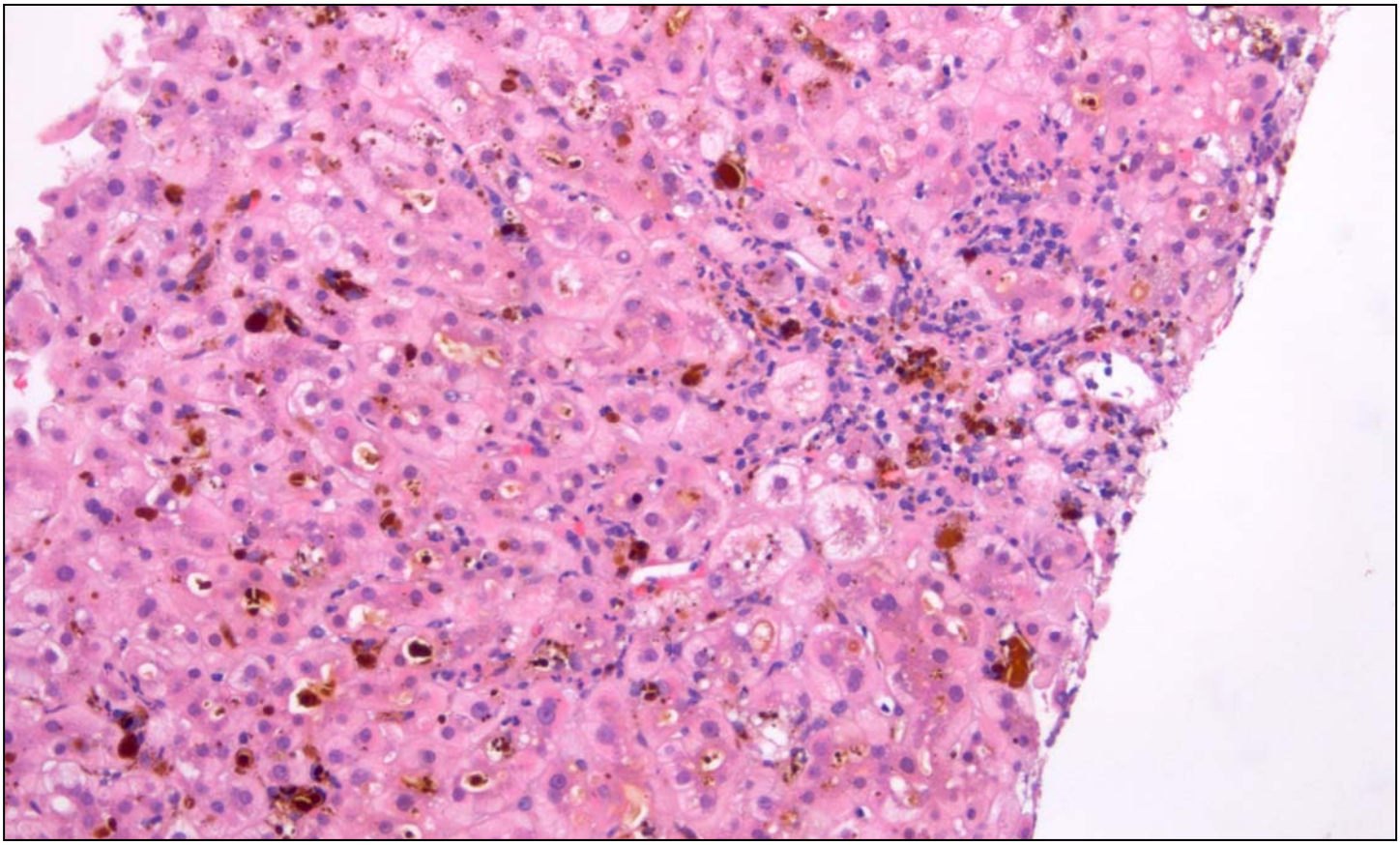
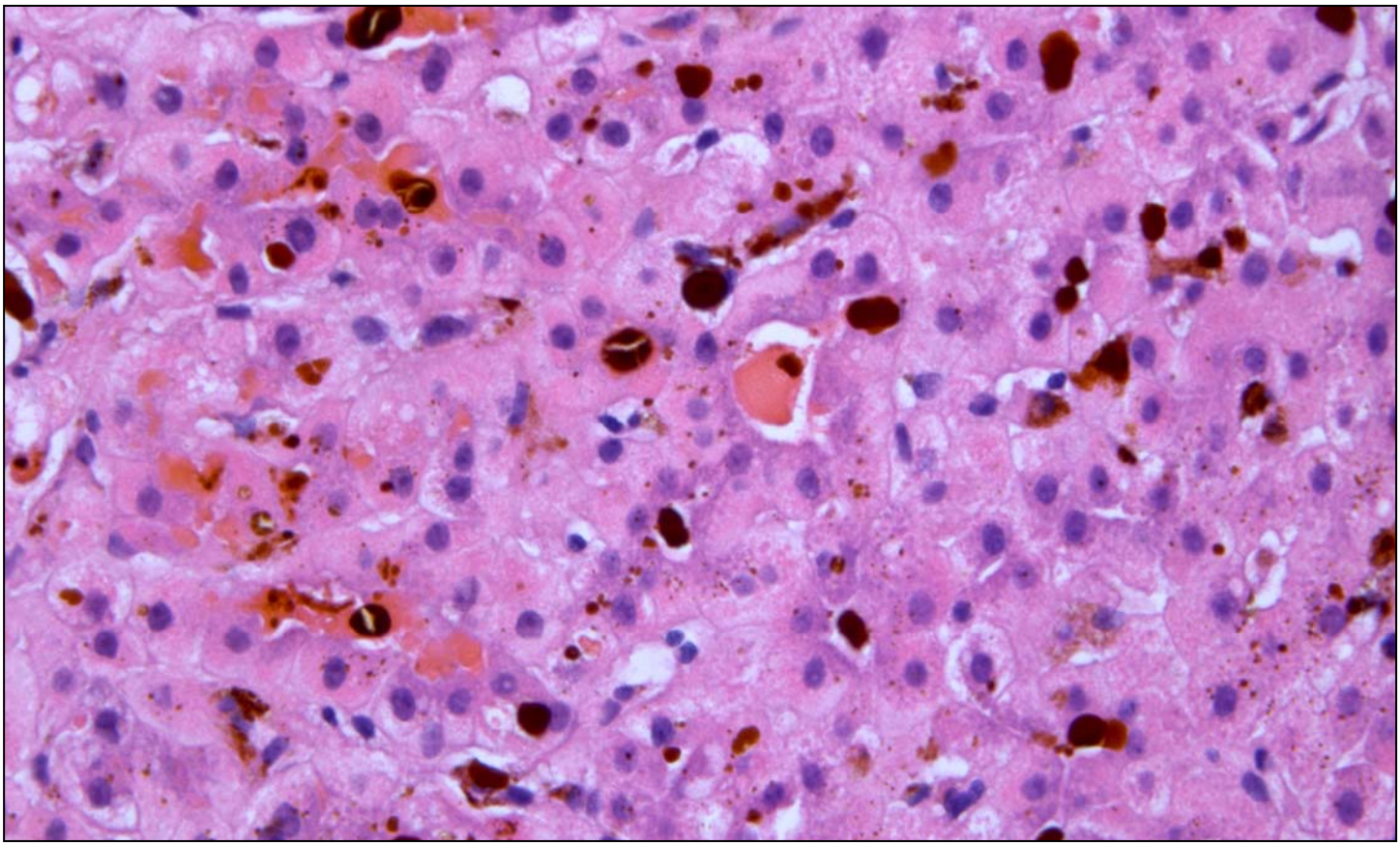
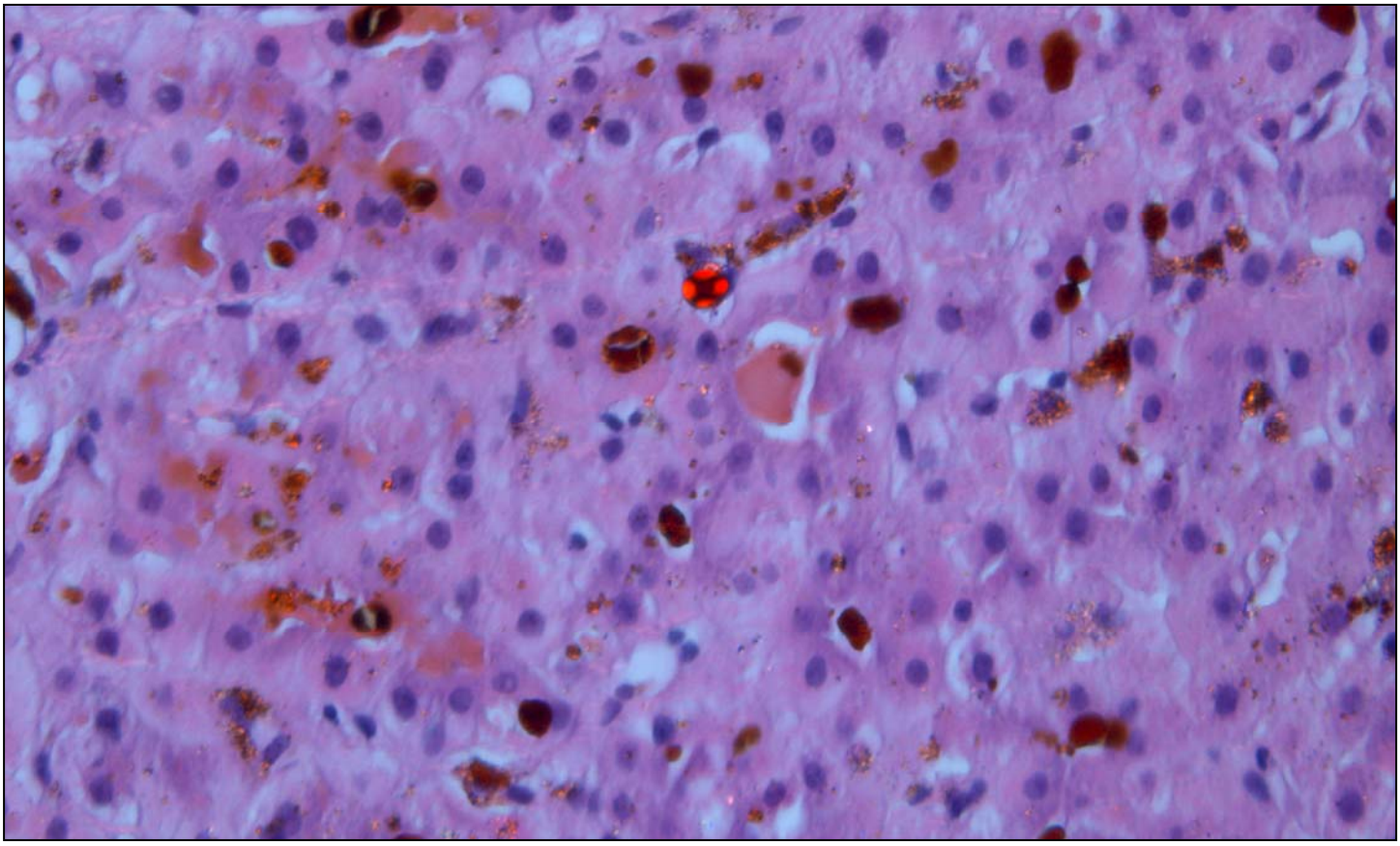
Case: 55 year old woman with liver failure of unknown etiology. Patient has a history of breast carcinoma in 2001, status post chemotherapy and radiation. Markedly elevated total and direct bilirubin, Alk Phos, AST and ALT. Ceruloplasmin and iron studies are normal. Hepatitis A, B, and C serologic tests are negative. Representative images of the liver biopsy are shown below.







Polarized

What is your diagnosis?

A. Dubin Johnson syndrome
B. Primary sclerosing cholangitis
C. Hemochromatosis
D. Erythropoietic protoporphyria
E. Wilson's disease

Answer and Discussion:
D. Erythropoietic protoporphyria

COMMENT:
Representative photos show severe cholate stasis and bile duct reaction in a background of mild portal and lobular inflammation and occasional acidophil bodies. The sinusoids and bile ductules contain yellow brown bile. The hepatocytes, Kupffer cells and sinusoids also contain abundant red-brown pigmented material with bright red birefringence under polarized light. Less common, larger globular red material demonstrates a Maltese-cross pattern under polarized light.

Choice A is incorrect. Dubin-Johnson is characterized by diffuse, coarsely granular, brown pigment in hepatocytes, more concentrated in the perivenular zone. Patients usually have a conjugated hyperbilirubinemia with otherwise normal liver enzymes and no other evidence of hepatic dysfunction.

Choice B is incorrect. Although a biliary process such as PSC may have some bile duct plugging, the bile would not have bright red birefringence.

Choice C is incorrect. Hemochromatosis is characterized by hepatocellular iron deposition beginning in the periportal hepatocytes and progressively extending to involve all zones.

Choice E is incorrect. Wilson's disease is due to copper overload, with low levels of serum ceruloplasmin. Typical findings in liver biopsy include glycogenated nuclei in periportal hepatocytes, steatosis, abnormal copper storage and presence of Mallory Denk Bodies in periportal hepatocytes.

The correct answer is D. The above changes have been described previously in liver biopsies of patients with erythropoietic protoporphyria. The defective step in heme synthesis is due to a mutated enzyme, ferrochelatase. Excess protoporphyrin is secreted by hepatocytes into bile, but hepatobiliary transport can become overwhelmed leading to insoluble crystal porphyrin aggregates in hepatocytes, canaliculi and proximal bile ducts. The liver appears black grossly. Hematin has been the most successful therapy, but liver transplantation is appropriate in patients with liver failure or cirrhosis.

Reference:
Akazawa N, Yanase M, Masaki N. Erythropoietic Protoporphyria. Clinical Gastroenterology and Hepatology 2010;8e82.

Anstey AV, Hift RJ. Liver disease in erythropoietic protoporphyria: insights and implications for management. Postgrad Med J. 2007 Dec;83(986):739-48.

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