with the EPP phenotype in Europe and North America. Rare patients with EPP symptoms and elevated erythrocyte protoporphyrin IX levels do not have mutations in *FECH* or *ALAS2* on genetic testing. In an affected family with EPP symptoms and accumulation of protoporphyrin IX, an autosomal dominant mutation was found in human CLPX, a modulator of heme biosynthesis.

Clinical Features In EPP and male XLP patients, skin photosensitivity, which differs from that in other cutaneous porphyrias, usually begins in early childhood. The initial symptoms on sun exposure consist of tingling, stinging, itching, or heat/burning sensations on the exposed skin occurring within <10 to 30 min of exposure in >60% of patients; most will have these prodromal symptoms within an hour of sun exposure. The prodromal symptoms are the “warning signal” to get out of the sun, thereby avoiding a severe incapacitating painful attack that can last from 2–5 days. Photosensitivity is associated with substantial elevations in erythrocyte protoporphyrin IX and occurs only in patients with genotypes that result in FECH activities below ~35% of normal. Vesicular lesions are uncommon. Redness and swelling develop after prolonged sun exposure and resemble angioedema **(Fig. 416-4)**. Pain symptoms may seem out of proportion to the visible skin involvement. Chronic skin changes may include lichenification, leathery pseudovesicles, labial grooving, and nail changes. Severe scarring is rare, as are pigment changes, friability, and hirsutism. Unless hepatic or other complications develop, protoporphyrin IX levels and symptoms of photosensitivity tend to remain remarkably stable over many years in most patients. Factors that exacerbate the hepatic porphyrias play no role in EPP or XLP.