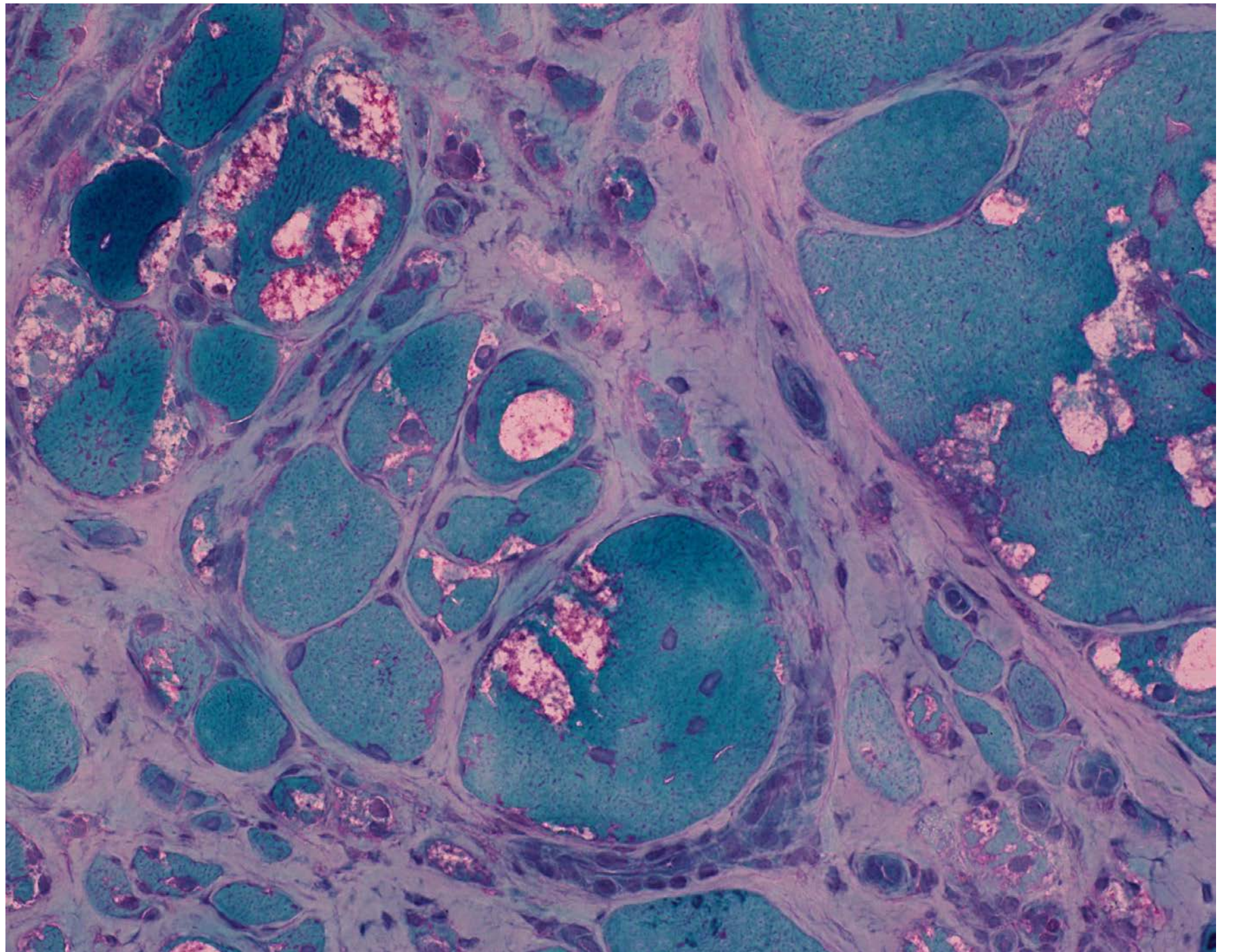
Masson trichrome



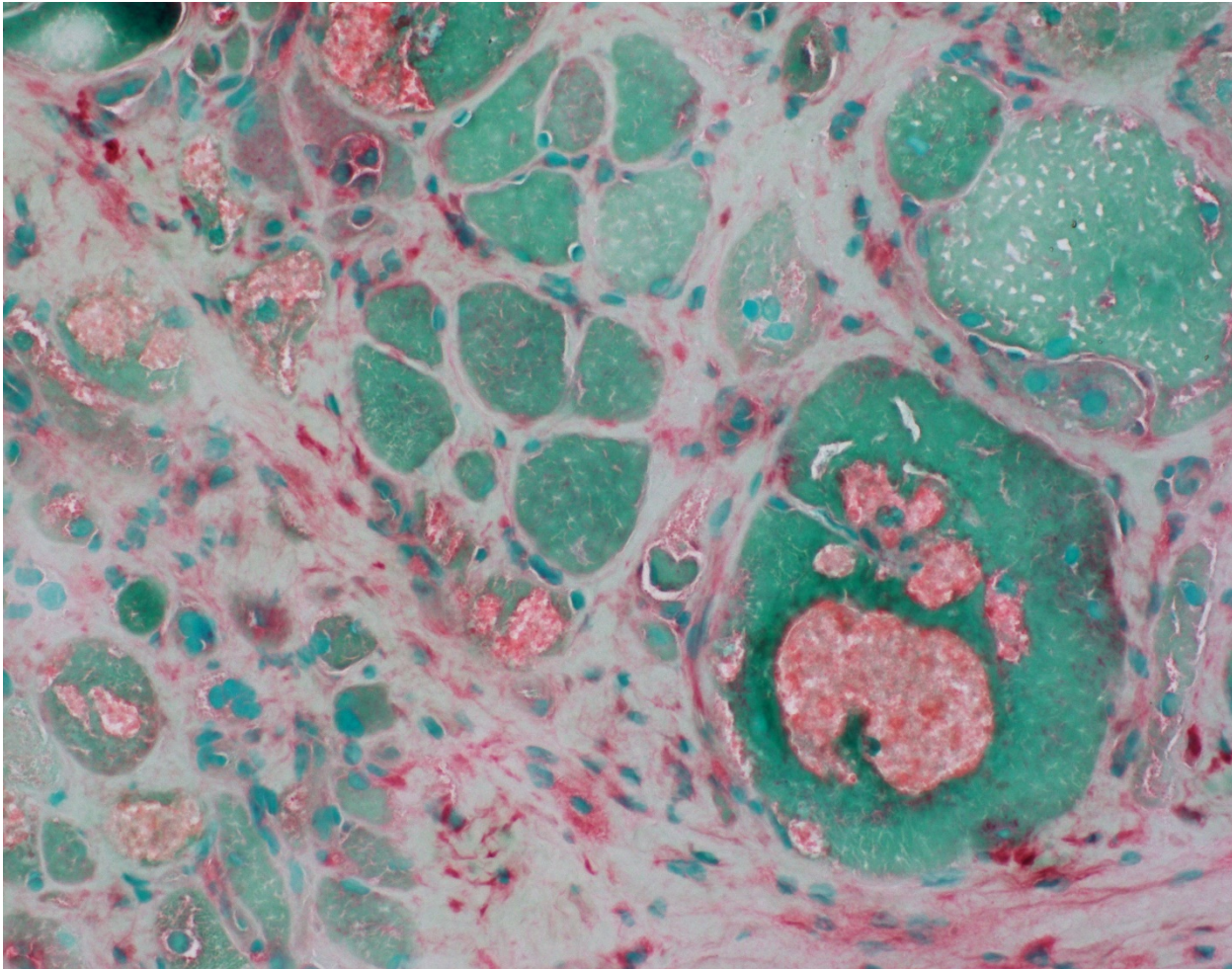
H&E



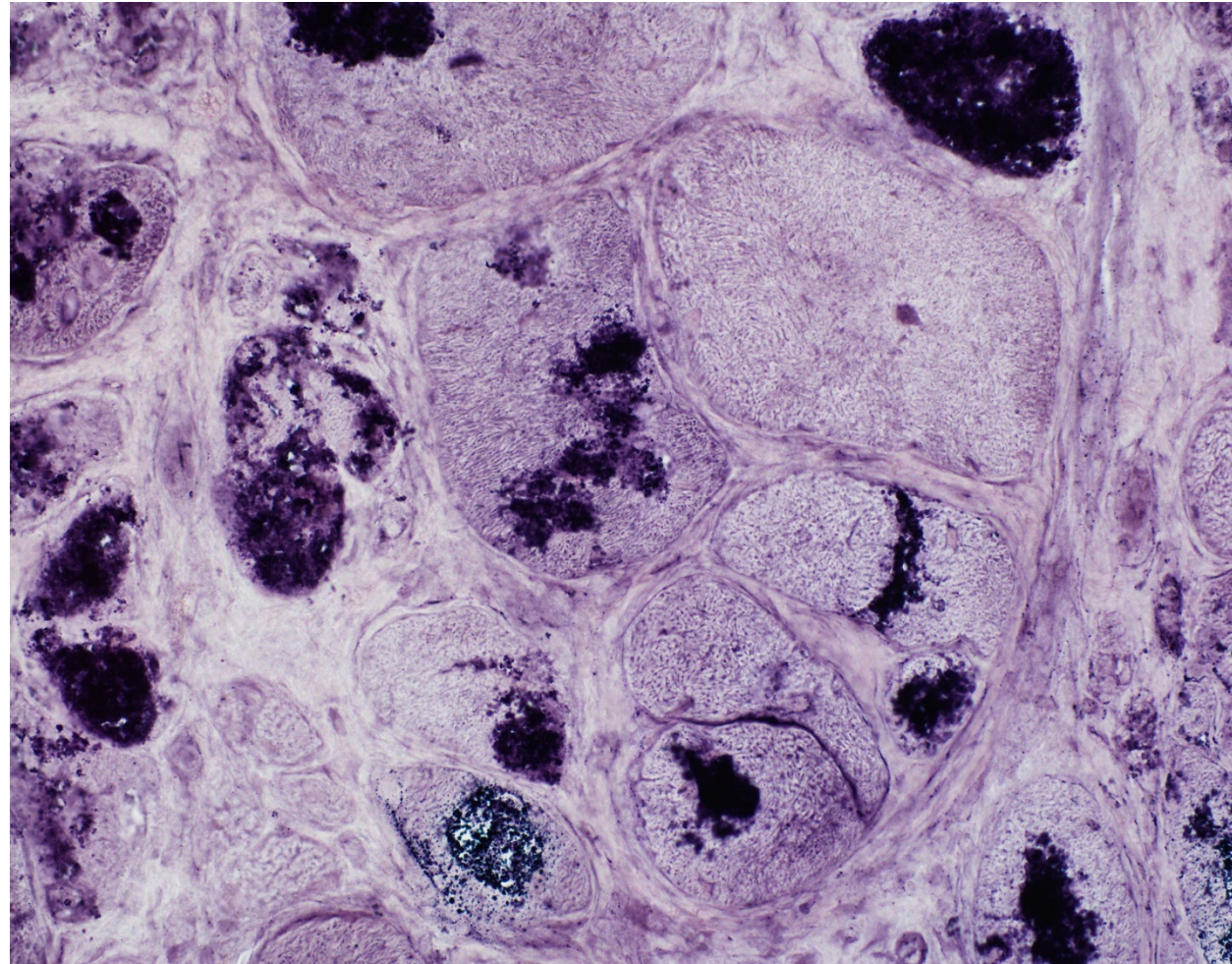
Gomori trichrome



Acid phosphatase



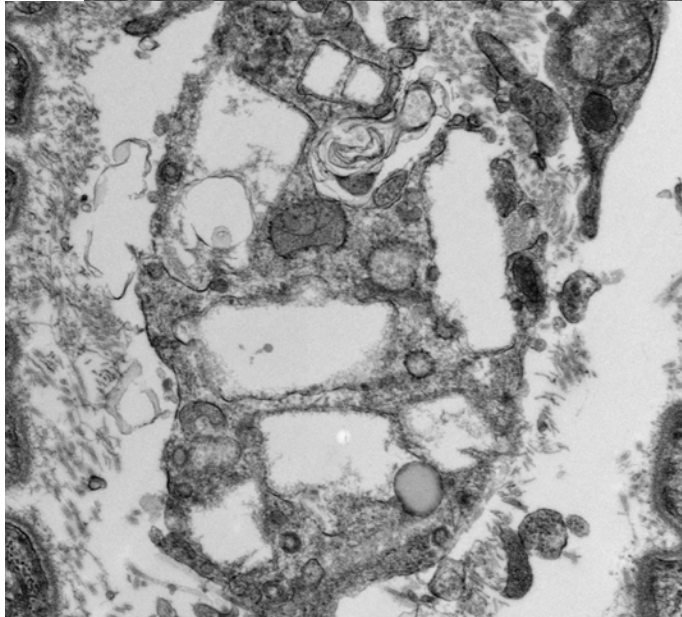
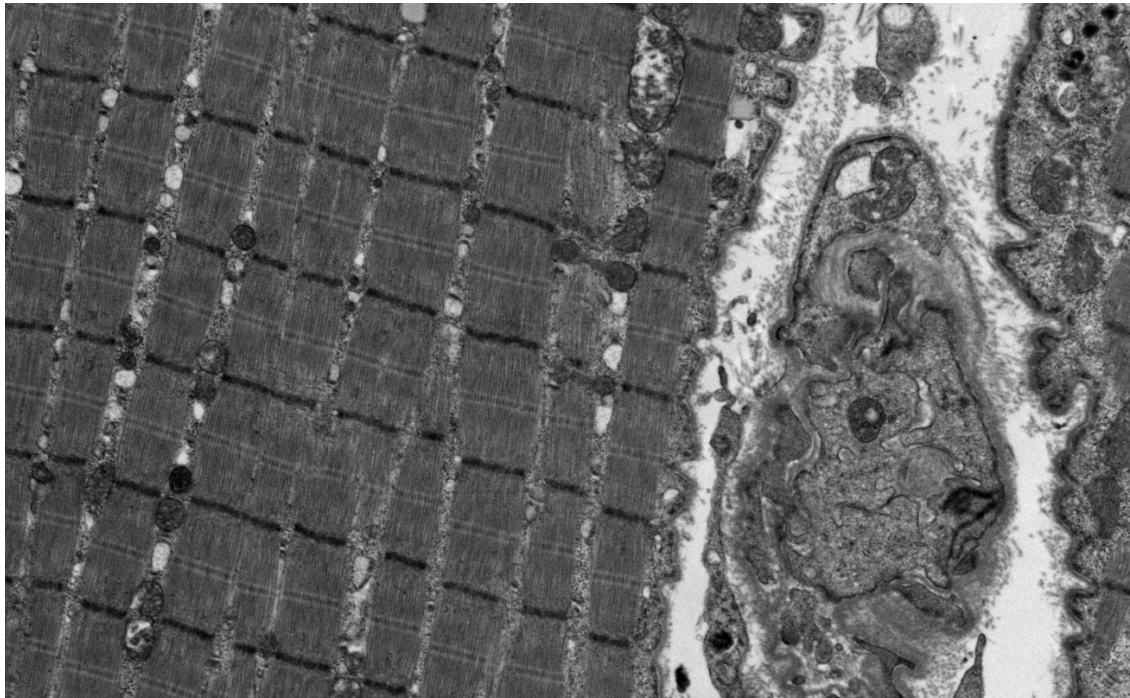
Myoadenylate deaminase (AMDA)



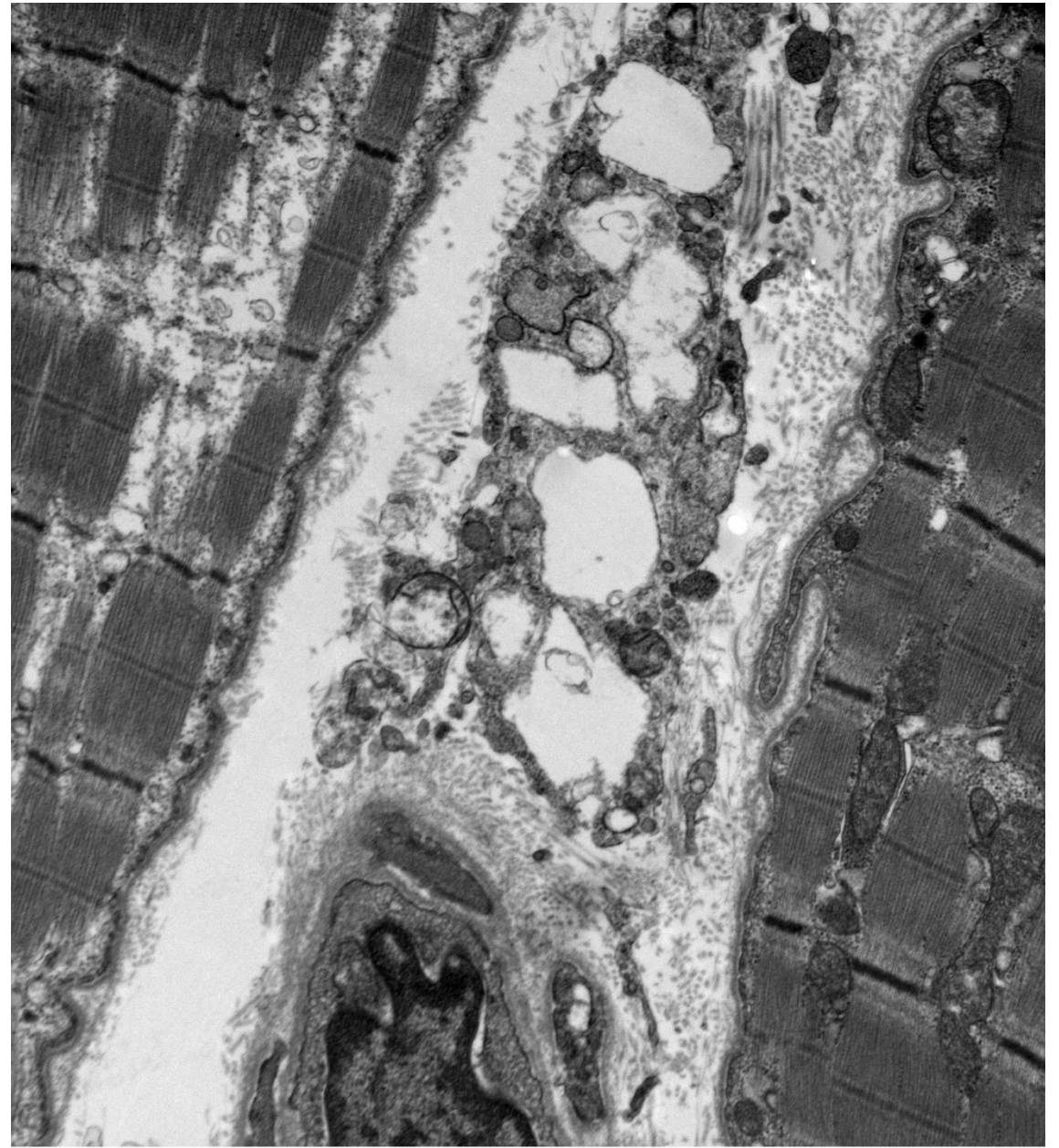
Diagnosis?

Chronic myopathy with red rimmed vacuoles

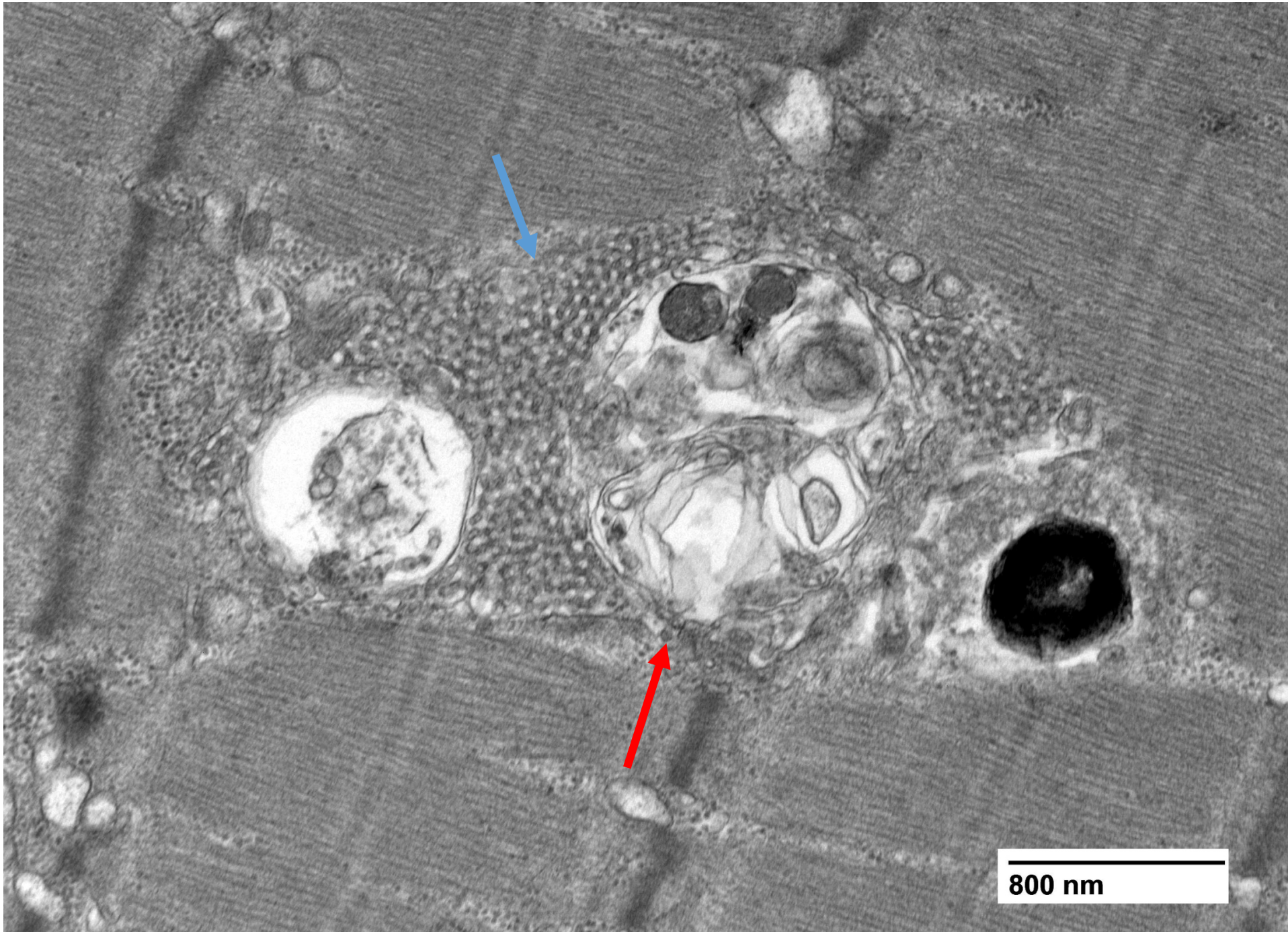
- DDX
 - Inclusion body myositis
 - Acquired IBM
 - Hereditary IBM (VCP, GNE1, desmin, MYH2)
 - Lysosomal storage diseases
 - Acid maltase deficiency
 - Cystinosis
 - Autophagic vacuolar myopathies
 - X-linked myopathy with excessive autophagy (XMEA)
 - Danon disease
 - Drug induced vacuolar myopathy
 - Chloroquine/hydroxychloroquine
 - Colchicine



2 μ m



1 μ m



Additional history

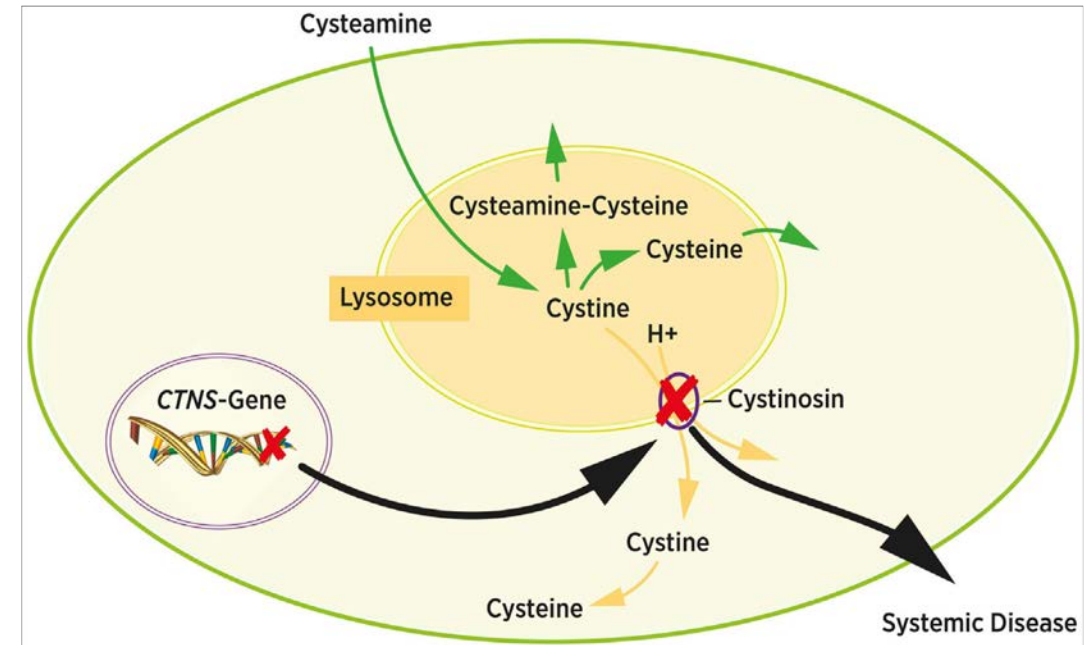
The patient has history of cystinosis diagnosed at age of 14 months, status post cysteamine treatment and two renal transplants in 1993 and 2005. He also has associated features of cystinosis, including poor vision, diabetes mellitus, hypothyroidism, and short stature.

Final diagnosis

- Cystinosis vacuolar myopathy

Cystinosis

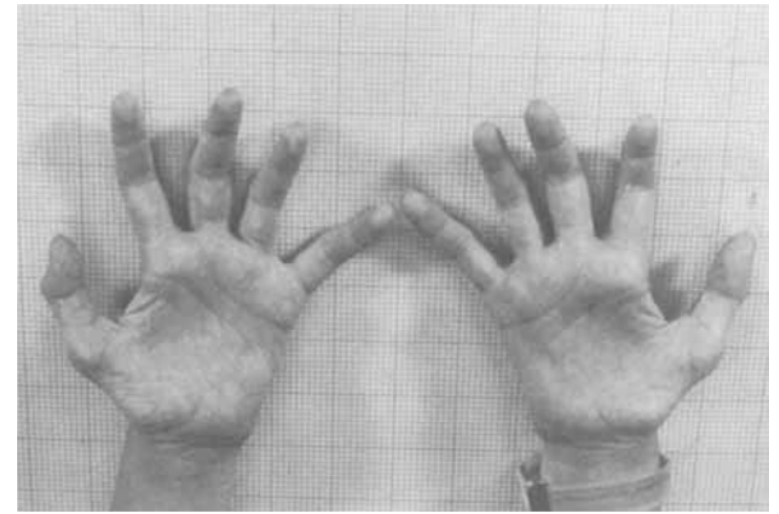
- Autosomal recessive
- 1-2 of 100,000 live births
- Mutations in the *CTNS* gene on chromosome 17p13
- Cystinosin - lysosomal transporter
- Three different forms: infantile nephropathic cystinosis, which is the most common form, juvenile nephropathic, and non-nephropathic cystinosis



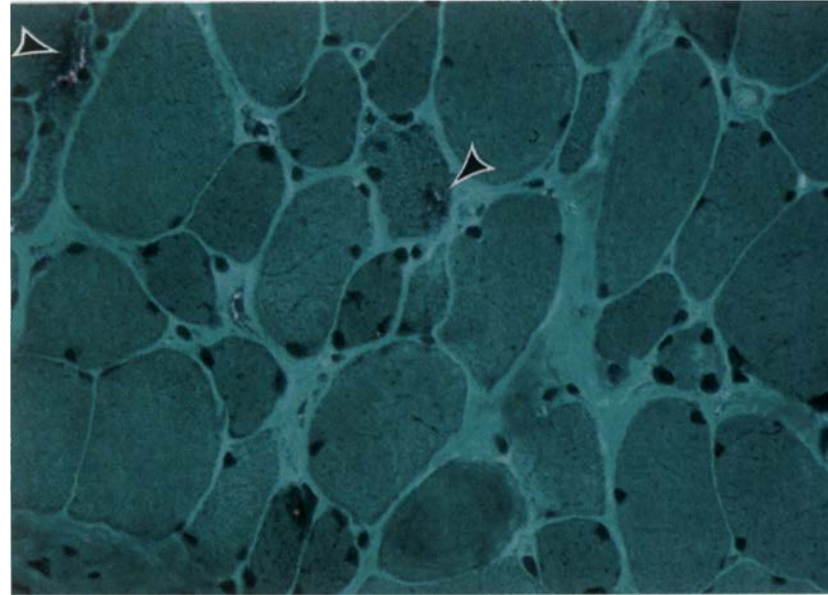
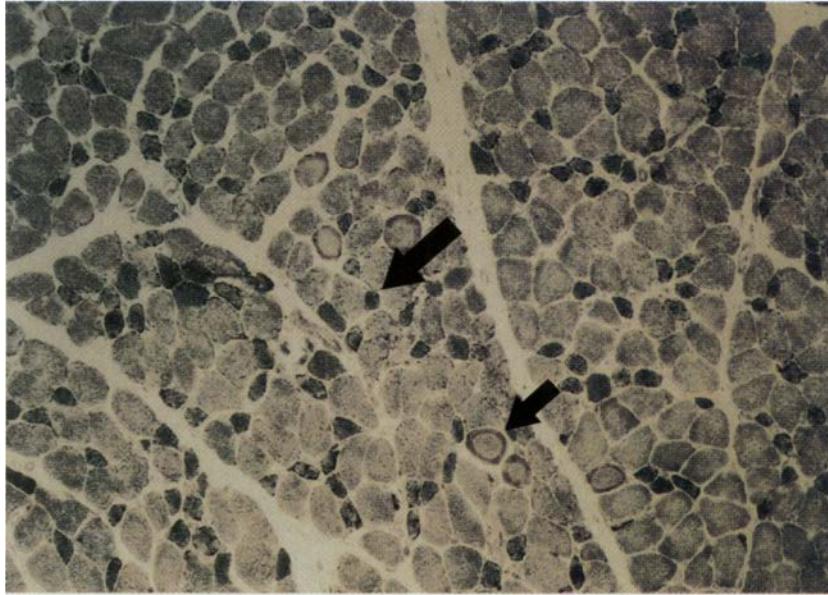
Front Pediatr. 2018;6:58

Cystinosis distal myopathy

- The first case reported in 1988
- Cystinosis myopathy frequency: 24 to 69%
- Hand muscles are the earliest and more severely involved
- Distal muscles of the lower extremities and proximal muscles can become affected later
- Dysphagia reported in 60% of patients
- Respiratory insufficiency in 69% of patients
- Normal reflexes, normal sensory function, and a normal or elevated CK level



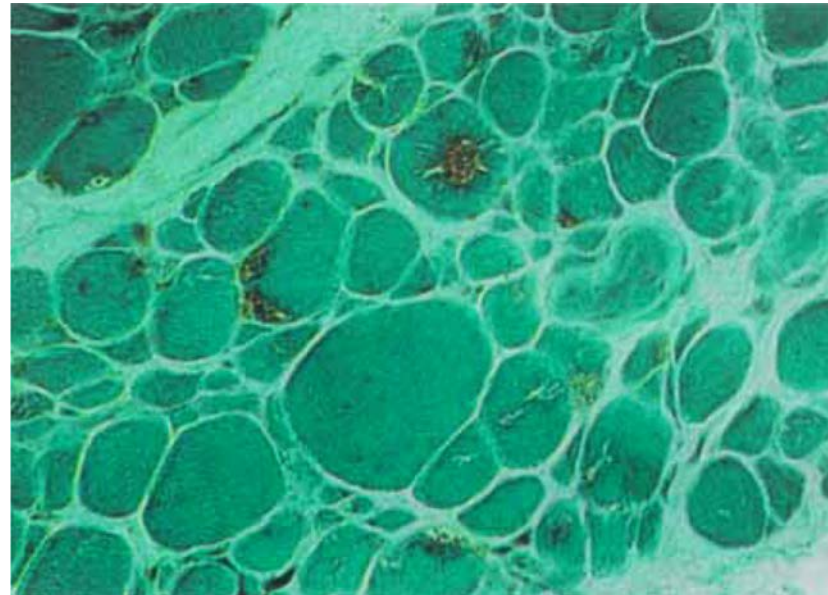
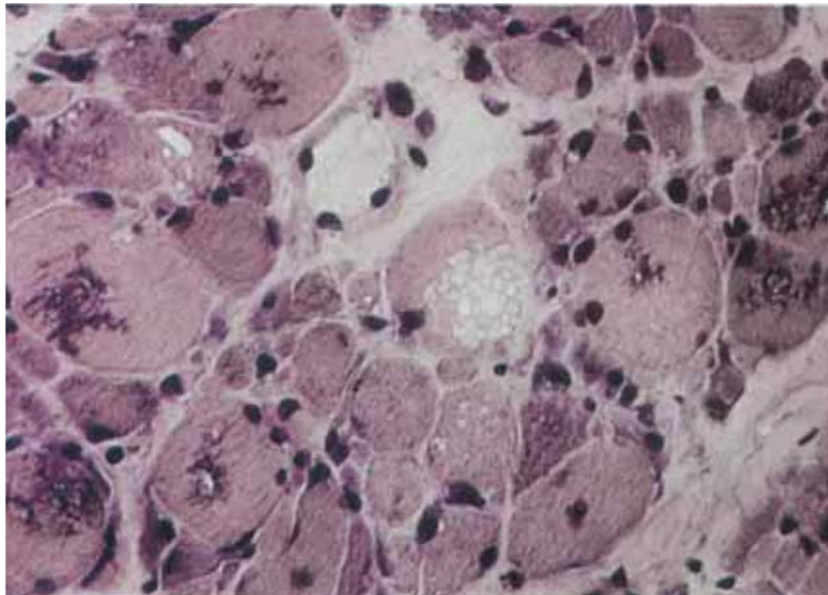
NADH



Trichrome

N Engl J Med 1988;319:1461

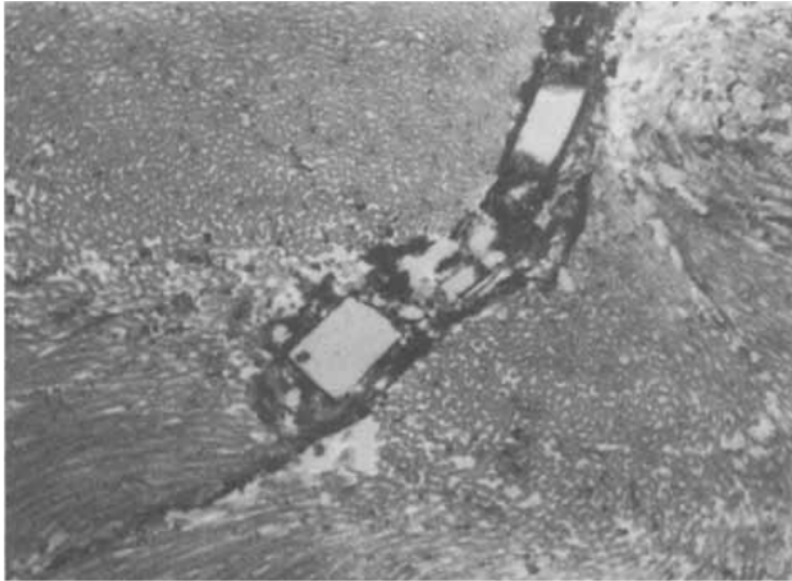
H&E



Acid phosphatase

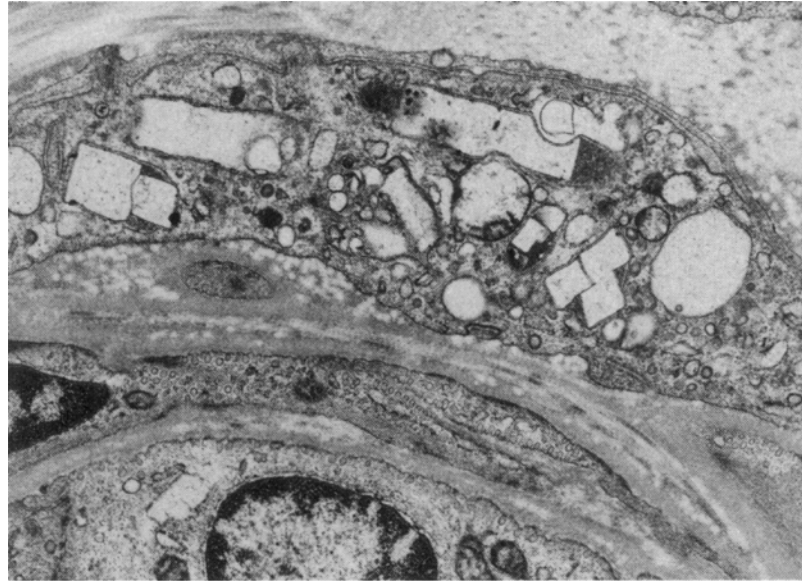
Ann Neurol 1994;35:181

Perimysial and endomysial spaces



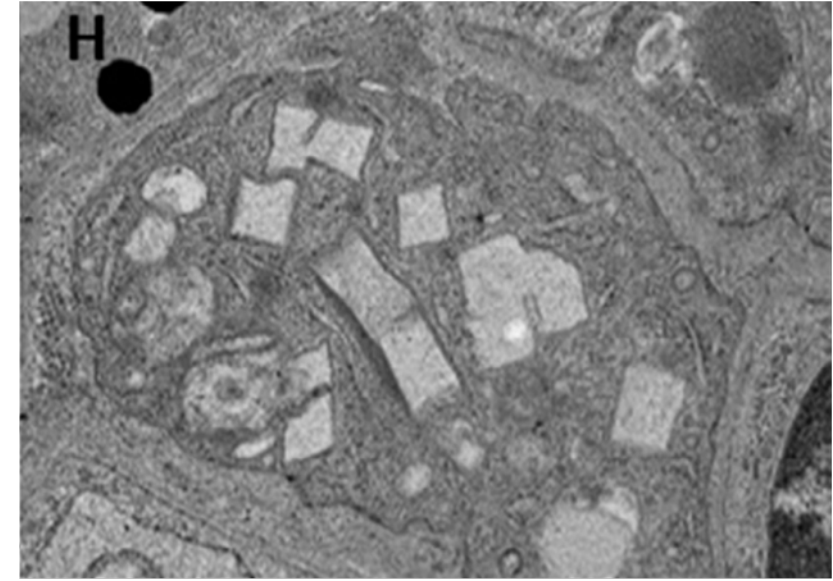
Ann Neurol 1994;35:181

Fibroblasts



N Engl J Med 1988;319:1461

Macrophages



Neuromuscular Disorders 2017;27:873

Reference

- Nephropathic Cystinosis: Symptoms, Treatment, and Perspectives of a Systemic Disease. *Front Pediatr.* 2018;6:58
- Distal vacuolar myopathy in nephropathic cystinosis. *Ann Neurol* 1994;35:181
- Cystinosis distal myopathy, novel clinical, pathological and genetic features. *Neuromuscul Disord* 2017;27:873
- Myopathy and cystine storage in muscles in a patient with nephropathic cystinosis. *N Engl J Med* 1988;319:1461
- A pattern-based approach to the interpretation of skeletal muscle biopsies. *Mod Pathol.* 2019;32:462