Porphyria cutanea tarda in a child with acute lymphoblastic leukemia

R. Thawani¹, A. Moghe², T. Idhate¹, M. Kalra¹, A. Mahajan¹ and K.E. Anderson²

From the ¹Department of Pediatric Hematology/Oncology, Indraprastha Apollo Hospitals, Sarita Vihar, New Delhi, India and ²Department of Preventive Medicine and Community Health, University of Texas Medical Branch, Galveston, TX, USA

Address correspondence to Dr R. Thawani, F-61/B, Gangotri Enclave, Alaknanda, New Delhi 110019, India. email: rajat13@gmail.com

Learning point for clinicians
Chemotherapeutic drugs, including commonly used drugs like methotrexate, maybe attributable to development of symptoms of porphyria in children who, otherwise, have no symptoms. Precautions may be needed in such patients to avoid exacerbations. More research needs to be done on the role of chemotherapeutic drugs in the pathogenesis of porphyrias.

Introduction
Porphyria cutanea tarda (PCT) arises from inhibition of hepatic uroporphyrinogen decarboxylase (UROD) activity to less than ~20% of normal.¹ A UROD inhibitor is formed in liver in the presence of iron and oxidative stress, and has been isolated from mice with PCT.² Accumulated porphyrinogens in the liver are oxidized to the correspondent porphyrins, which circulate in the plasma causing phototoxic skin manifestations. Multiple susceptibility factors contribute including alcohol, estrogens, smoking, hepatitis C virus, human immunodeficiency virus and HFE and UROD mutations. Heterozygous UROD mutations, accompanied by additional factors, occur in ~20% of adults with PCT but are more common in rare childhood cases.³ The disease may occur with methotrexate, multi-agent chemotherapy or bone marrow transplantation in children.³,⁴ We report a child with documented familial PCT after chemotherapy for acute lymphoblastic leukemia (ALL) without other identifiable susceptibility factors.

Case report
An 18-month-old girl responded well to chemotherapy with vincristine, daunorubicin, l-asparaginase, prednisolone, cyclophosphamide, 6-mercaptopurine, cytarabine and methotrexate for Standard Risk Precursor B ALL. Blistering photosensitivity developed during maintenance treatment with 6-mercaptopurine and methotrexate and persisted after chemotherapy ended. Serum transaminases were mildly elevated, urine porphyrins 5689 nmol/g creatinine (normal < 300)—consisting mostly of uroporphyrin (71%) and heptacarboxylporphyrin (18%) (normal—mostly coproporphyrin), plasma porphyrins 9.1 mcg/dl (normal < 0.9), plasma scanning showed a fluorescence peak at 620 nm and erythrocyte porphyrins were normal. Although there was no family history of porphyria and both parents had normal porphyrin levels, the patient and mother (but not the father) had a previously reported heterozygous UROD mutation (IVS1+1G>T), and decreased erythrocyte UROD activity (19.2 and 26.5 nmol/ml erythrocytes/hour, respectively, normal 30–60). Hepatitis C virus, human immunodeficiency virus, HFE mutations, estrogens, alcohol and smoking were excluded. After ophthalmological clearance, low-dose hydroxychloroquine lowered plasma porphyrins to 3.1 mcg/dl and urine porphyrins to 1065 nmol/g creatinine in 4 months; and symptoms improved.

Discussion
In this case of childhood familial PCT, multiple other susceptibility factors were excluded, supporting the role of...
Chemotherapy in activating the disease. Attribution to a single chemotherapeutic agent is not possible because she was exposed to multiple drugs. How chemotherapeutic agents might contribute in PCT is not established. Some may increase hepatic porphyrin and heme synthesis by inducing hepatic 5-aminolevulinic acid synthase-1 (ALAS1), the first and rate-limiting enzyme of heme biosynthesis.\textsuperscript{3} But the amounts of porphyrins excreted in PCT can be accounted for with little or no induction of ALAS1, suggesting that this effect is less important in PCT than in acute hepatic porphyrias. Whether some chemotherapeutic agents might contribute to iron-mediated oxidative stress and production of a UROD inhibitor in hepatocytes\textsuperscript{2} has, to our knowledge, not been studied.

Conflict of interest: None declared.

References