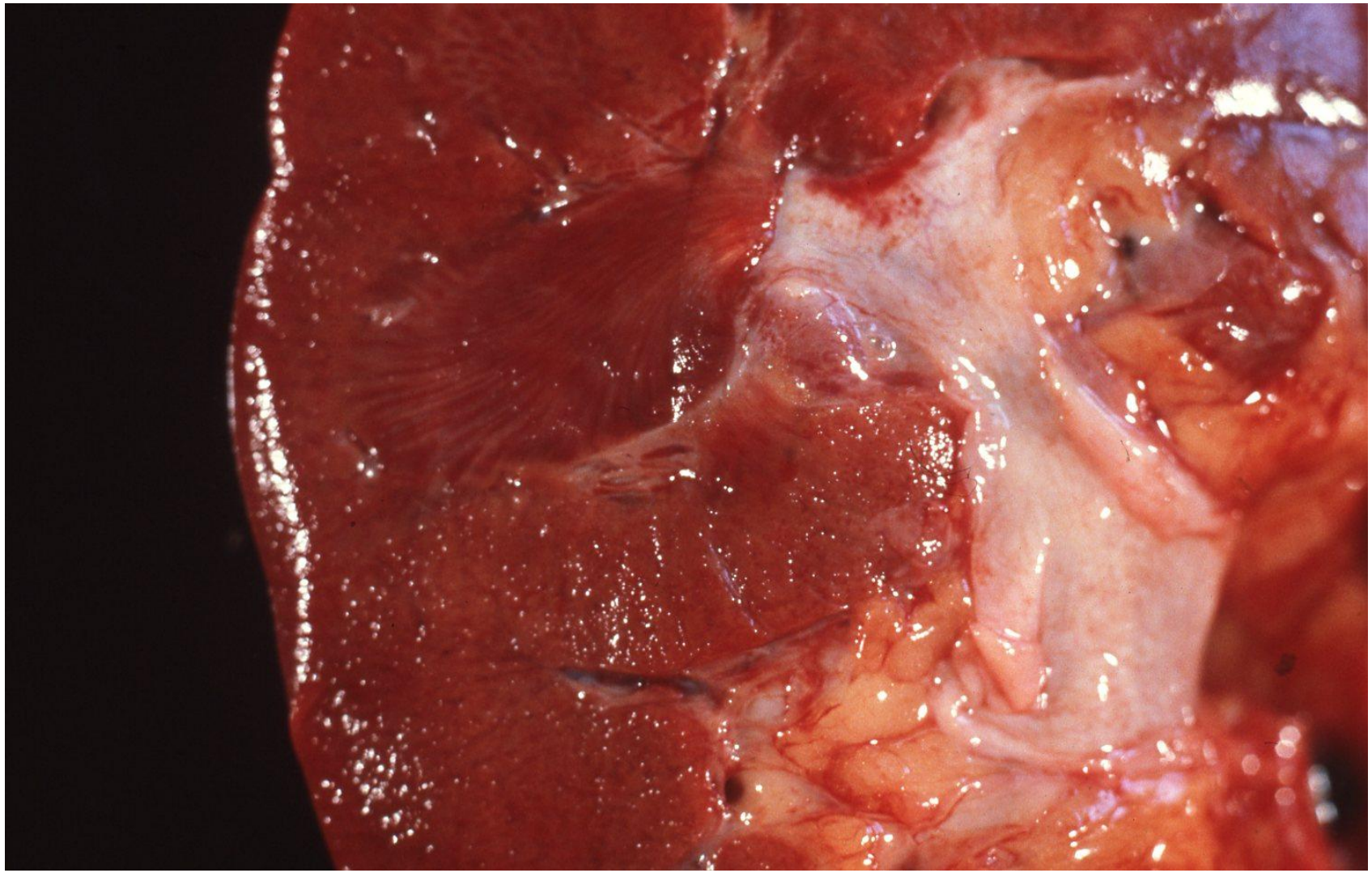
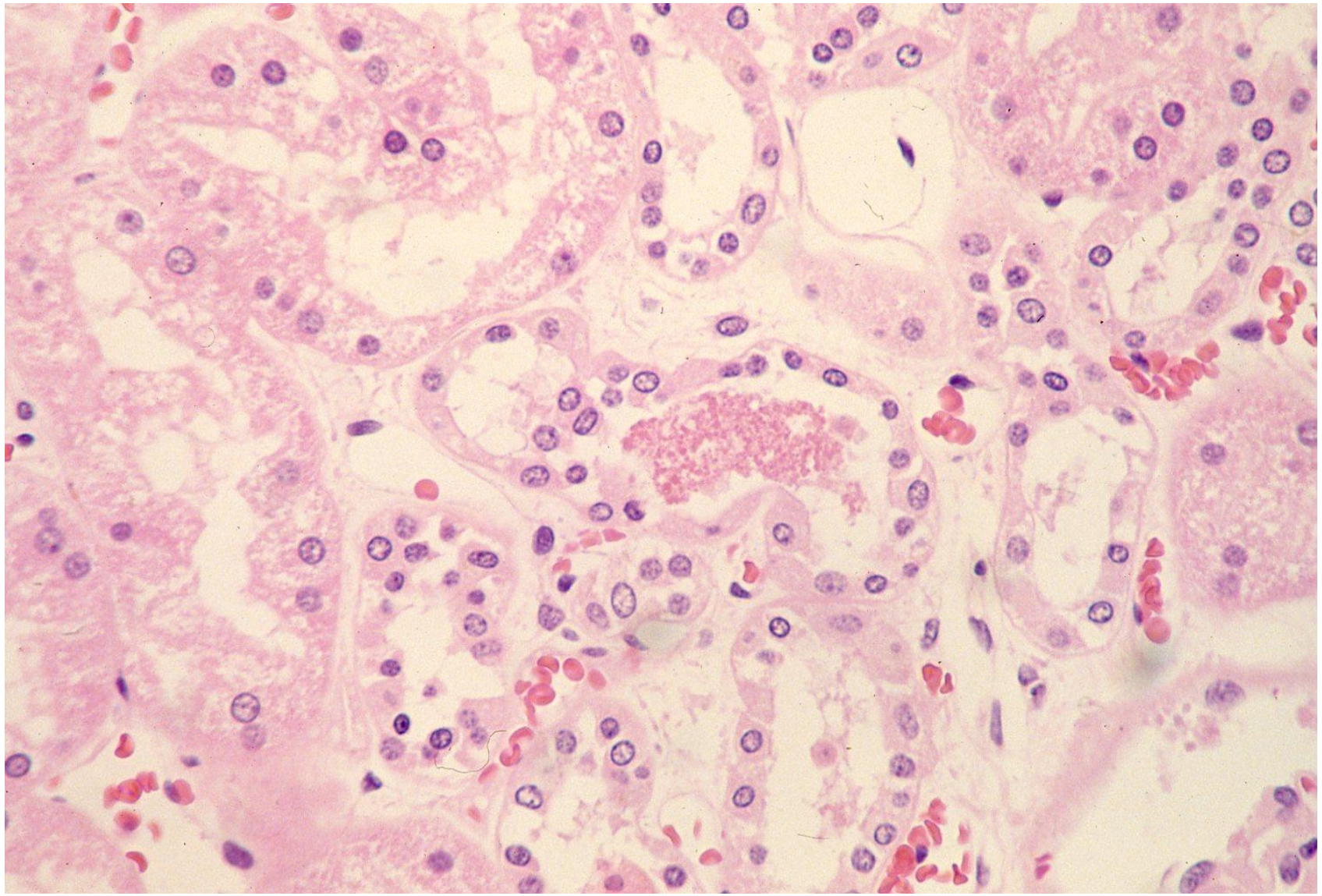
# Idiopathic rhabdomyolysis (idiopathic myoglobinuria)

A 43-year-old Danish man who had suffered from persistent occipito-nuchal pain for 10 years flew to Japan for sightseeing in June, 1979. He vomited in the airplane and complained of sever malaise. Next day, progressive muscle weakness and dyspnea on exertion appeared. On day 3, myalgia of both thighs started, and marked sweating happened on day 4. He was admitted to a local hospital in Tokyo on day 5. Urine excretion was kept, but the urine color was black. He smoked cigarettes and drank alcohol, but did not use any special medication. No family history of muscle disease was recorded. On admission, his mental status was clear. Hypothermia (35C), tachycardia (120/minutes) and hypertension (150-170/100-120 mmHg) were pointed out. He complained of cold sensation on the lower extremities. Because of systemic myalgia with tenderness, he could not sit up on the bed. Decrease of urine volume (415 mL/day) with black-colored appearance persisted. The laboratory data on admission included neutrophilia (20,000/μL), blood urea nitrogen 42 mg/dL, creatinine 2.0 mg/dL, aspartate transaminase 700 IU/L, alanine aminotransferase 130 IU/L, lactate dehydrogenase 1,860 IU/L, sodium 137 mEq/L, potassium 5.4 mEq/L, chloride 95 mEq/L, and calcium 3.7 mEq/L. The urine revealed macroscopic hematuria but without red cells in the sediment. Myoglobin was immunologically detected in his urine. On day 7, he expired suddenly and unexpectedly. No dialysis therapy was given throughout his illness. At autopsy, the striated muscles were grossly unremarkable, but microscopically reveals features of rhabdomyolysis. The heme casts in formalin-fixed, paraffin-embedded sections of the kidney were immunoreactive for myoglobin. For the author, this experience became the turning point to apply the immunoperoxidase method to diagnostic pathology using formalin-fixed paraffin-embedded sections. The authors believes that this was the very beginning of immunoperoxidase-assisted diagnostic pathology in Japan. In these days, the immunoperoxidase technique had been utilized as a research seed by using paraformaldehyde-fixed frozen sections, but scarcely used for the diagnostic pathology. A brief history of early development of chromogenic immunostaining in diagnostic pathology in Japan is summarized in the reference below.

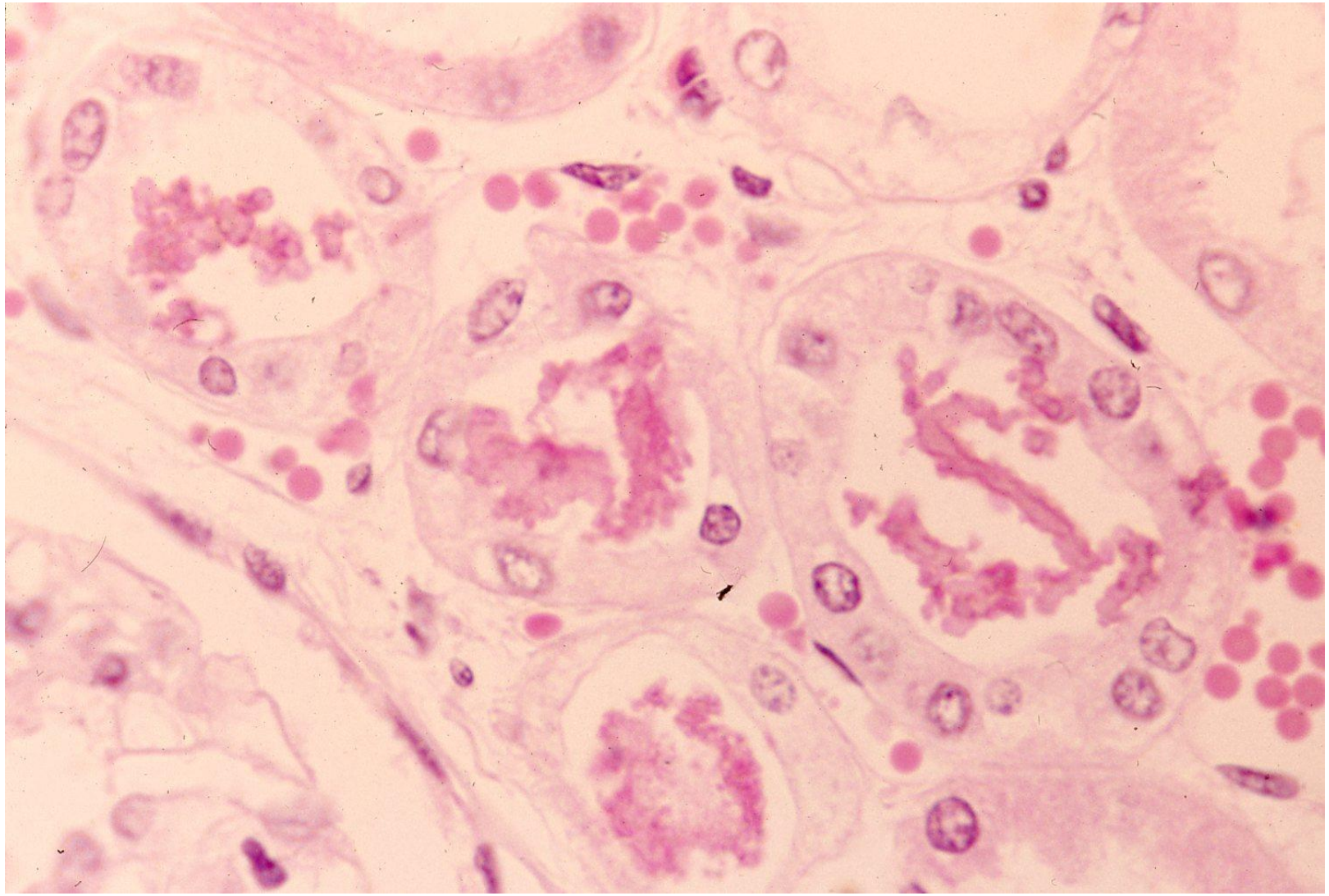
Ref.: Tsutsumi Y. An autopsy case of idiopathic rhabdomyolysis in 1979: immunoperoxidase detection of myoglobin casts in formalin-fixed, paraffin-embedded sections of the kidney. Cureus 2021; 13(10): e18922. doi: 10.7759/cureus.18922



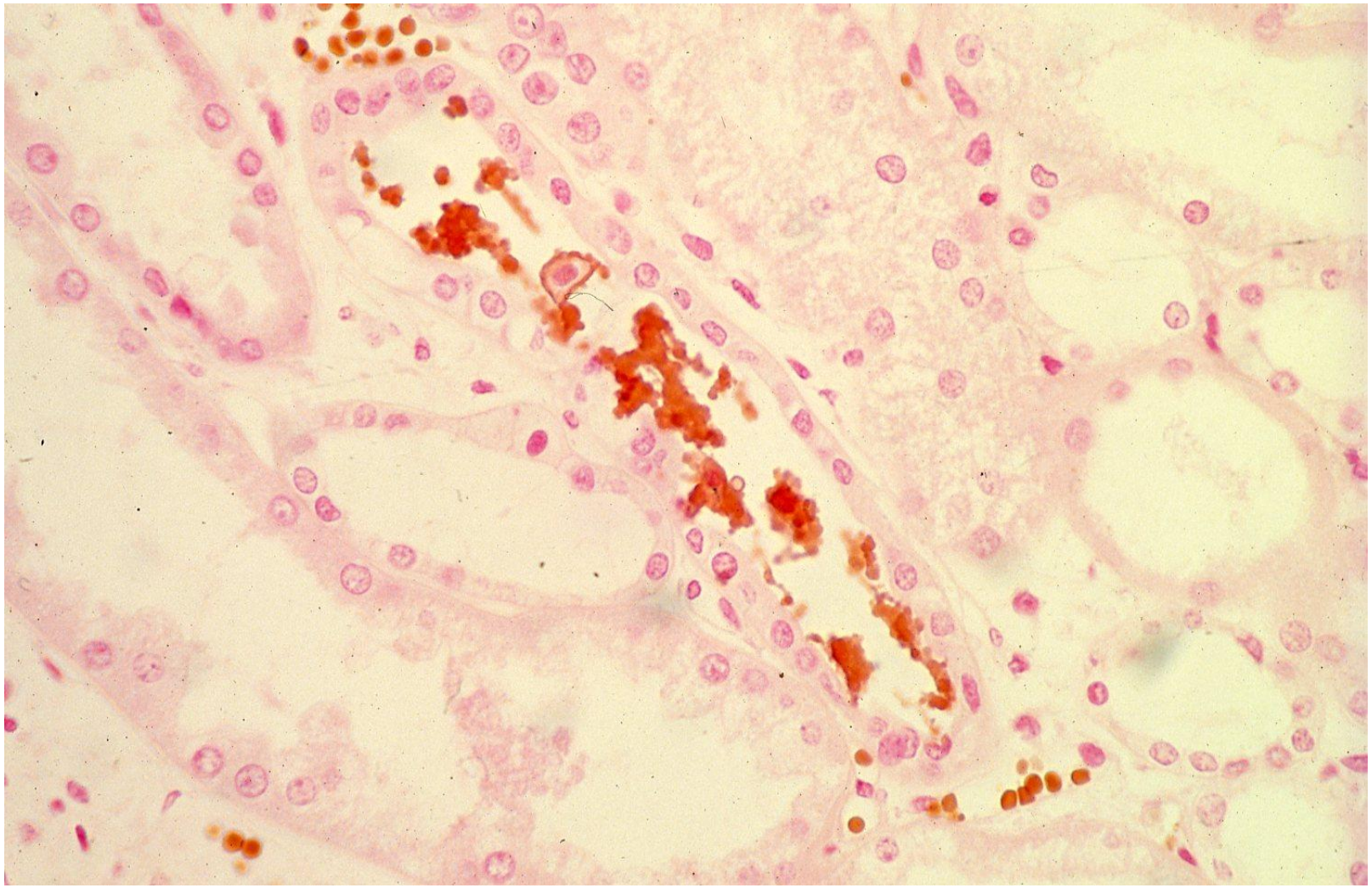
Idiopathic myoglobinuria in a 43 y-o Danish man.  The kidneys (left 160 g, right: 140 g) are grossly unremarkable, except for mild congestion.



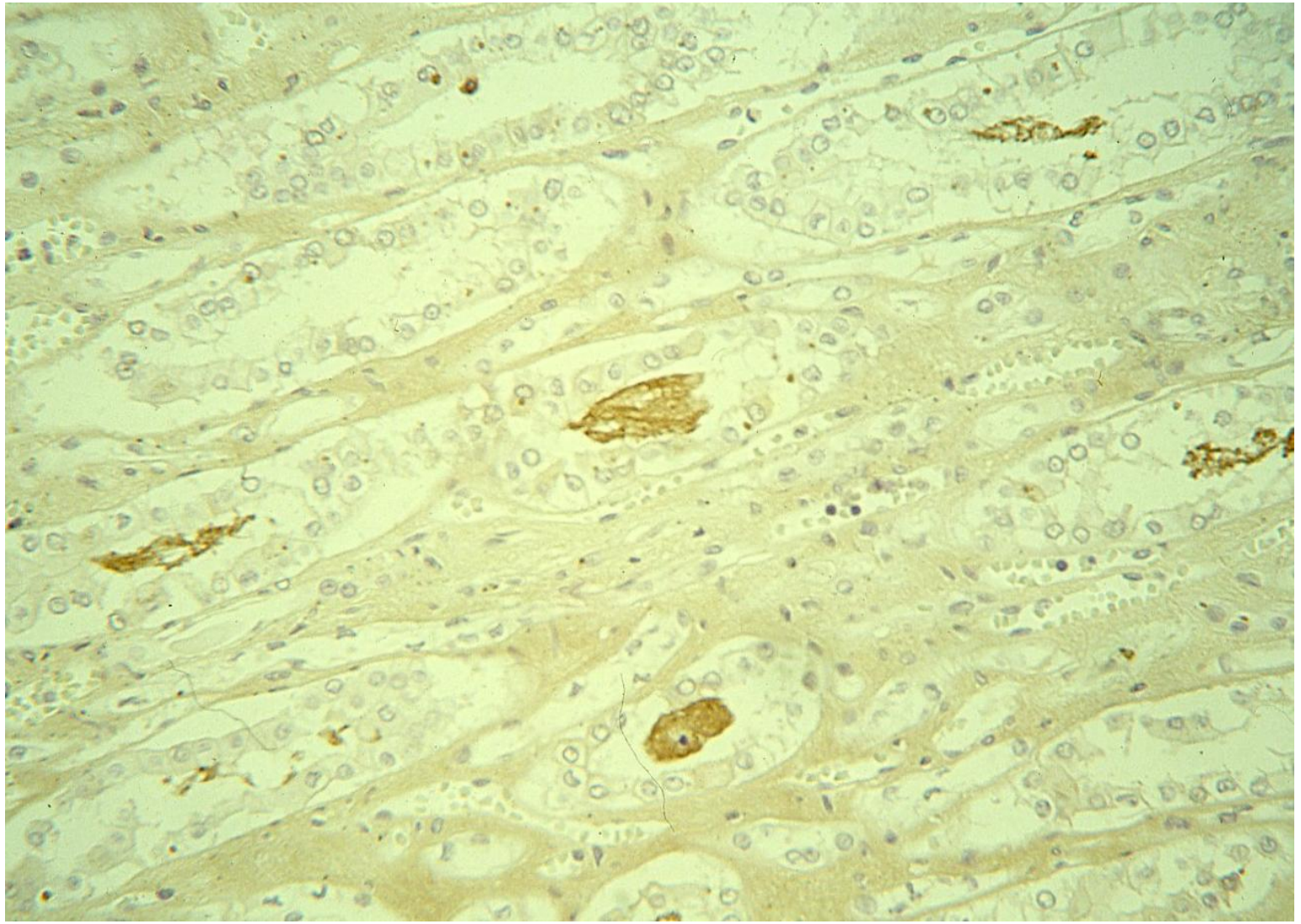
Idiopathic myoglobinuria in a 43 y-o Danish man.  Microscopically, heme casts (granular casts) are seen in the proximal renal tubules (H&E-1).



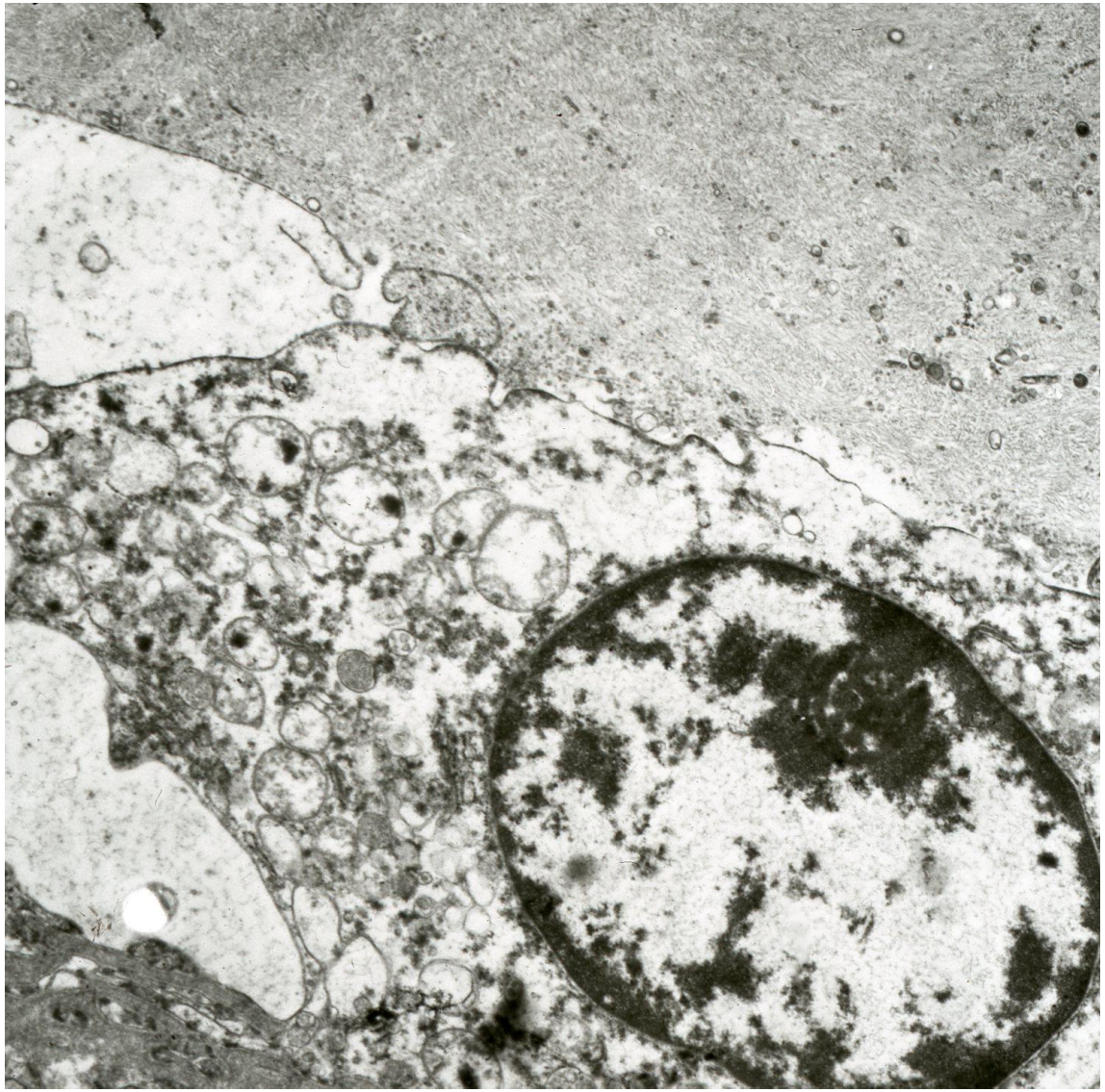
Idiopathic myoglobinuria in a 43 y-o Danish man.  Microscopically, heme casts (granular casts) are seen in the proximal renal tubules (H&E-2).



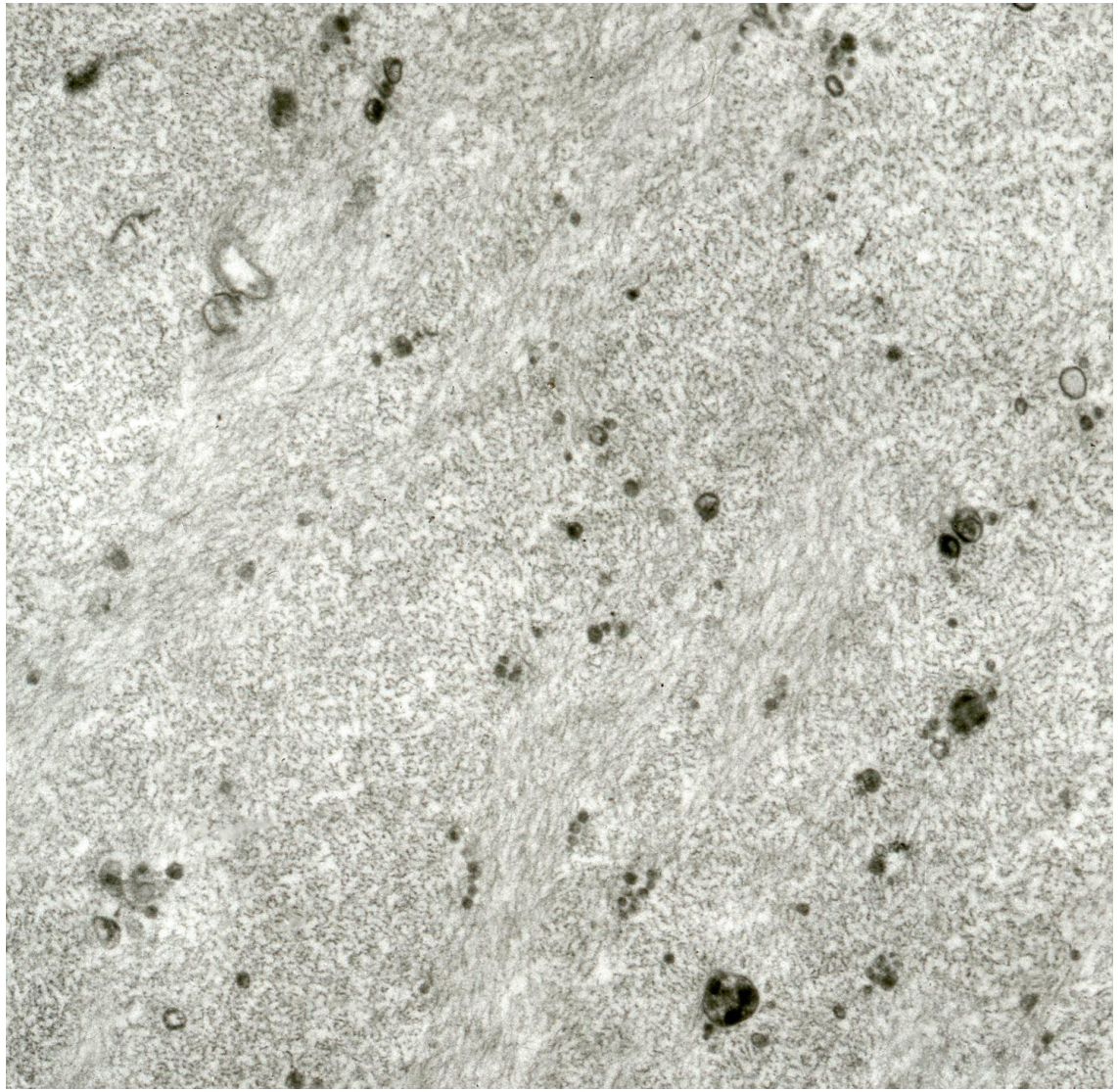
Idiopathic myoglobinuria in a 43 y-o Danish man.  Microscopically, heme casts (granular casts) in the proximal renal tubules are positive with benzidine reaction, indicating the presence of heme protein in the casts.



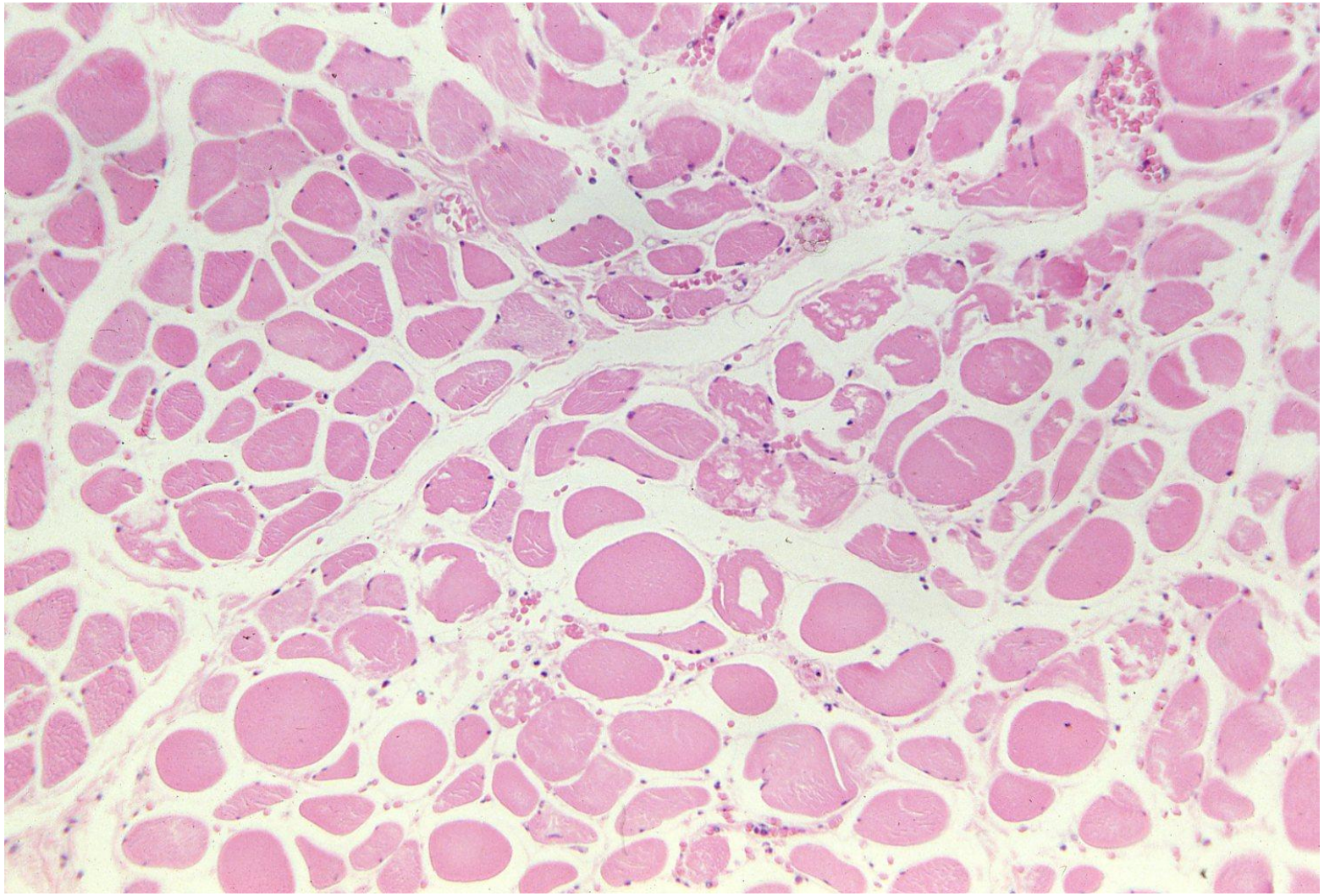
Idiopathic myoglobinuria in a 43 y-o Danish man.  Microscopically, heme casts (granular casts) in the proximal renal tubules are immunoreactive for myoglobin with peroxidase-antiperoxidase (PAP) method.  This was the very first experience of myoglobin visualization in formalin-fixed, paraffin-embedded sections.



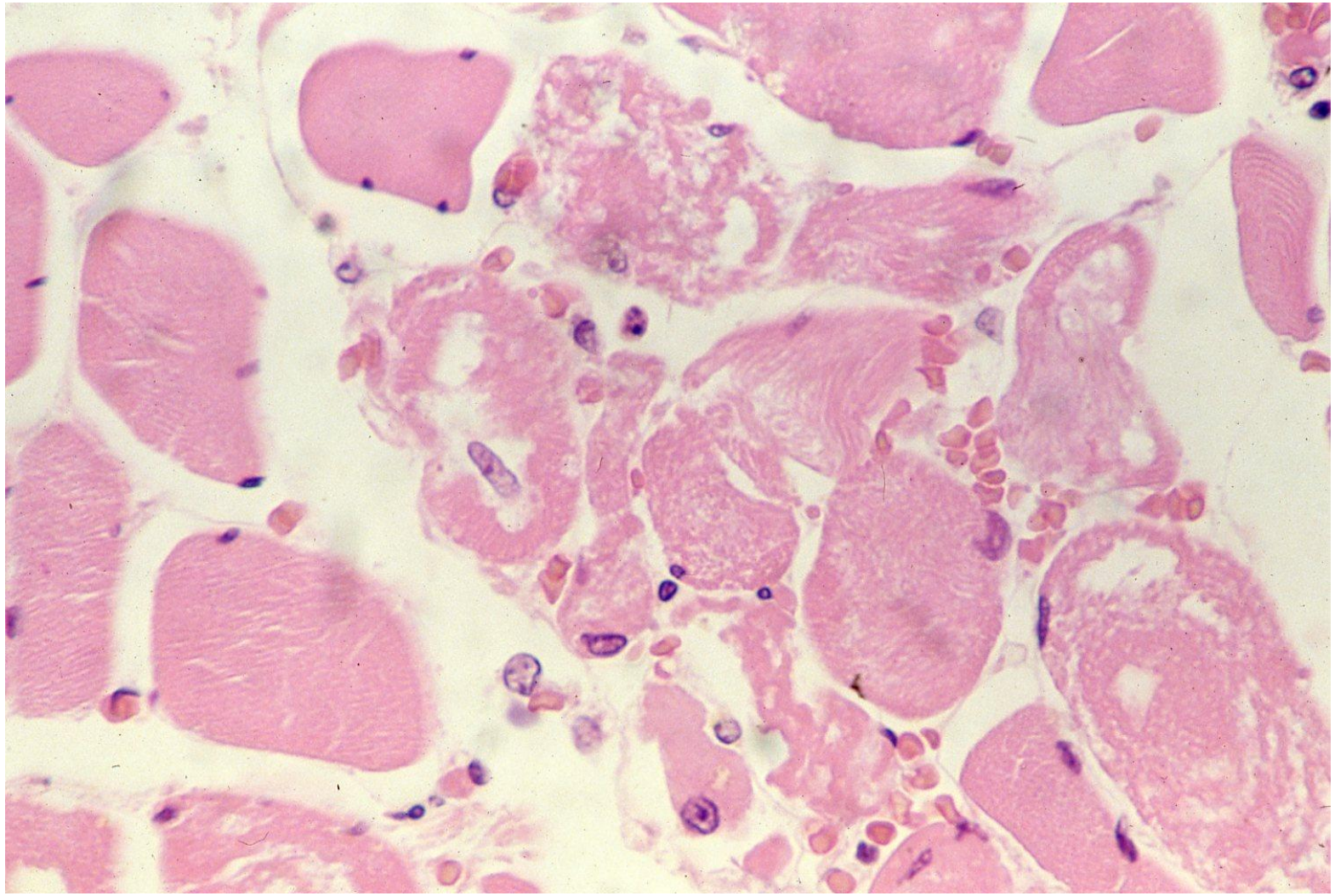
Idiopathic myoglobinuria in a 43 y-o Danish man.  Ultrastructurally, the heme cast is seen on the proximal renal tubular epithelial cell rich in mitochondria. The cast consists of fibrillar substances and electron-dense dot-like material.



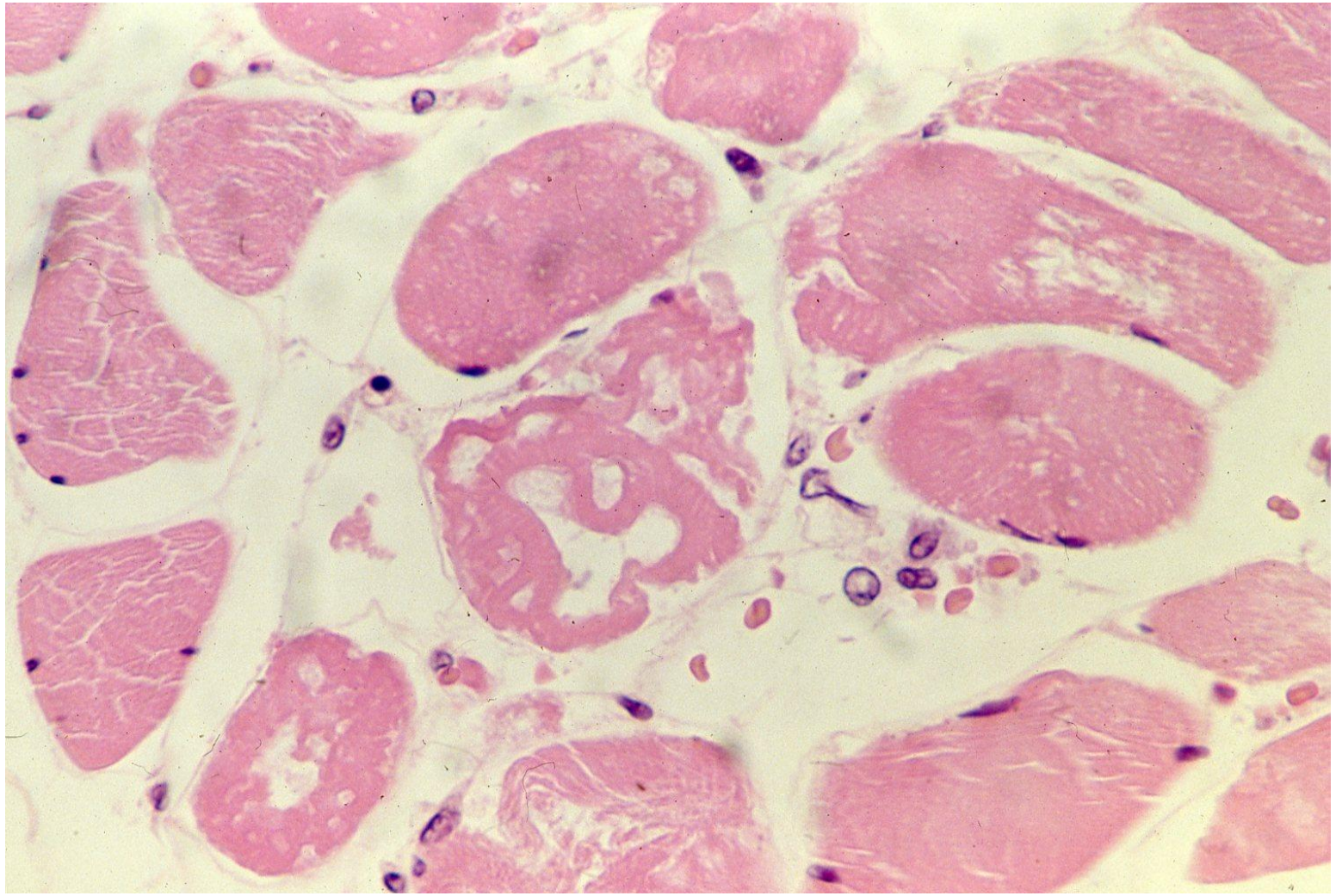
Idiopathic myoglobinuria in a 43 y-o Danish man.  Ultrastructurally, the heme cast in the lumen of the proximal renal tubule consists of fibrillar substances intermingled with electron-dense dot-like material, probably representing clusters of heme-containing proteins.



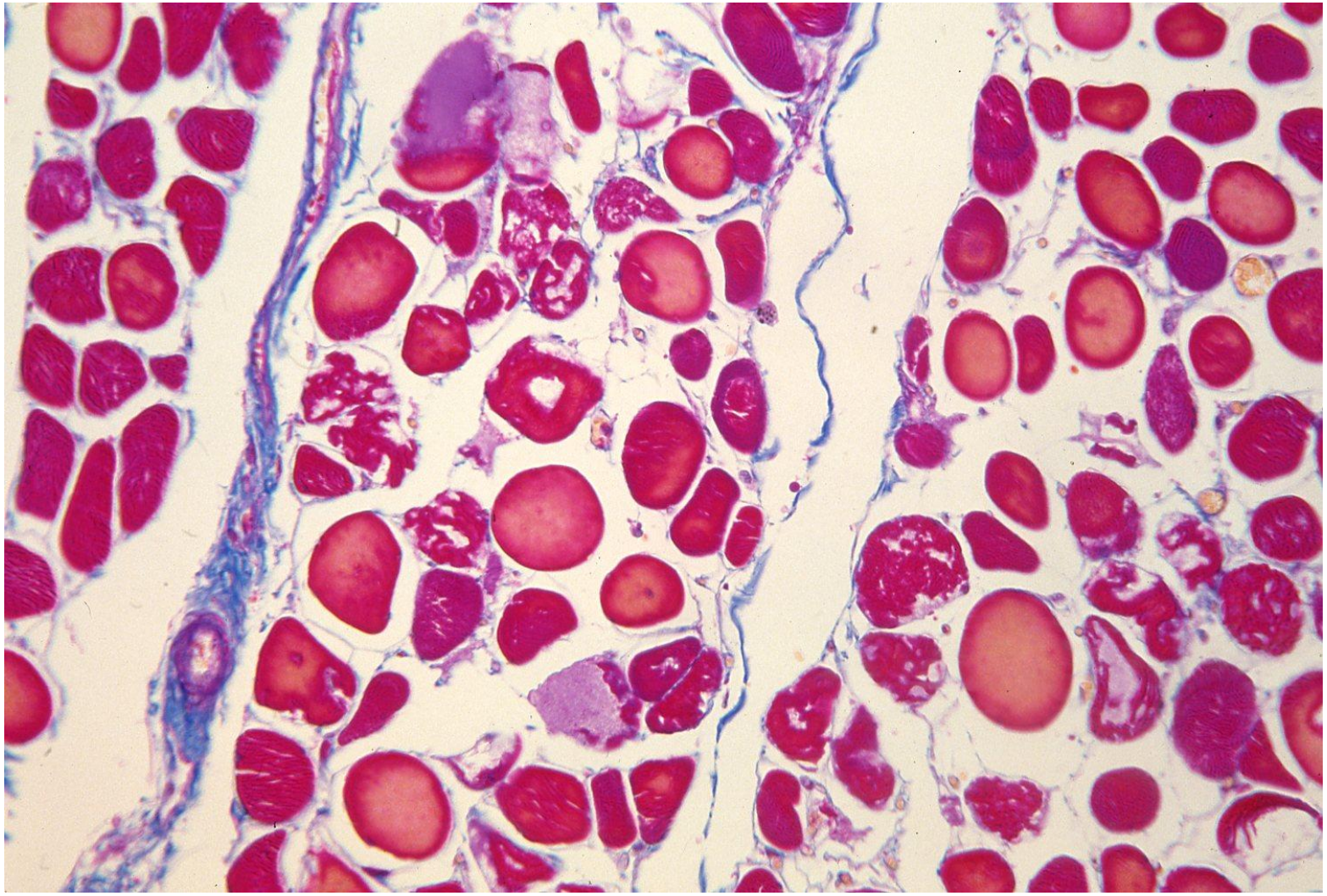
Idiopathic myoglobinuria in a 43 y-o Danish man.  Striated muscle cells often show myolytic changes (rhabdomyolysis) (H&E-3).



Idiopathic myoglobinuria in a 43 y-o Danish man.  Striated muscle cells often show myolytic changes (rhabdomyolysis) (H&E-4).



Idiopathic myoglobinuria in a 43 y-o Danish man.  Striated muscle cells often show myolytic changes (rhabdomyolysis) (H&E-5).



Idiopathic myoglobinuria in a 43 y-o Danish man.  Striated muscle cells often show myolytic changes (rhabdomyolysis) (Azan-Mallory).

## Summary of etiological factors in the present case (idiopathic rhabdomyolysis)

### *A) Clinical aspects*

1) No previous similar attack
2) No distinct family history
3) No exertional episode
4) No metabolic disorders
5) No addiction of heroin or alcohol
6) No distinct intake of drugs or toxins
7) No signs and symptoms of infection

### *B) Pathological aspects*

1) No deposition of glycogen or lipid in the striated muscle
2) No heavy metals or arsenic chromatographically identified in the liver
3) No detectable viruses or bacteria in the muscle and kidney
   (immunofluorescence analysis and viral isolation study: negative)
4) No viral particles identified in the striated muscle cells by EM