Erythropoietic protoporphyria in the house mouse. A recessive inherited ferrochelatase deficiency with anemia, photosensitivity, and liver disease.

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Abstract

A viable autosomal recessive mutation (named fch, or ferrochelatase deficiency) causing jaundice and anemia in mice arose in a mutagenesis experiment using ethylnitrosourea. Homozygotes (fch/fch) display a hemolytic anemia, photosensitivity, cholestasis, and severe hepatic dysfunction. Protoporphyrin is found at high concentration in erythrocytes, serum, and liver. Ferrochelatase activity in various tissues is 2.7-6.3% of normal. Heterozygotes (+/fch) are not anemic and have normal liver function; they are not sensitive to light exposure; ferrochelatase activity is 45-65% of normal. Southern blot analysis using a ferrochelatase cDNA probe reveals no gross deletion of the ferrochelatase gene. This is the first spontaneous form of erythropoietic protoporphyria in the house mouse. Despite the presence in the mouse of clinical and biochemical features infrequent in the human, this mutation may represent a model for the human disease, especially in its severe form.

Images.
Liver transplantation for erythropoietic protoporphyria liver disease. Liver Transplant 2005;11:1590–1596. Harms, J, Lautenschlager, S, Minder, CE, Minder, EI. An alpha-melanocyte-stimulating hormone analogue in erythropoietic protoporphyria. N Engl J Med 2009;360:306–307. Fontanellas, A, Mazurier, F, Landry, M, et al. Erythropoietic protoporphyria in the house mouse: a recessive inherited ferrochelatase deficiency with anemia, photosensitivity, and liver disease. J Clin Invest 1991;88:1730–1736. Lindberg, RL, Martini, R, Baumgartner, M, et al. Motor neuropathy in porphobilinogen deaminase-deficient mice imitates the peripheral neuropathy of human acute porphyria. J Clin Invest 1999;103:1127–1134. Phillips, JD, Jackson, LK, Bunting, M, et al. Erythropoietic protoporphyria (EPP) is a rare inherited metabolic disorder caused by a deficiency of the enzyme ferrochelatase (FECH), which results from changes (mutations) in the FECH gene. Due to abnormally low levels of this enzyme, excessive amounts of protoporphyrin accumulate in the bone marrow, blood plasma, and red blood cells. Some patients with symptoms of EPP have a genetic change in a different gene called ALAS2. The liver in protoporphyria. Hepatology. 1988;8:402–7. INTERNET Balwani M, Bloomer J, Desnick R; Porphyrias Consortium of the NIH-Sponsored Rare Diseases Clinical Research Network (see Chapter Notes, Acknowledgments). Erythropoietic Protoporphyria, Autosomal Recessive. 2012 Sep 27 [Updated 2014 Oct 16]. Erythropoietic protoporphyria (EPP) is the most common inherited porphyria in children and is diagnosed in most individuals after the onset of cutaneous manifestations. Hepatobiliary disease affects the minority of individuals with EPP and usually manifests in patients with an established diagnosis of EPP. We report on a classic but rare case of EPP that masqueraded as cholestasis. Hyperlipidemia and atherosclerosis associated with liver disease in ferrochelatase-deficient mice. J Lipid Res. 2001;42(1):41–50pmid:11160364. Erythropoietic protoporphyria (EPP) is a rare inherited disorder that causes the skin to become painful when exposed to sunlight. In this article, we explore what EPP is, what symptoms it causes, and how to treat it. We also look at related conditions and describe when to see a doctor. Pictures. What is it? In a person with EEP, mutations in the FECH gene cause the body to have a deficiency of the enzyme ferrochelatase. When there is not enough ferrochelatase, the body is unable to convert the compound protoporphyrin into heme, a molecule that enables blood to carry oxygen. As a result, protoporphyrin builds up in blood vessels under the skin. Sunlight exposure activates the accumulated protoporphyrin, generating a reaction that leads to inflammation and severe pain. Erythropoietic Protoporphyria (Protoporphyria, Heme synthetase deficiency, Ferrochelatase deficiency, X-linked dominant protoporphyria [XLDPP], Erythrohepatic protoporphyria [no longer used]). Bryan Anderson. Amar Patel. Photosensitivity in the absence of bulla is a characteristic feature seen when diagnosing EPP. EPP should be considered in the differential diagnosis of any child with photosensitivity. A history of sun exposure inducing redness, vesiculation, burning, and stinging is notable. The photosensitivity associated with EPP is acute and painful in sun-exposed areas and include signs of erythema (Figure 1), edema, petechiae, stinging, and burning; however, as noted previously, bullae should not be seen. Areas afflicted include any exposed to sun.