Letters

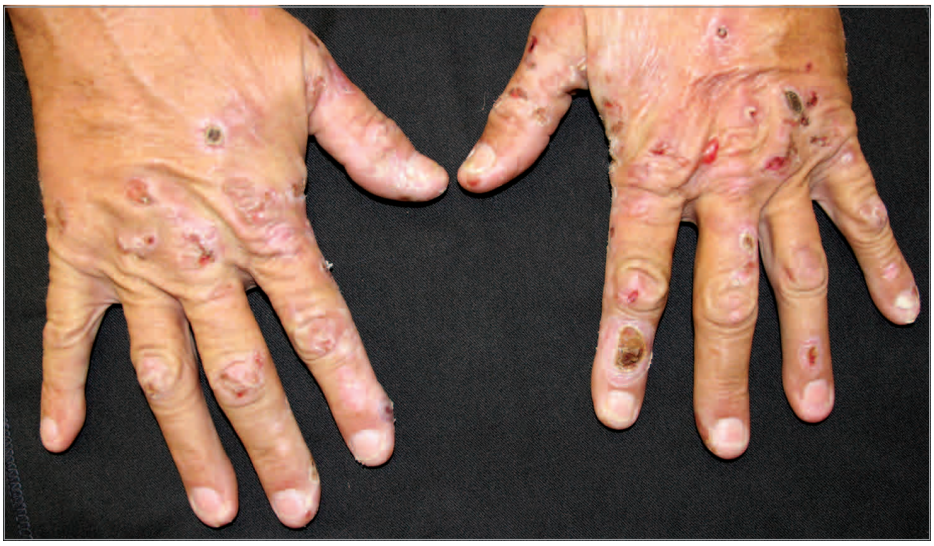
OBSERVATION

Resolution of Porphyria Cutanea Tarda in Patients With Hepatitis C Following Ledipasvir-Sofosbuvir Combination Therapy

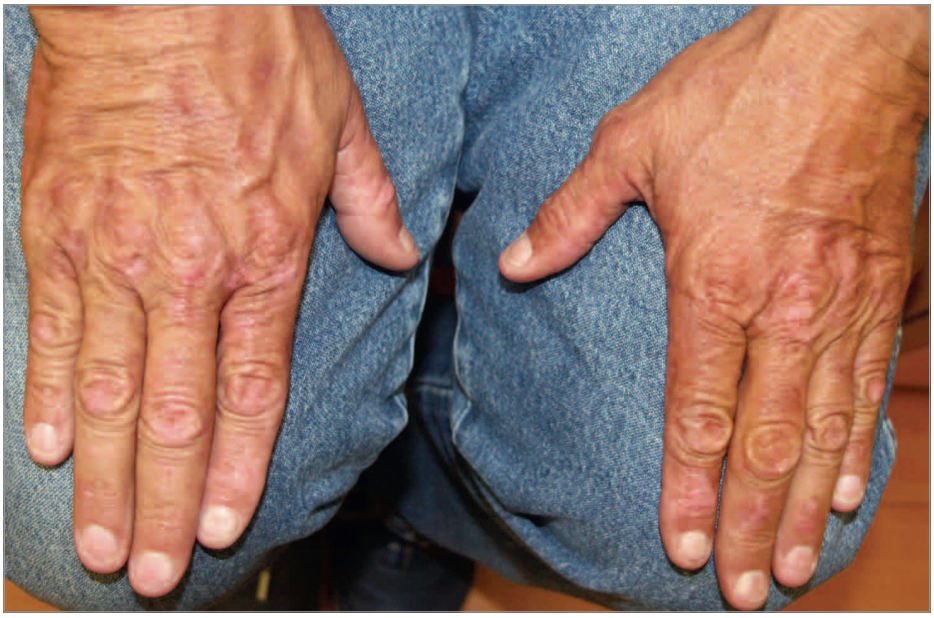
Porphyria cutanea tarda (PCT) is the most common porphyria, caused by a decrease in uroporphyrinogen decarboxylase (UROD) activity.[1] There is a strong association between the sporadic form of PCT and hepatitis C virus (HCV) infection. Depending on the country, 40% to 50% of patients with PCT have been found to be infected with HCV.[2] Chronic hepatitis C infection unmasks the UROD enzyme deficiency in genetically predisposed patients by causing oxidative stress from iron overload.[3] In addition, PCT occurs in the highest rates in

Figure. Clinical Images of Patient 1

A Before treatment



B After treatment



A, Bullae and erosions of porphyria cutanea tarda are seen in a patient with hepatitis C before treatment. B, Five months after completing an 8-week regimen of combination therapy with ledipasvir and sofosbuvir, the lesions are cleared.

Table. Patient and Clinical Characteristics

Characteristic	Patient 1	Patient 2	Patient 3
Sex (age)	Male (60s)	Male (50s)	Male (50s)
Chief complaint or examination findings	Several years of erythematous scaly plaques with bullae and vesicles (Figure, A)	Numerous open sores, bullous lesions, and erythematous plaques on dorsum of hands for several months	3-Month history of eruption and erosions of the hands
Hepatitis C history	Previously diagnosed	Newly diagnosed	Newly diagnosed
Laboratory values	24-Hour fractionated porphyrin urine tested positive for several fractions; total porphyrin level, 2099.3 µg/24 h	HCV antibody, 24.30 points above signal cutoff; shave biopsy findings consistent with PCT	HCV antibody, 30.3 points above signal cutoff; 24-hour fractionated urine porphyrin level, 4499.4 µg/24h; shave biopsy findings consistent with PCT
Treatment	8-Week course of ledipasvir-sofosbuvir combination therapy	Interim treatment with clobetasol showed minimal improvement; 12-week course of ledipasvir-sofosbuvir combination therapy	12-Week course of ledipasvir-sofosbuvir combination therapy
Follow-up	Complete resolution of PCT 3 months after treatment regimen completed (Figure, B)	Complete resolution of PCT 5 months after ledipasvir-sofosbuvir treatment regimen completed	Markedly decreased number of lesions 1 month after treatment; no new spontaneous lesions after completion of therapy

Abbreviations: HCV, hepatitis C virus; PCT, porphyria cutanea tarda.

patients with HCV-related liver cirrhosis, which suggests that cirrhosis may play a role in disease development.[4]

Report of Case | Previous HCV treatments, such as interferon, have shown mixed responses in the resolution of PCT.[3] One case report demonstrated the resolution of PCT after HCV treatment with the direct-acting antiviral (DAA) agent boceprevir.[5] Boceprevir, however, still requires interferon therapy in the treatment regimen, which may have contributed to PCT resolution. We describe 3 men with HCV who had resolution of their PCT manifestations months after completing an 8- or 12-week combination regimen of ledipasvir, 90 mg and sofosbuvir, 400 mg (**Figure** and **Table**).

Discussion | A literature search revealed 1 case report of successful PCT clearance following treatment with another DAA agent, boceprevir.[5] This suggests that the marked improvement in PCT is likely related to the cure of HCV that can be achieved by DAA agents in general and not necessarily only ledipasvir-sofosbuvir combination therapy.

Hepatitis C is an infectious disease that primarily affects the liver potentially leading to cirrhosis and hepatic cancer. As many as 170 million people worldwide are infected with HCV chronically.[6] The ushering of a greater understanding of the HCV genome has facilitated the dawn of a new age of treatments for hepatitis C capable of 95% sustained virologic response with DAA agents.[6] Direct-acting antiviral agents target specific steps in HCV replication. The improvement of PCT following DAA treatment further suggests that viral activity is directly linked with disease severity and may provide important insight into therapeutics for HCV-associated PCT.

The development of DAA agents heralds a new direction for infectious diseases and hepatology in the fight against hepatitis C. Our case series highlights the potential secondary benefits in improving cutaneous skin diseases of hepatitis C with DAA agents. Further investigations are needed to corroborate our findings regarding PCT resolution in patients with HCV following DAA treatment. Hepatitis C also has known associations with other extrahepatic manifestations such as mixed cryoglobulinemia and lichen planus, which require further investigation.

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