X-linked agammaglobulinemia with brown bowel syndrome

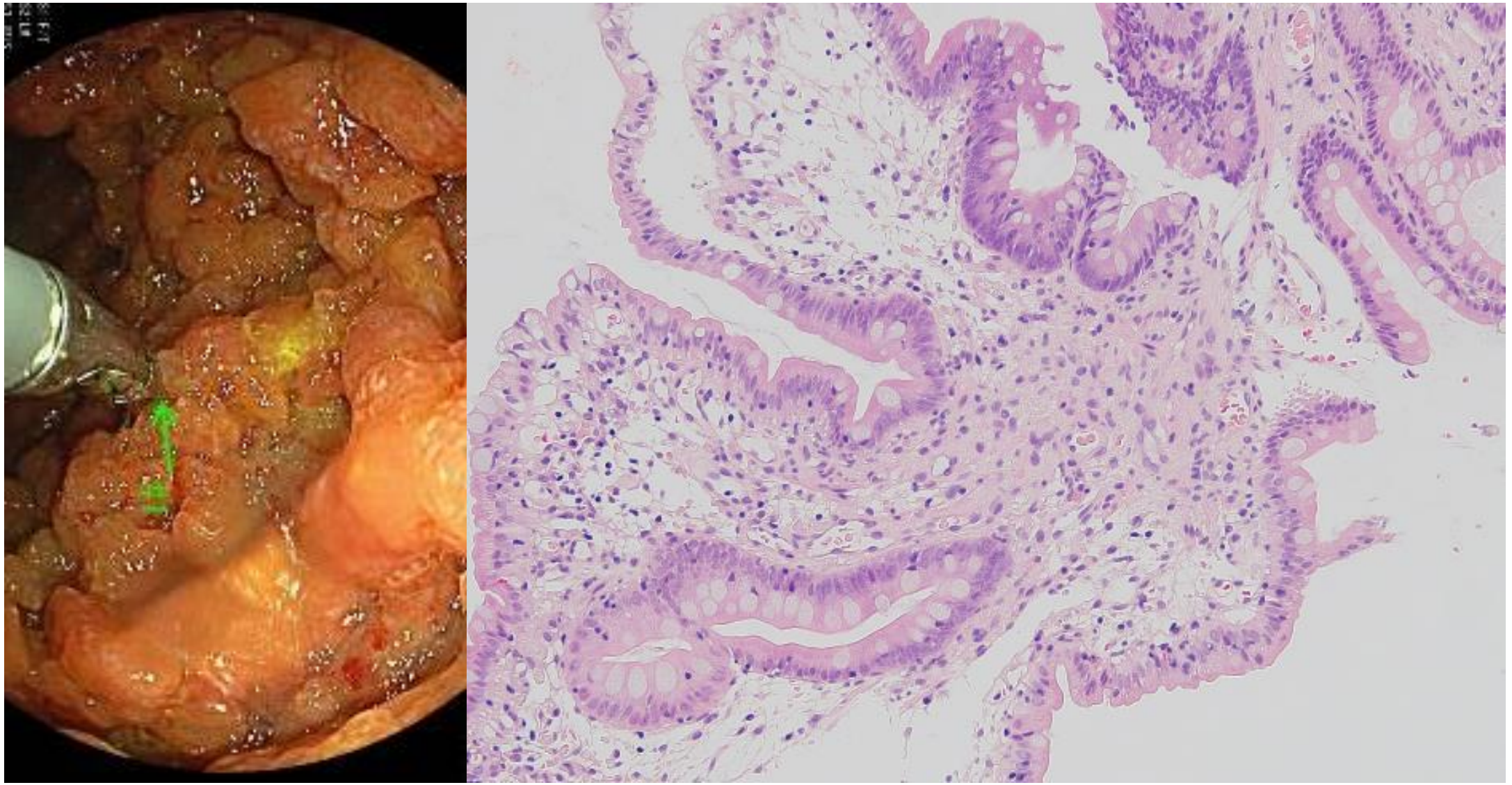
X-linked agammaglobulinemia of Bruton type is caused by a single gene mutation on the X chromosome (Xq21.3-q22). The impaired Bruton's tyrosine kinase (Btk) in male patients leads to a severe block in B cell development at the pre-B cell to immature B cell stage with a markedly reduced immunoglobulin production. B-lymphocytes are absent in the peripheral blood. The lymphoid tissues (the spleen, lymph nodes, tonsils and Peyer's patches) are underdeveloped, and no plasma cells are seen microscopically.

Ref.-1: El-Sayed ZA, et al. X-linked agammaglobulinemia (XLA): phenotype, diagnosis, and therapeutic challenges around the world. World Allergy Organ J 2019; 12(3): 100018. doi: 10.1016/j.waojou.2019.100018

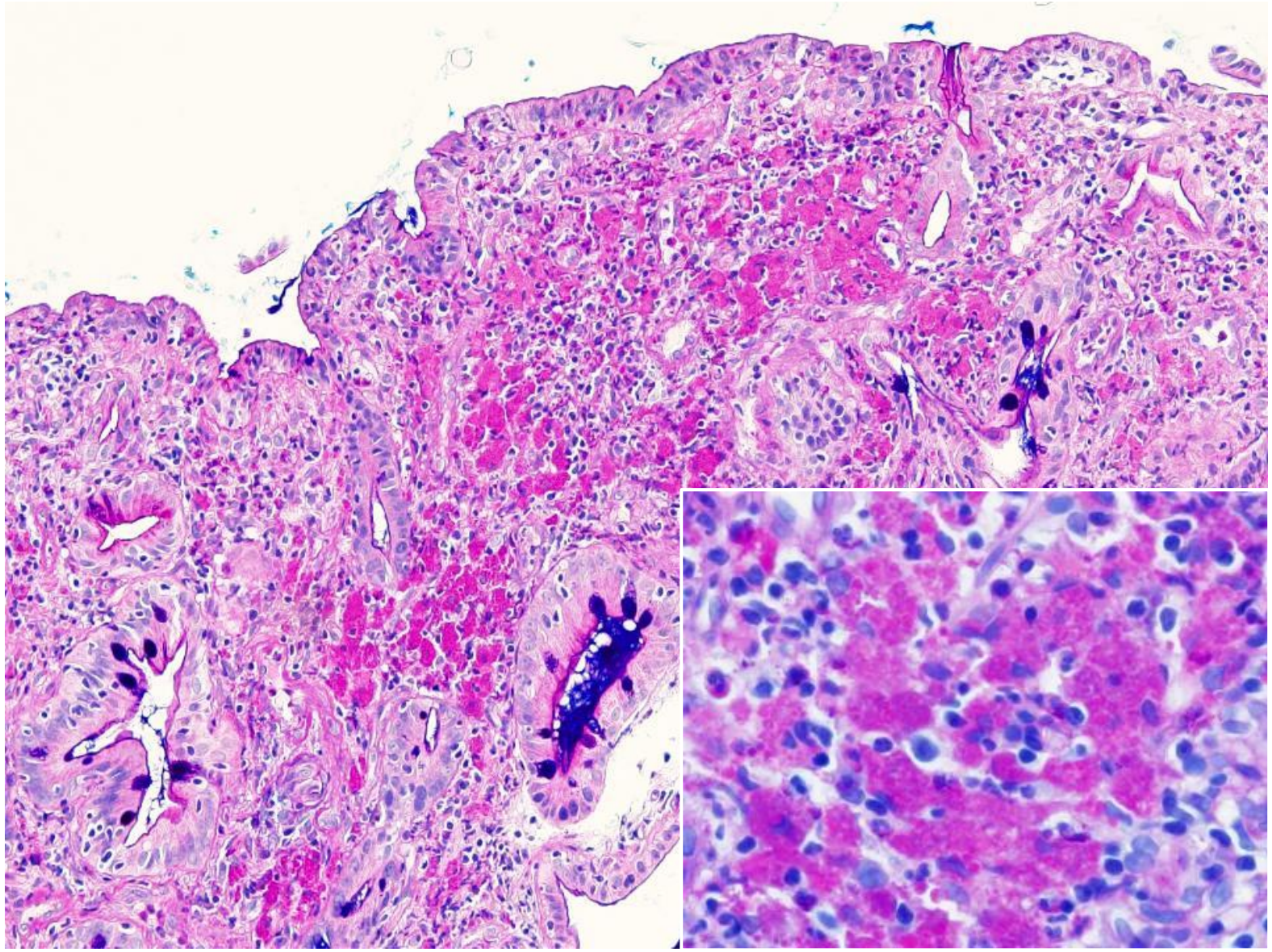
Ref.-2: Barmettler S, et al. Gastrointestinal manifestations in X-linked agammaglobulinemia. J Clin Immunol 2017; 37(3): 287-294. doi: 10.1007/s10875-017-0374-x

Case presentation

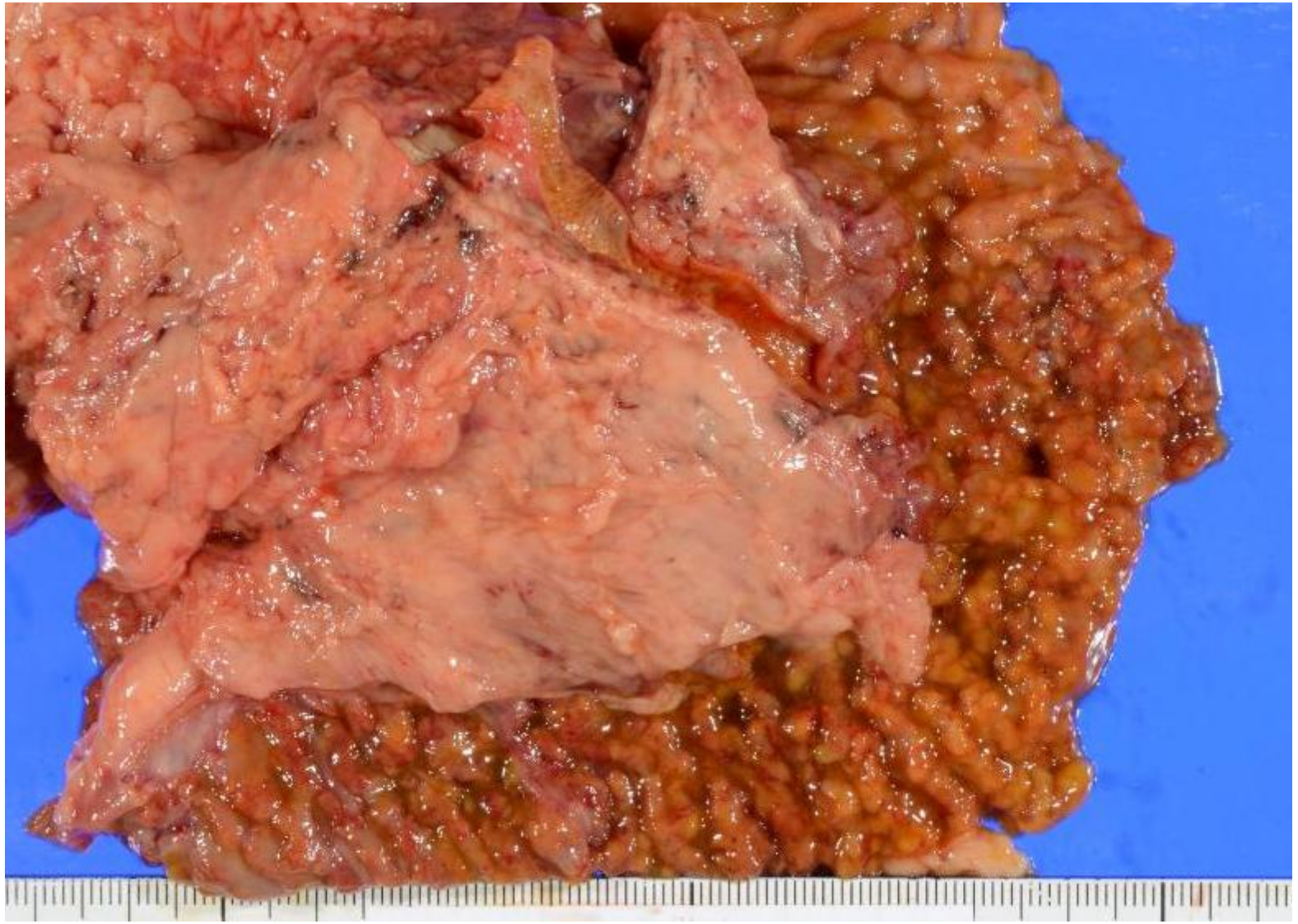
A 40-year-old autopsy male patient with X-linked agammaglobulinemia (XLA) of Bruton type is presented. The diagnosis of XLA was made at the age of 4 years. Infectious episodes were repeated thereafter. At the age of 35, he was diagnosed as non-viral liver cirrhosis. Panperitonitis with retention of ascites was repeated, and he died of hepatic encephalopathy. The liver showed features of non-cirrhotic portal hypertension, and brown bowel syndrome is extensively seen in the small intestine. The lymphoid tissue in the spleen and lymph nodes is atrophic.



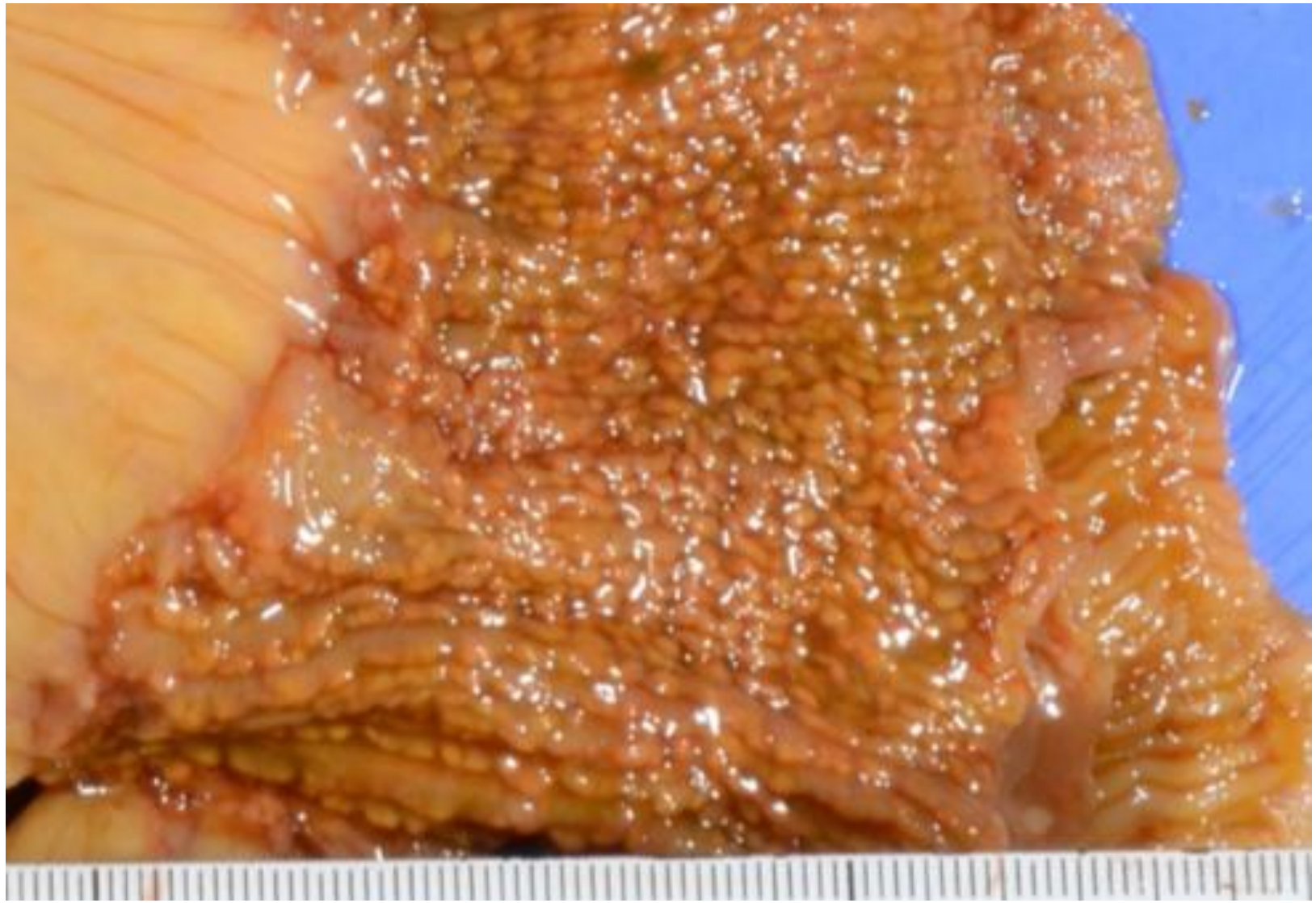
Duodenal biopsy from a 40-year-old man with XLA. Endoscopically, multiple polypoid projections are seen in the duodenal mucosa. Microscopically, accumulation of ceroid-containing macrophages is seen in the lamina propria mucosae. H&E-1



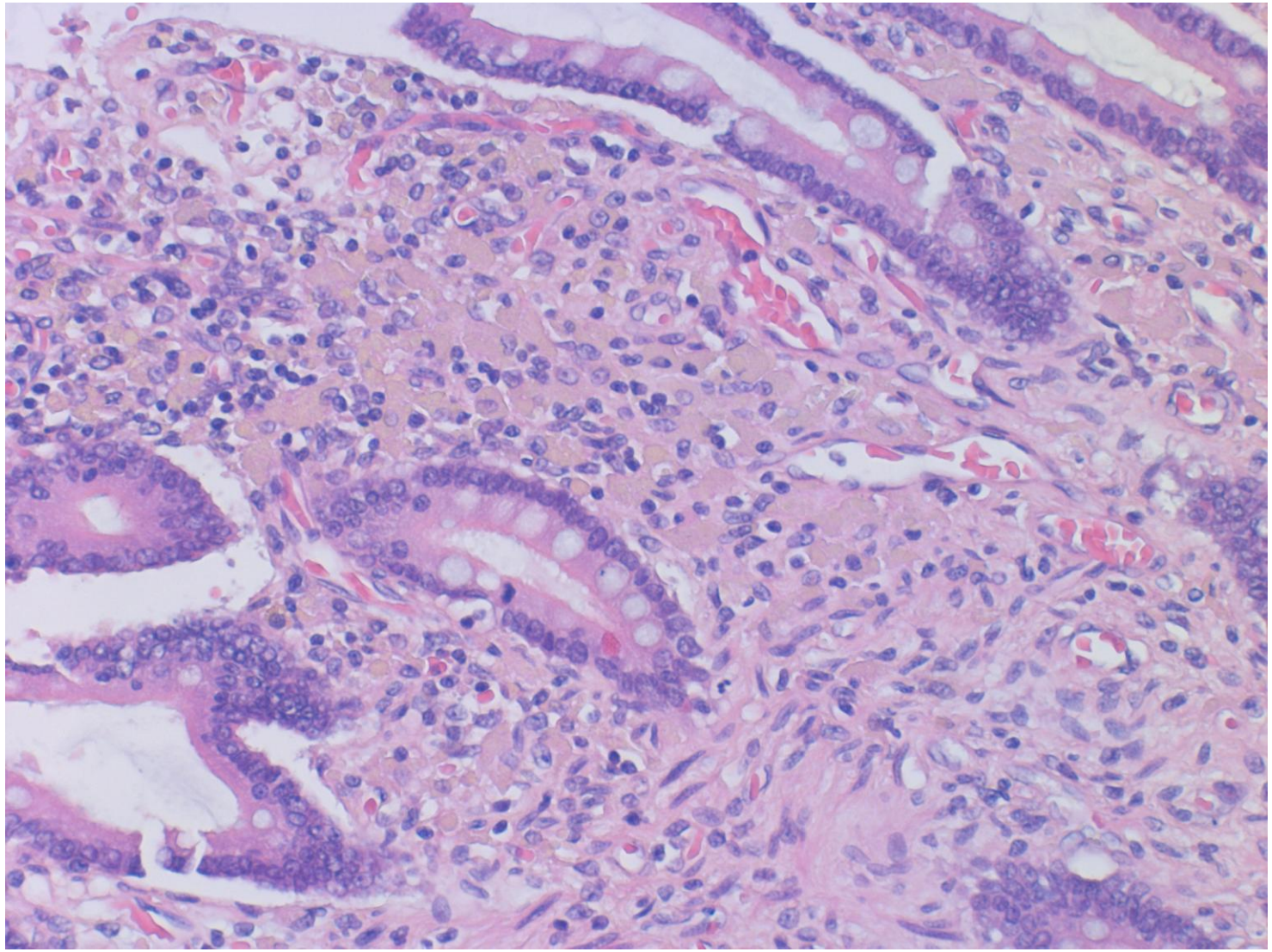
Duodenal biopsy from a 40-year-old man with XLA. Accumulation of PAS-reactive ceroid-containing macrophages is seen in the lamina propria mucosae. Inset: Close-up view of the PAS-reactive macrophages. Alcian blue-PAS



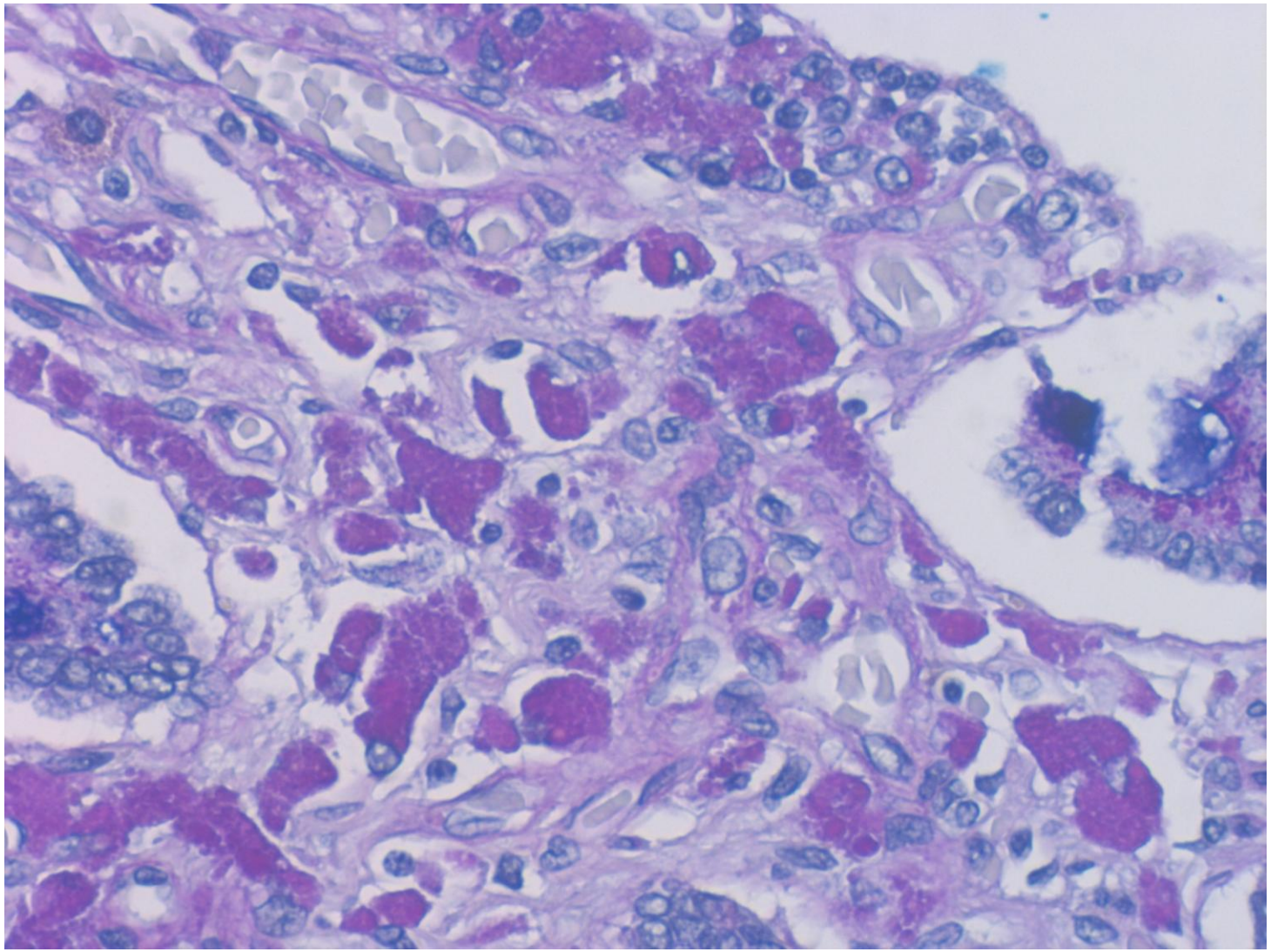
The duodenal mucosa at autopsy of a 40-year-old man with XLA. Yellowish brown-colored polypoid projections are multifocally seen in the duodenal mucosa, being consistent with brown bowel syndrome. The peritoneum is turbid and thickened due to chronic peritonitis. Ascites 8,300 mL is retained.



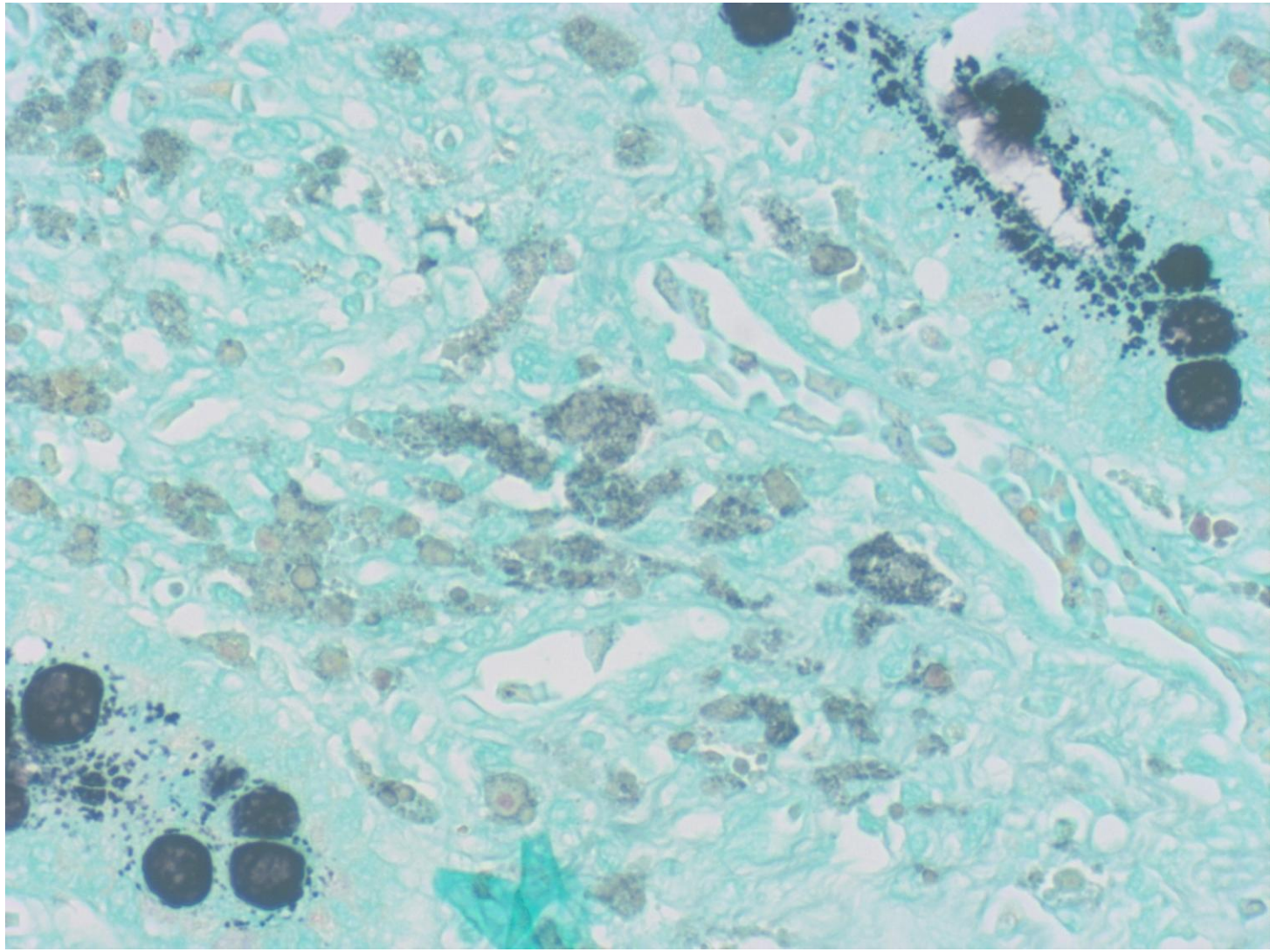
The jejunal mucosa at autopsy of a 40-year-old man with XLA. Yellowish brown-colored polypoid projections are multifocally seen in the jejunal mucosa. The features are consistent with brown bowel syndrome.



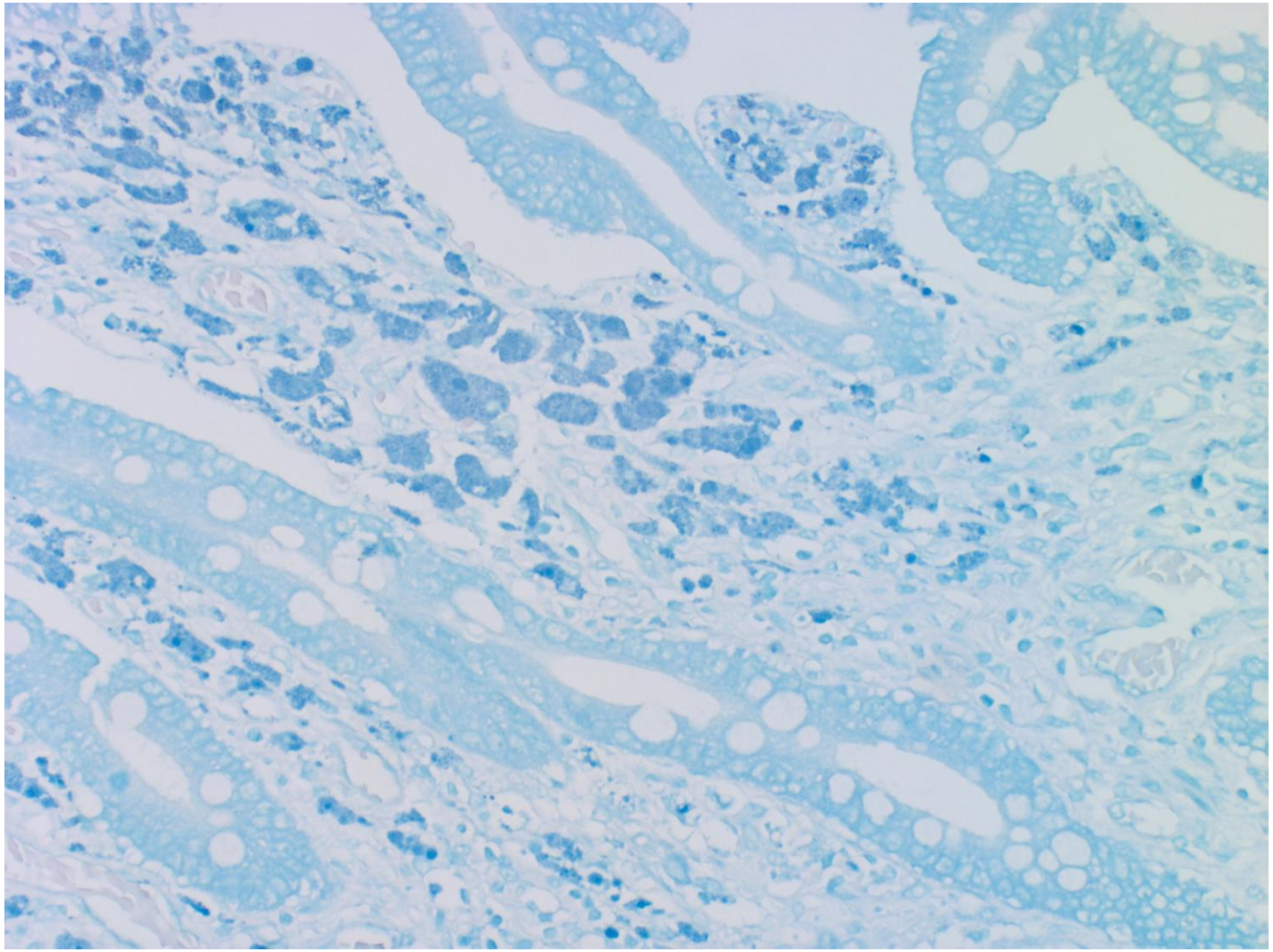
In the duodenal mucosa at autopsy of a 40-year-old man with XLA, ceroid-containing macrophages are accumulated in the lamia propria mucosae. No plasma cells are seen. H&E



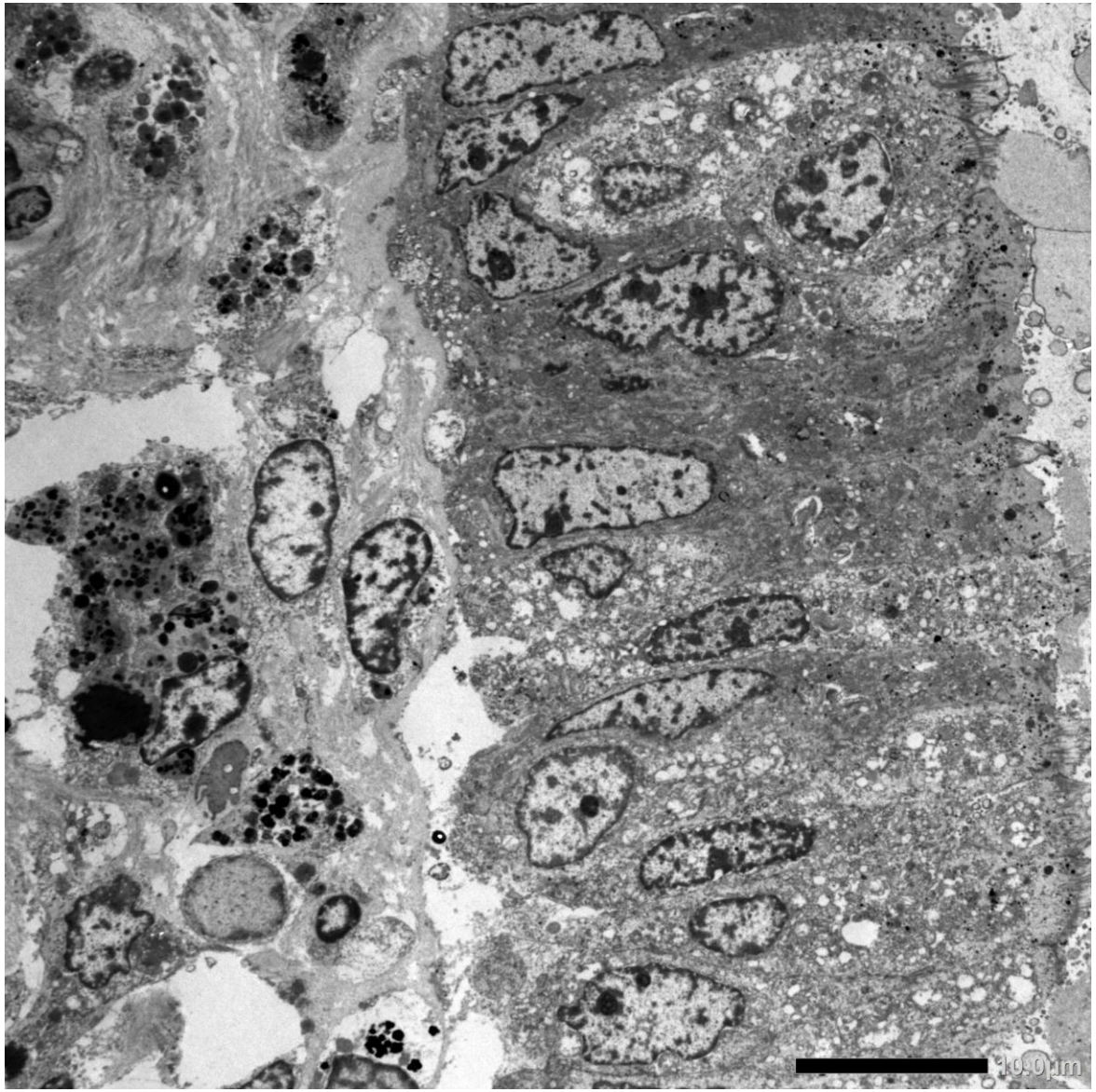
In the duodenal mucosa at autopsy of a 40-year-old man with XLA, PAS-reactive ceroid-containing macrophages are accumulated in the lamia propria mucosae. PAS



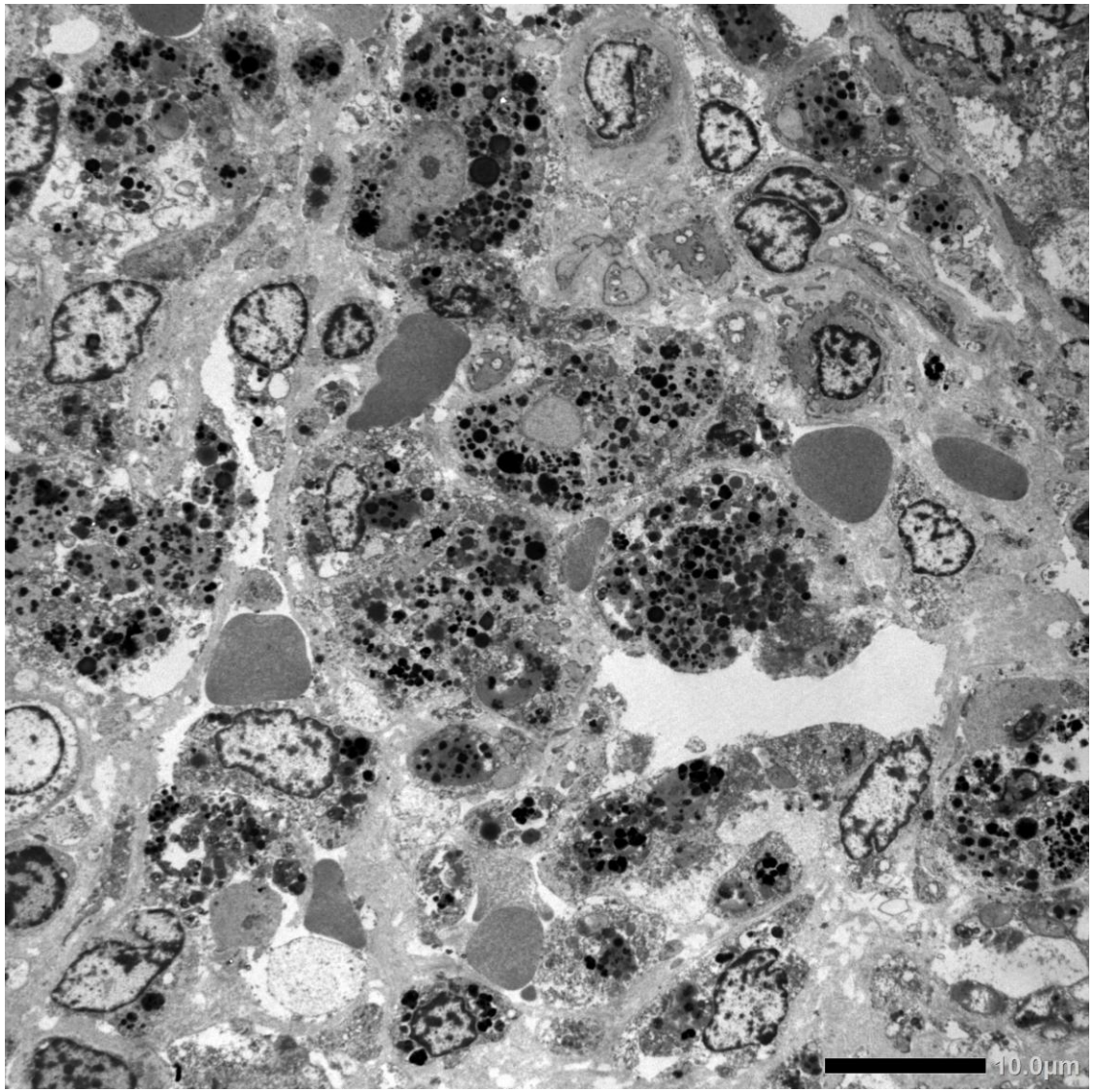
In the duodenal mucosa at autopsy of a 40-year-old man with XLA, Grocott staining is faintly reactive for ceroid pigments in the macrophages. Grocott



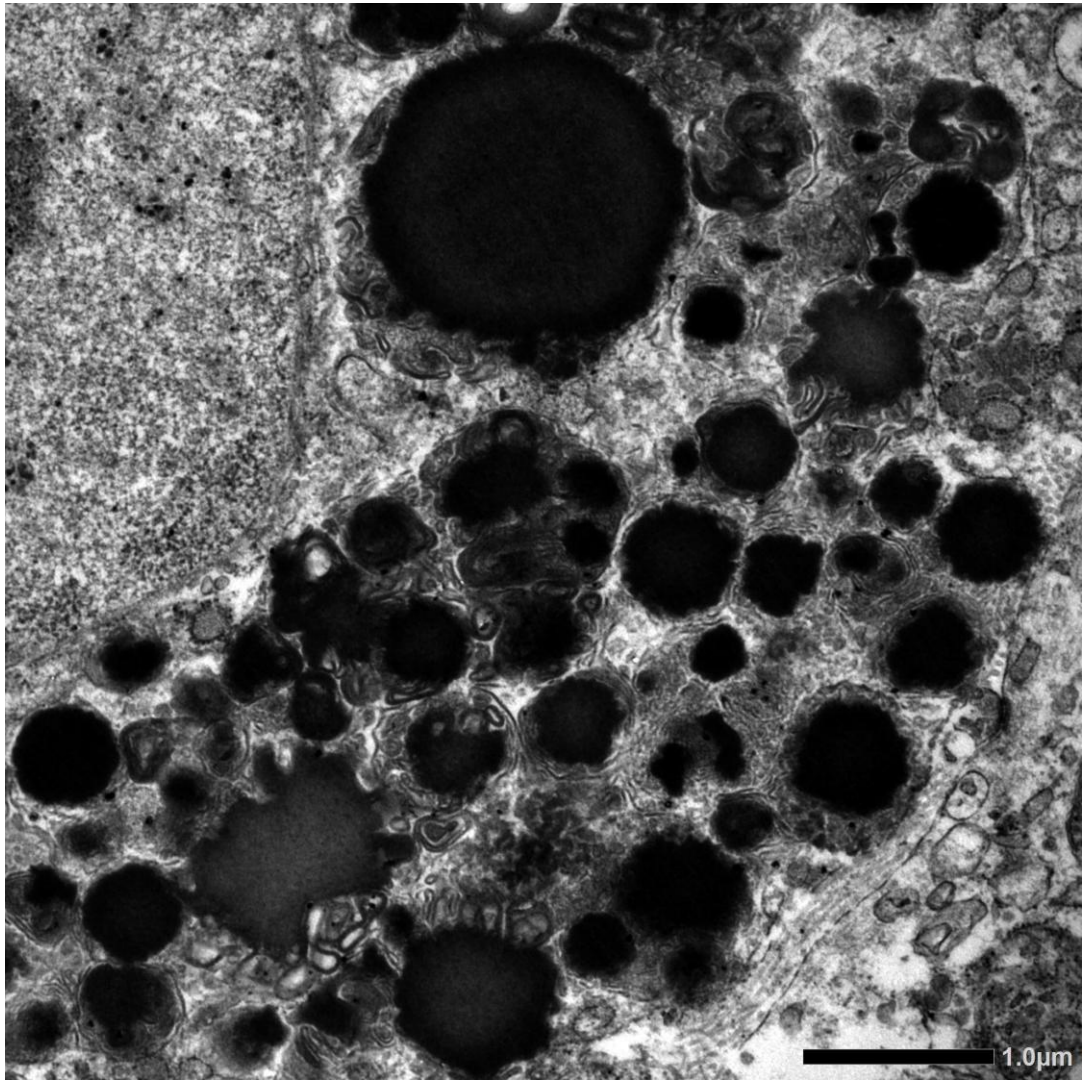
In the duodenal mucosa at autopsy of a 40-year-old man with XLA, Acid-fast staining is negative in the macrophages. Ziehl-Neelsen



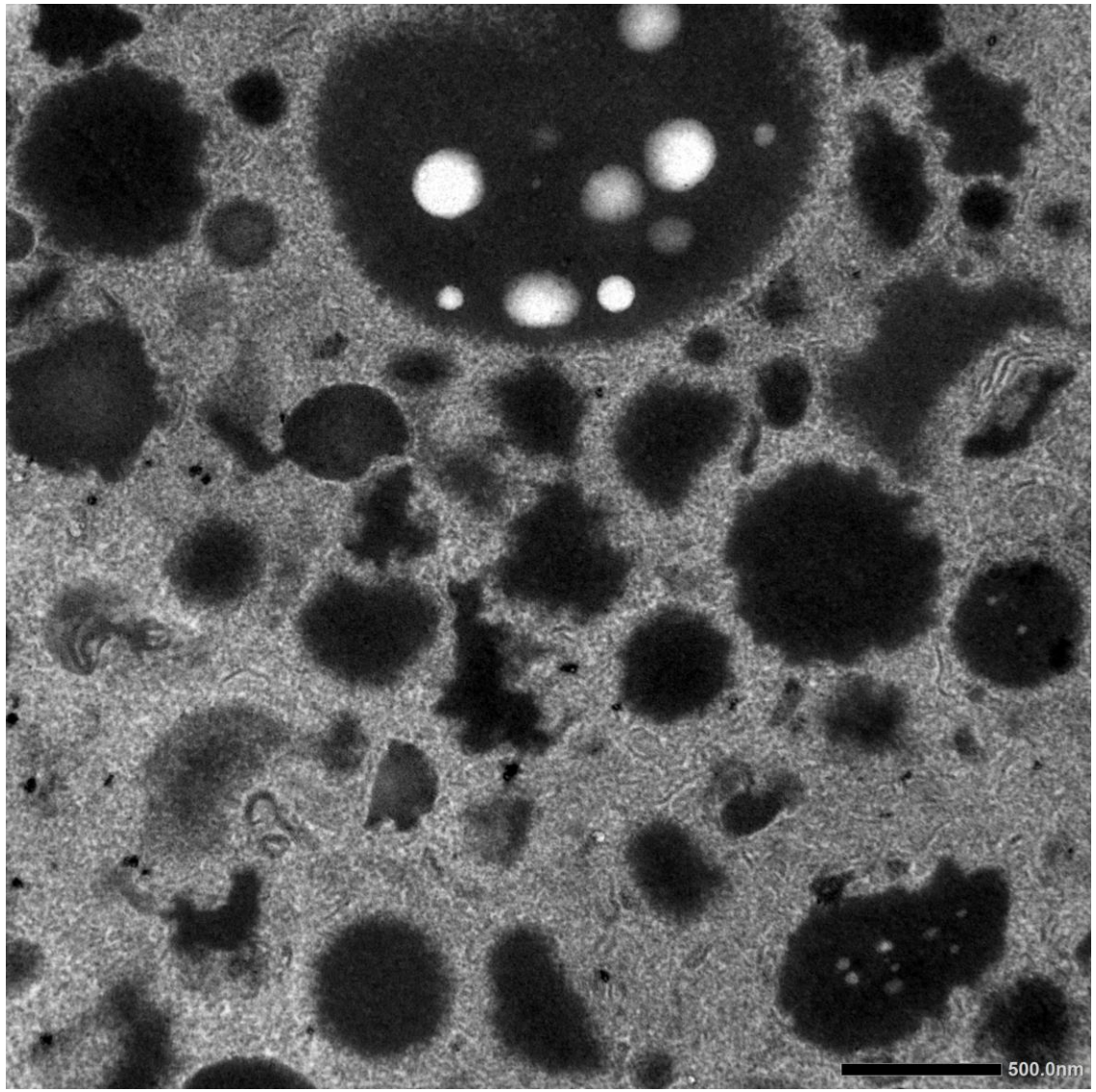
Ultrastructure of the duodenal mucosa at autopsy of a 40-year-old man with XLA. Macrophages containing electron-dense coarse granules are seen in the lamina propria mucosae. No plasma cells are seen. EM-1



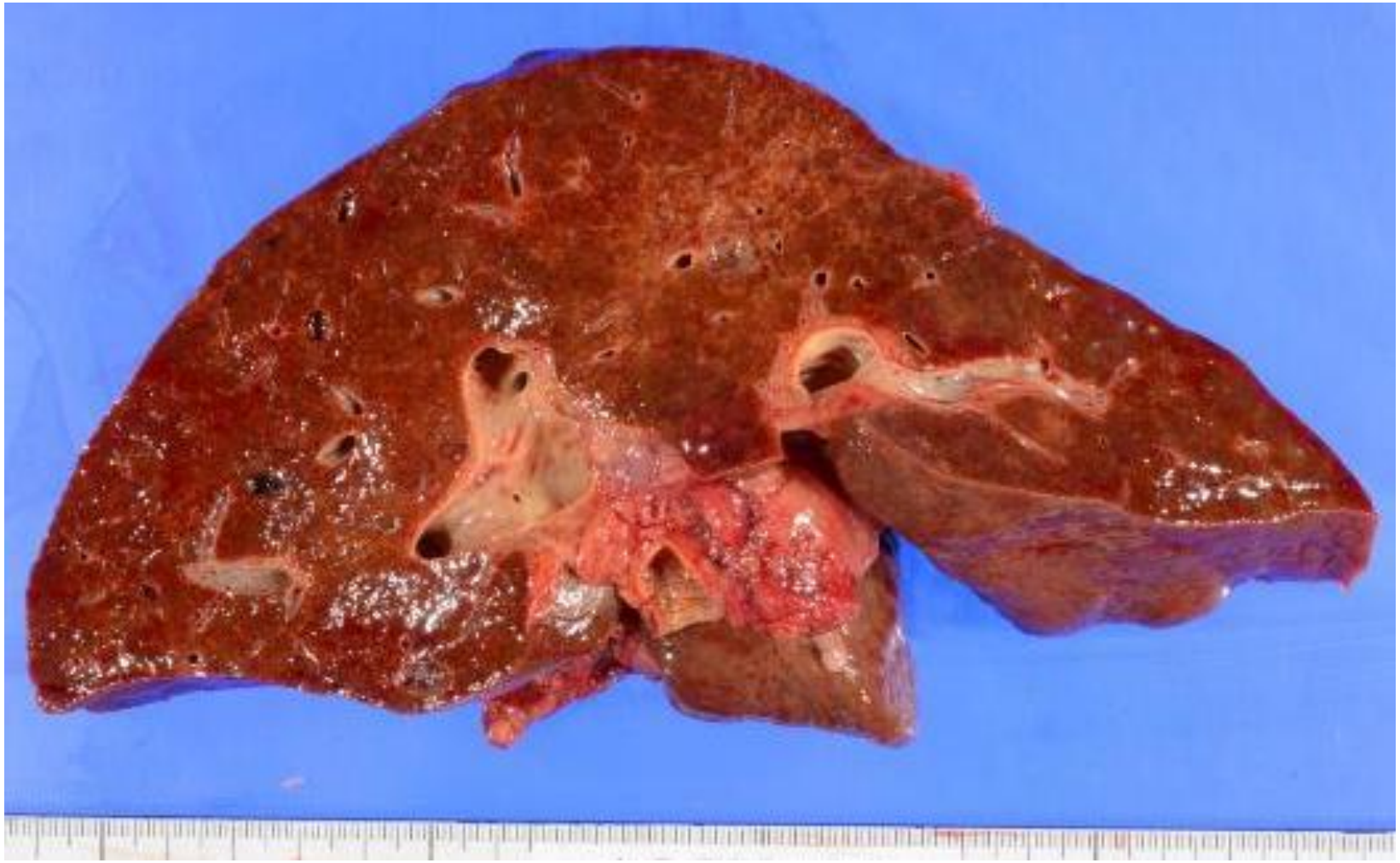
Ultrastructure of the duodenal mucosa at autopsy of a 40-year-old man with XLA. Macrophages containing electron-dense coarse granules are seen in the lamina propria mucosae. No plasma cells are seen. EM-2



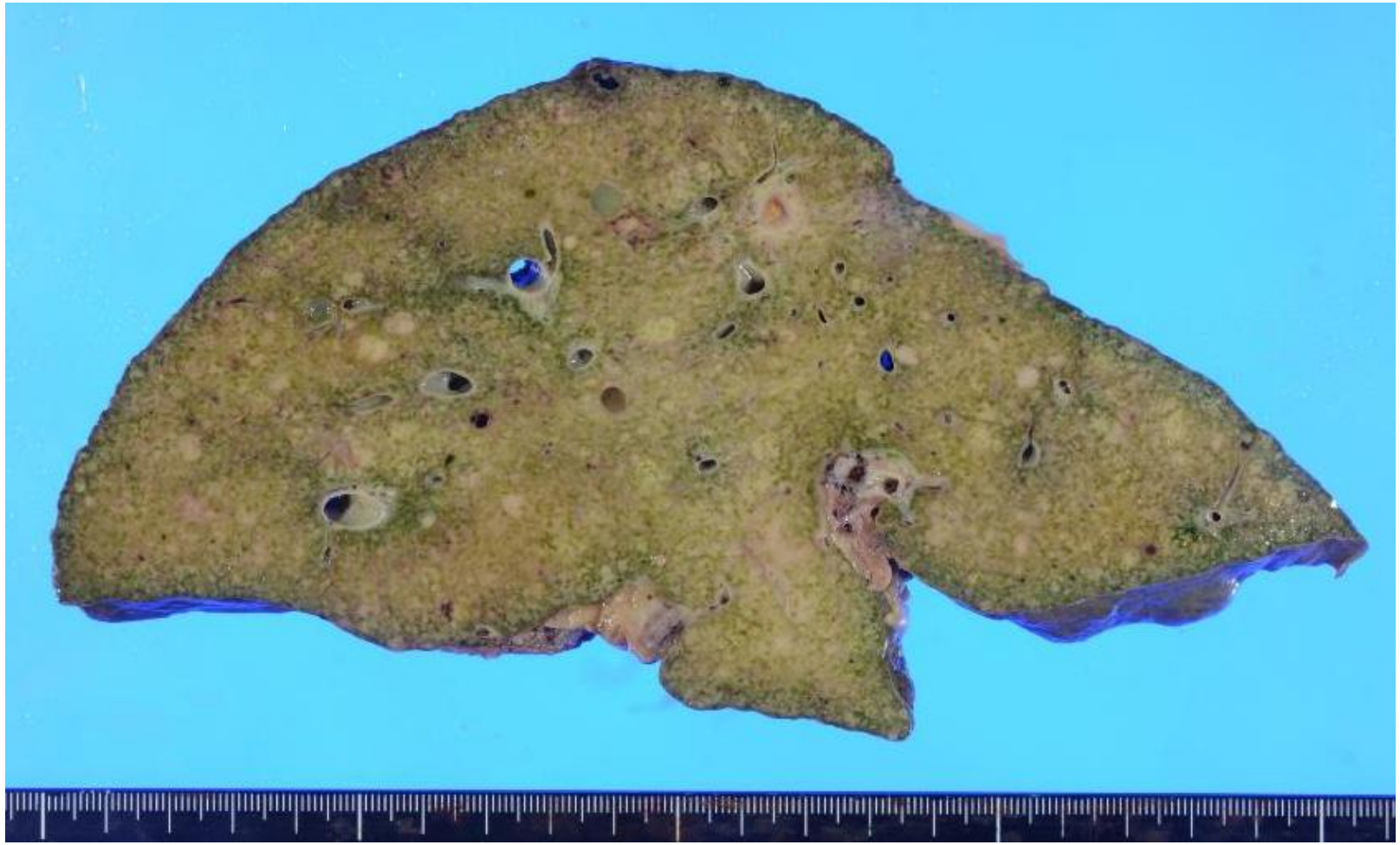
Ultrastructure of the duodenal mucosa at autopsy of a 40-year-old man with XLA. Macrophages containing electron-dense coarse granules are seen in the lamina propria mucosae. Ceroid pigments are phagocytized in lysosomes. EM-3



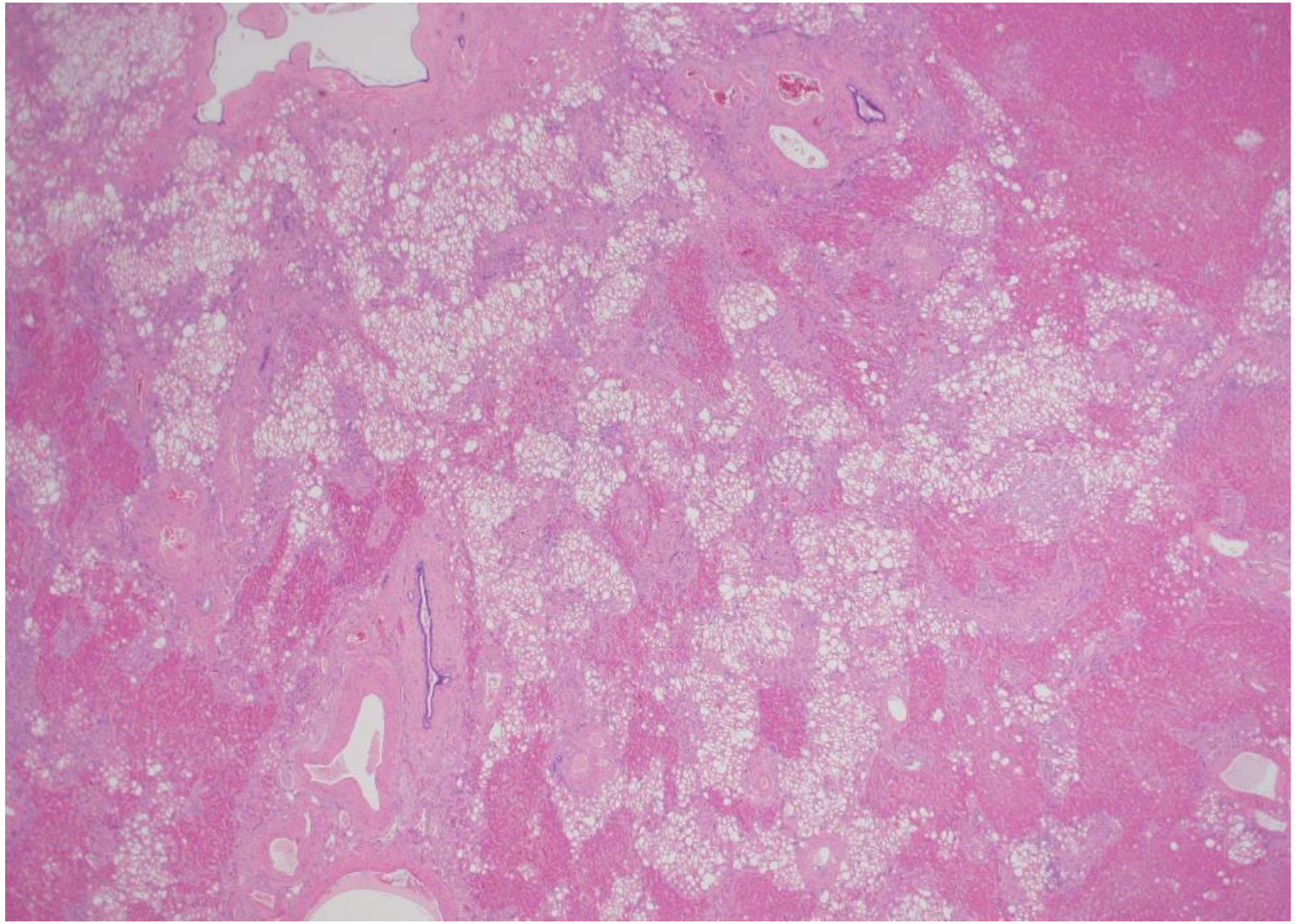
Ultrastructure of the duodenal mucosa at autopsy of a 40-year-old man with XLA. Macrophages containing electron-dense coarse granules are seen in the lamina propria mucosae. EM-4



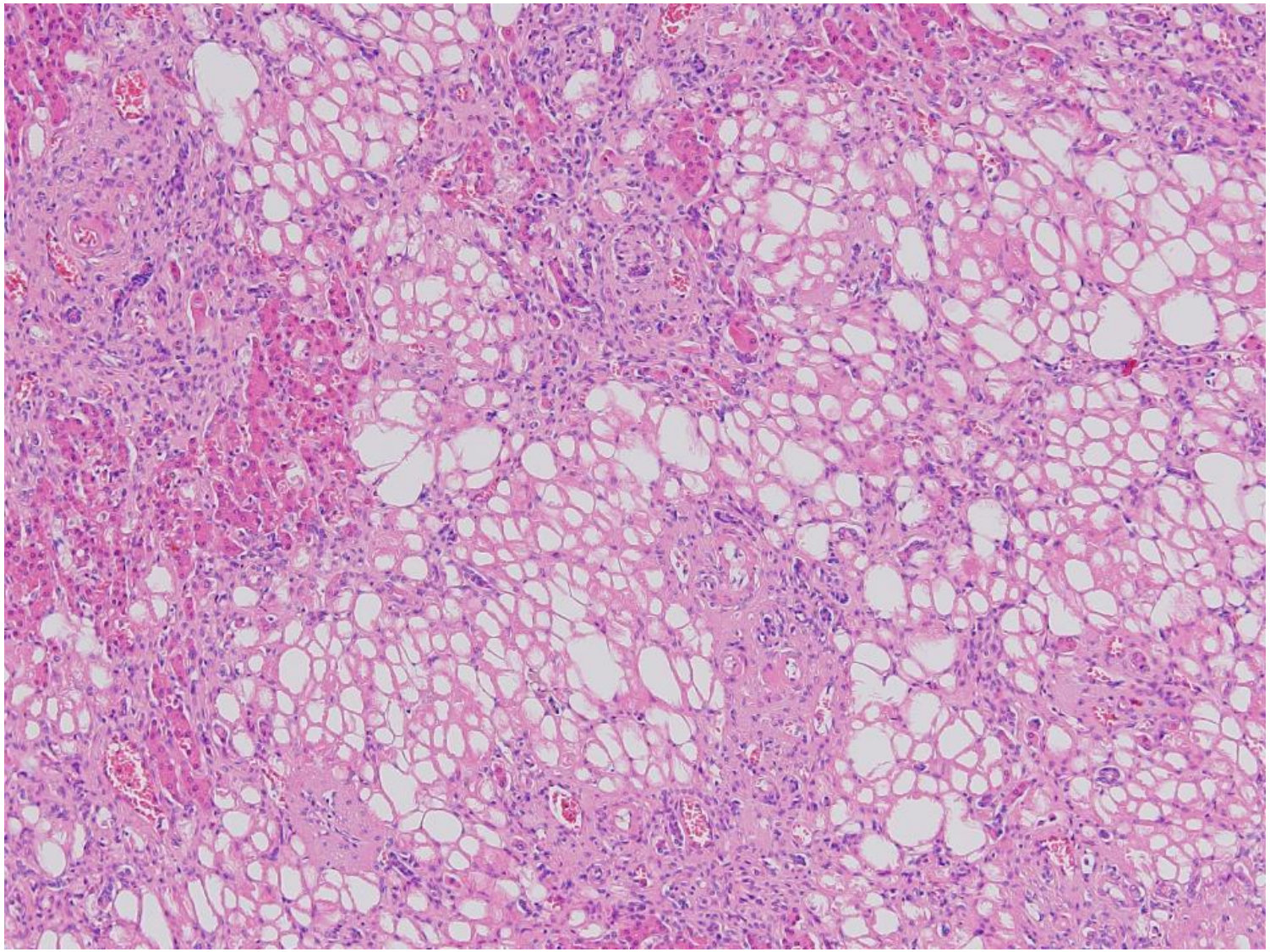
A cut surface of the liver at autopsy of a 40-year-old man with XLA,
The liver is atrophic (weight: 424 g) with focal and irregular fibrosis.



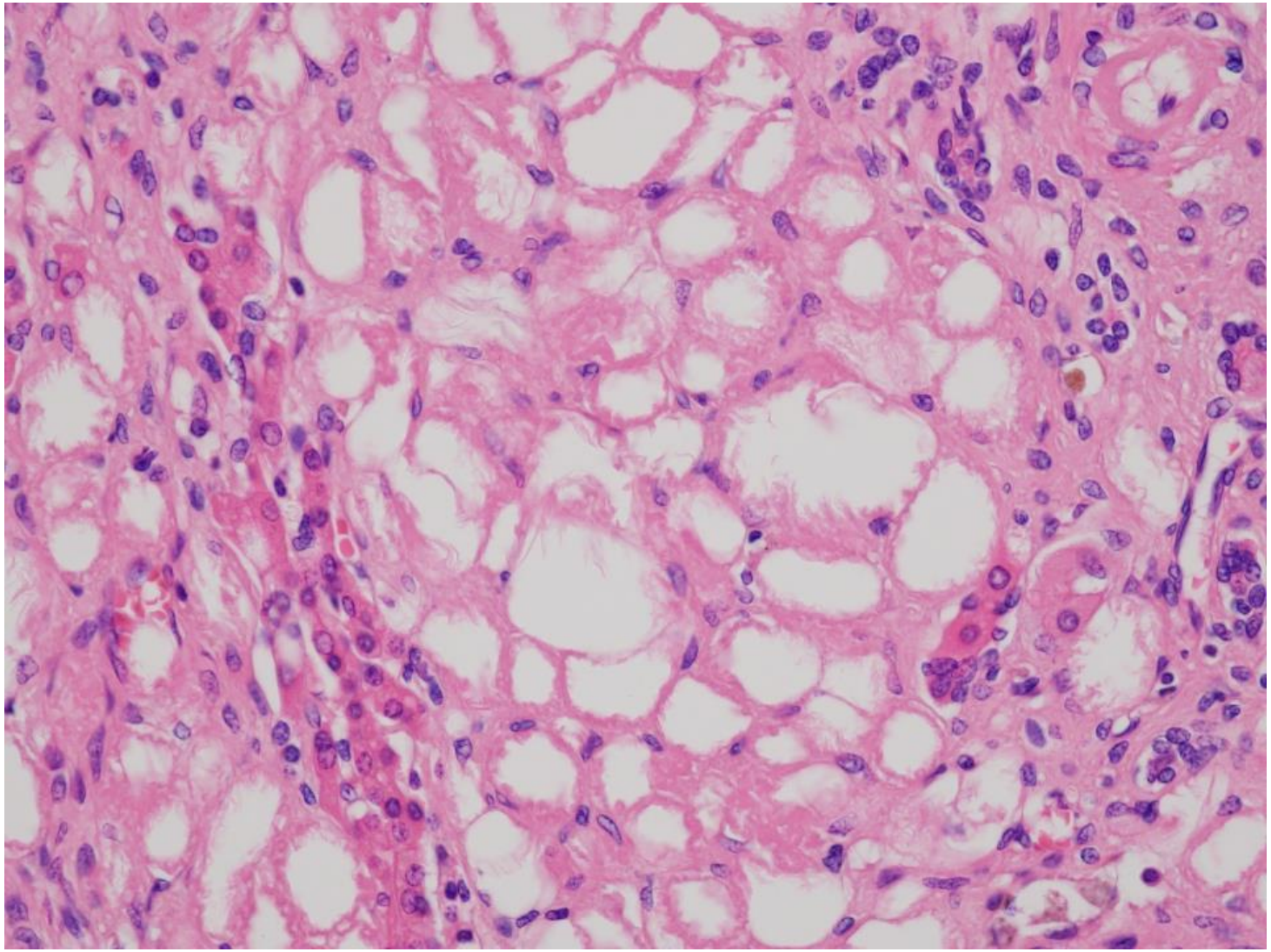
A cut surface of the liver after formalin fixation at autopsy of a 40-year-old man with XLA, The atrophic liver (weight: 424 g) contains multiple small gray nodules. The features are consistent with non-cirrhotic portal hypertension. Greenish color indicates intrahepatic cholestasis.



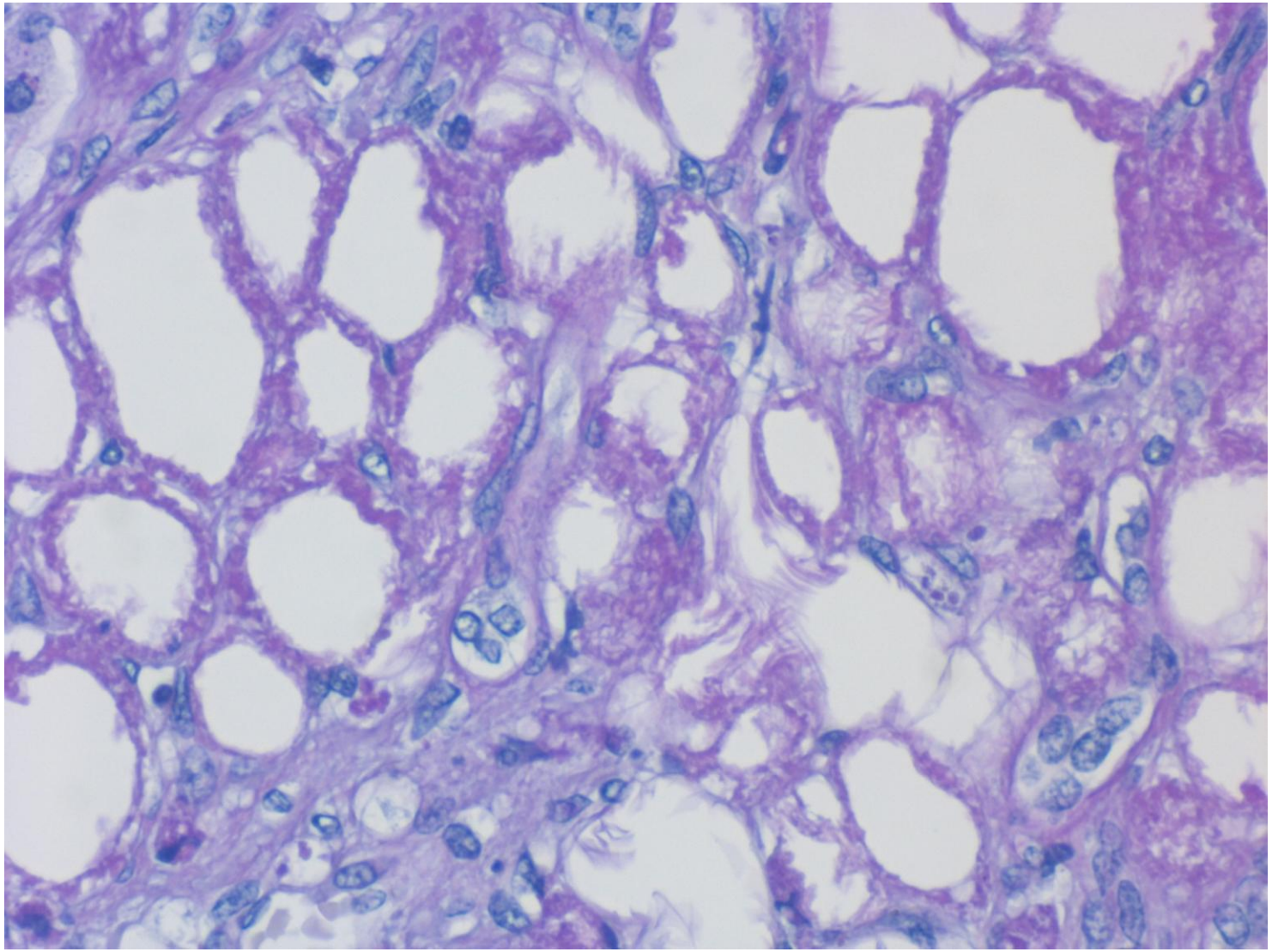
The liver at autopsy of a 40-year-old man with XLA reveals focal clustering of lipoid material is characteristic. H&E-a



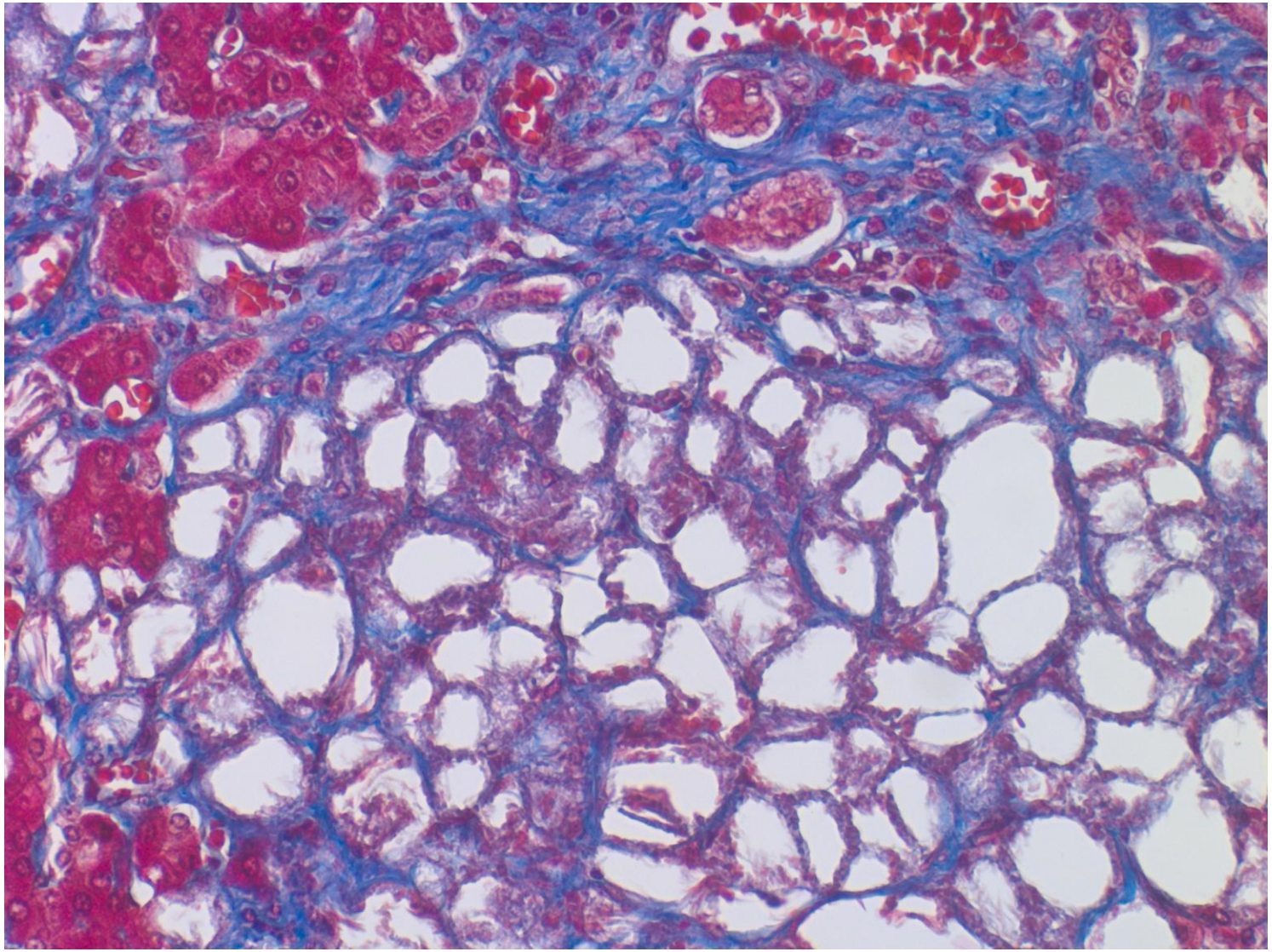
The liver at autopsy of a 40-year-old man with XLA reveals focal clustering of lipoid material. Accumulation of macrophages is associated. H&E-b



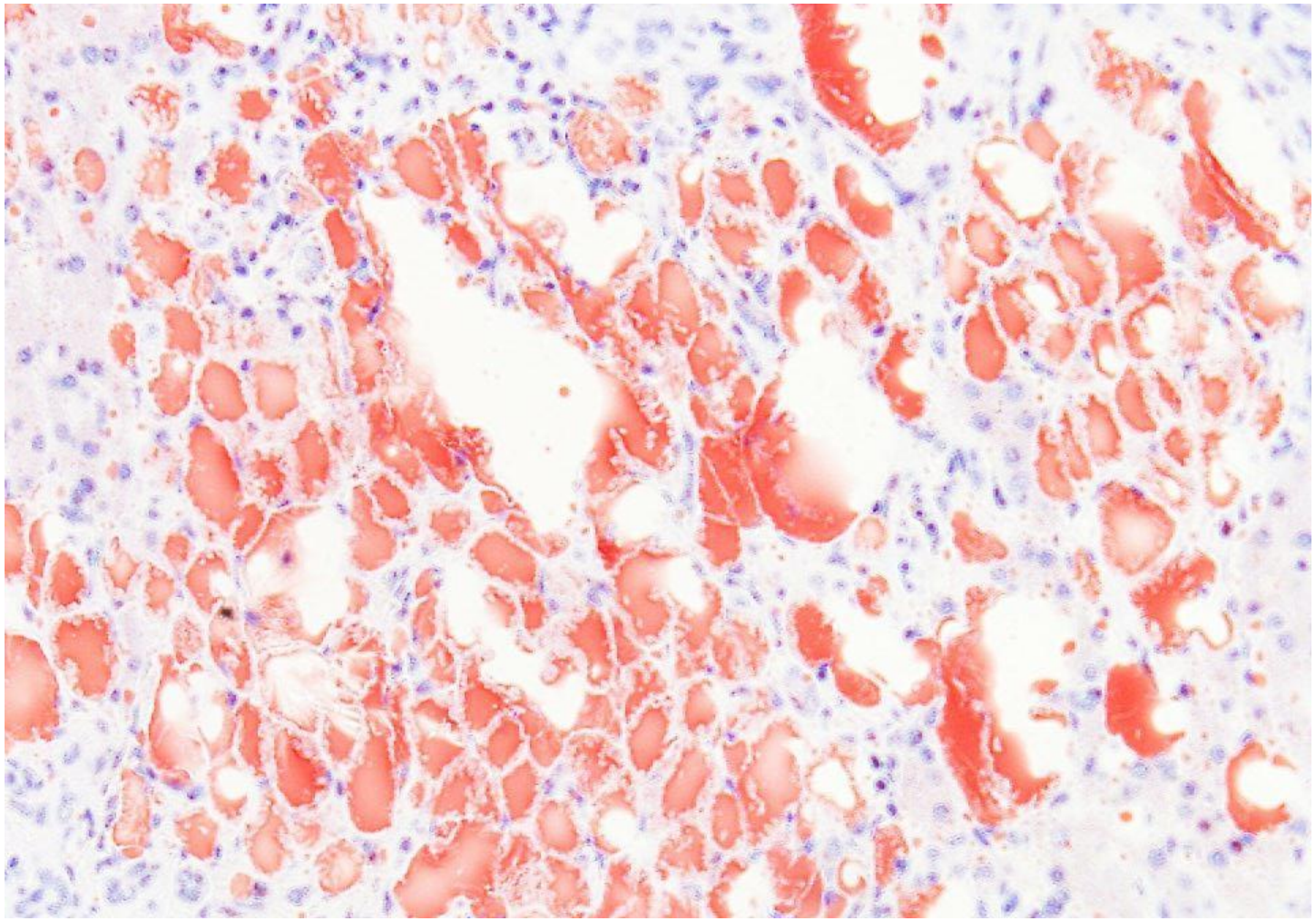
The liver at autopsy of a 40-year-old man with XLA reveals focal clustering of lipoid material with membranous lipodystrophy-type change. H&E-c



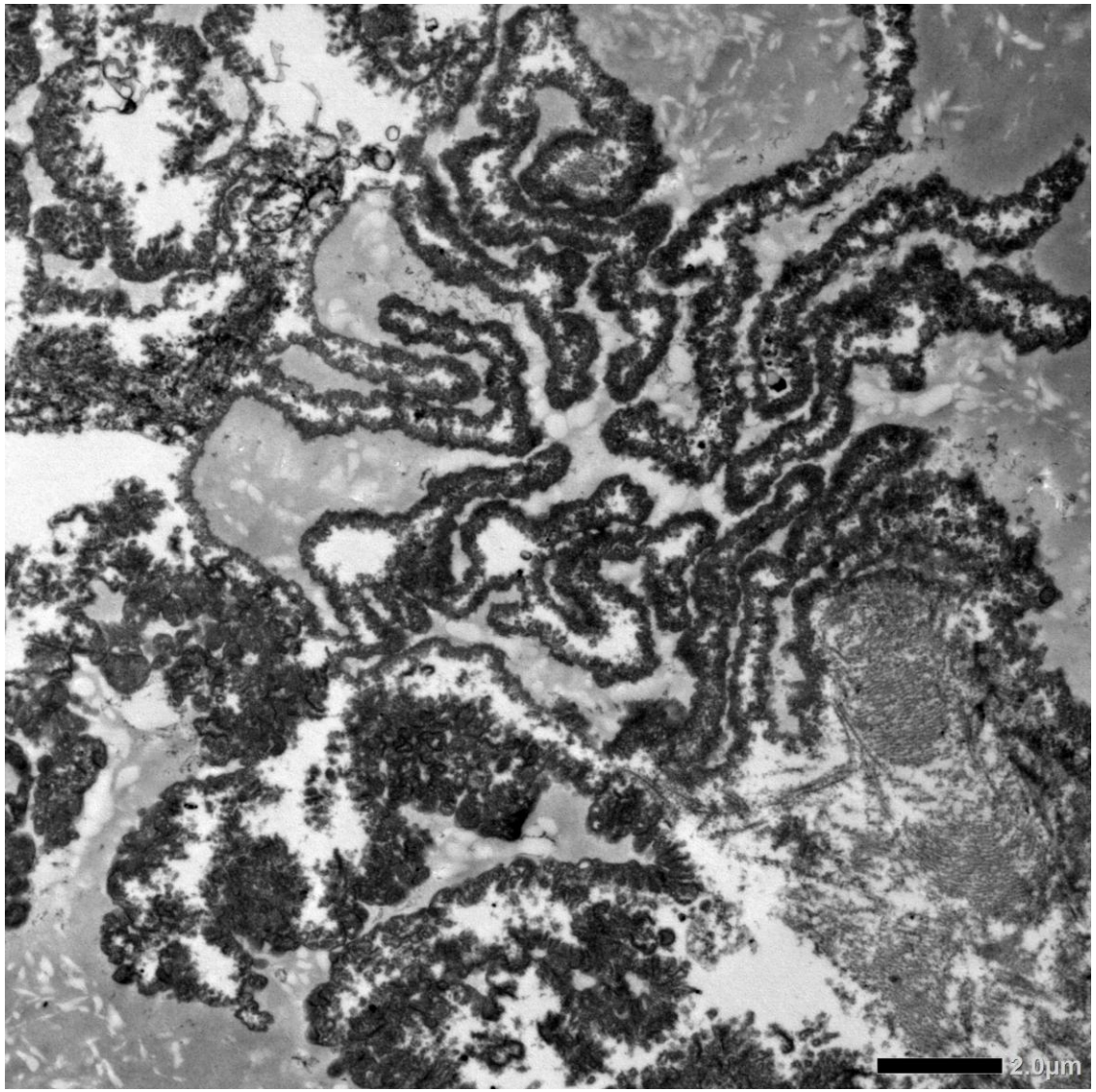
The liver at autopsy of a 40-year-old man with XLA reveals focal clustering of lipoid material with membranous lipodystrophy-type change. PAS



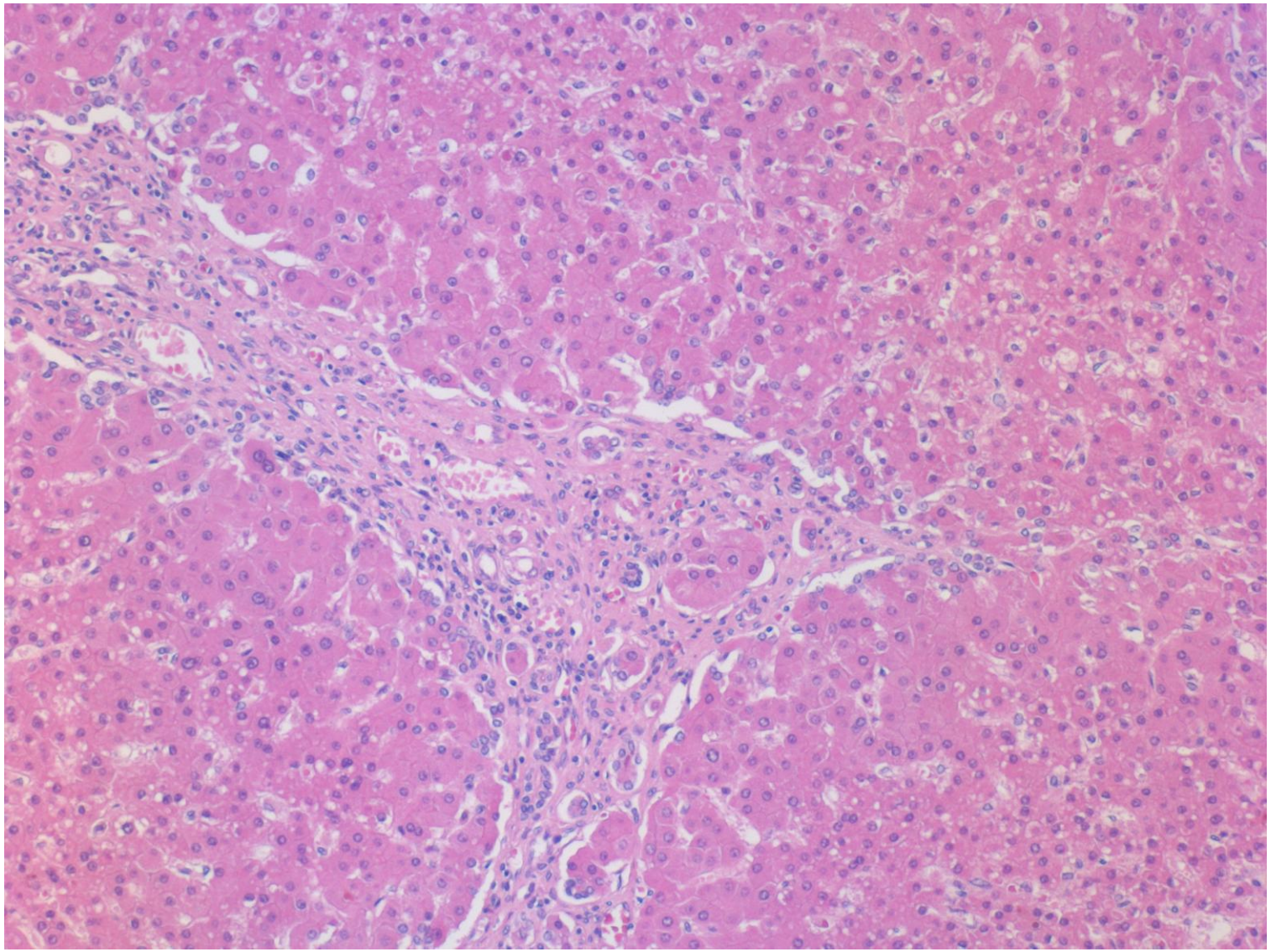
The liver at autopsy of a 40-year-old man with XLA reveals focal clustering of lipoid material with membranous lipodystrophy-type change. Masson trichrome



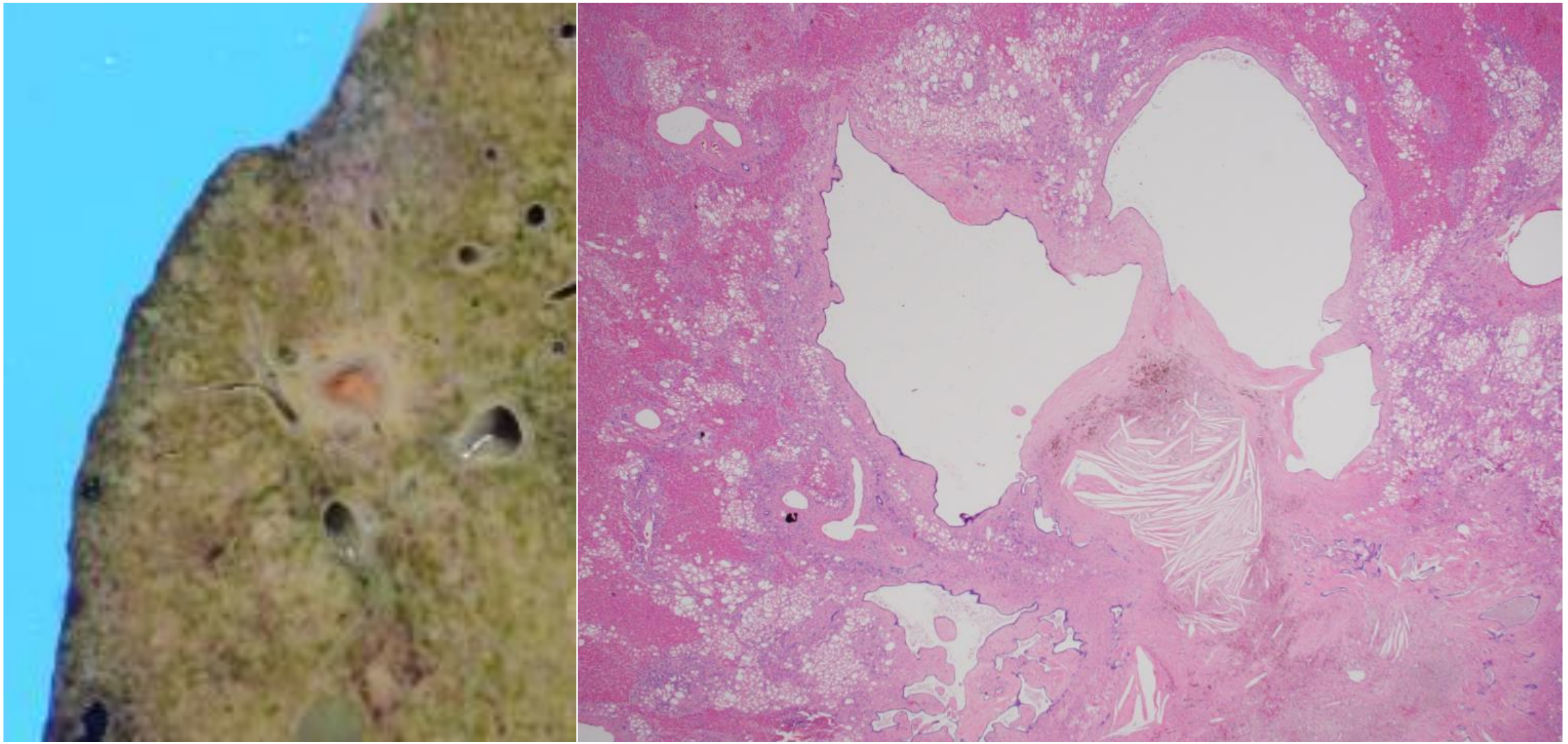
The liver at autopsy of a 40-year-old man with XLA. Oil red O staining reveals accumulation of neutral lipid in foci of the membranous lipodystrophy-like change. Oil red O



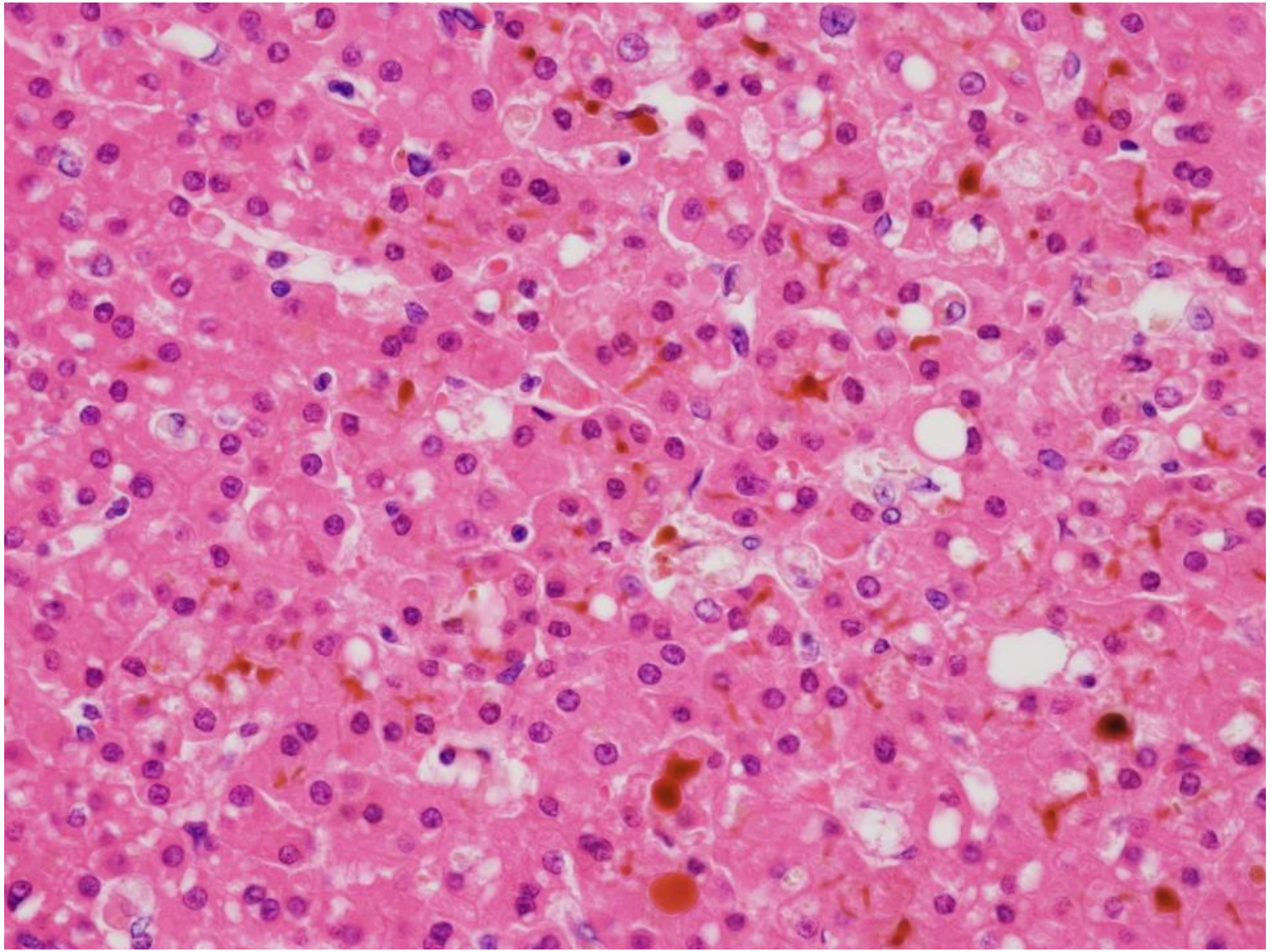
Ultrastructure of the liver at autopsy of a 40-year-old man with XLA. The membranous lipodystrophy-type lesion reveals accumulation of electron-dense wrinkling lipid materials. EM



The liver at autopsy of a 40-year-old man with XLA reveals focal septating fibrosis. H&E-d



The liver at autopsy of a 40-year-old man with XLA reveals irregular-shaped fibrotic nodules microscopically associated with focal dilatation of bile ducts. Left: cut surface after formalin fixation, right: H&E-e



The liver at autopsy of a 40-year-old man with XLA reveals marked intrahepatic cholestasis. Fatty change of the hepatocytes is mildly associated. H&E-f