Elevated Porphyrin Levels in End Stage Renal Disease: Pseudoporphyria or Porphyria Cutanea Tarda?

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Introduction

Porphyria Cutanea Tarda (PCT) is an acquired porphyria causing blistering of the skin on sun exposed surfaces. The disease is caused by a deficiency in uroporphyrinogen decarboxylase (UROD) which can occur in the setting of hepatitis, alcohol abuse and iron overload [1]. Porphyrin accumulation and elevation has been noted in ESRD patients irrespective of PCT and with or without manifestation of cutaneous symptoms and has been termed pseudoporphyria [2,3]. This is likely because standard dialysis does not effectively remove plasma uroporphyrin and due to a decrease in glutathione causing oxidative stress, but there is no deficiency in heme synthesis [4,5]. There have also been true cases of PCT being seen in ESRD patients, but these cases have been associated with iron supplementation and blood transfusions [6,7]. Here we present a case of blistering of the skin of the hands of a patient on ESRD without a clear diagnosis for PCT or pseudoporphyria.

Case Presentation

The patient is a male in his 60s with a past medical history of End Stage Renal Disease on dialysis and hepatic steatosis secondary to stain induced rhabdomyolysis who presented to the hematology office for blistering of the hands. The blistering began 4 months prior. The fluid filled blisters appeared on the dorsum on the hands bilaterally and healed with hyperpigmentation. The blisters reoccurred and worsened until initial presentation (Figure 1). The patient reported drinking 4 mixed drinks of standard size a week. The patient was not on any iron supplementation and had never received a blood transfusion previously. He has been very adherent with his dialysis schedule and is being evaluated for a renal transplant.

He was found to have hyperferritinemia and an elevated total serum porphyrin. Urine porphyrin studies were unable to be sampled due to a laboratory error. Hepatitis panels were negative for Hepatitis B and C. DNA mutation analysis identified one copy of the C282Y pathogenic variant in the HFE gene, commonly associated with hemochromatosis, an iron overload disorder [3]. Though not conclusive, this raises the possibility of primary hemochromatosis. A biopsy of the bullous lesion was performed which revealed a sub-epidermal blistering process, indicative of PCT.

Clinical Presentation

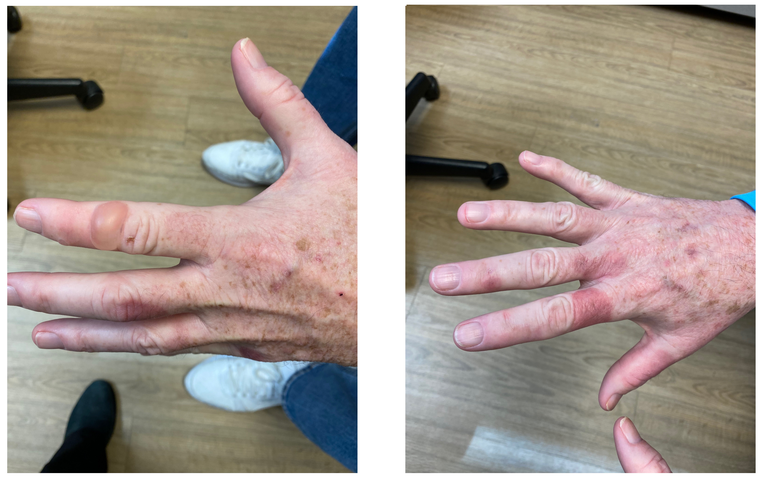

Figure 1

The patient's hands on initial presentation to the office. The left hand (left image) shows an active bullous skin lesion on the index finger. The right hand (right image) shows healed, well demarcated previous bullae on the left, middle finger, and thumb.

Laboratory Values

Labs	Value	Ref Range
Iron	121	35-150 ug/dL
Ferritin	**>1,500**	24-250 ng/mL
Iron Sat	42	15-45%
TIBC	288	270-460 ug/dL
WBC	6.2	3.8-10.5 K/uL
RBC	3.4	4.5-5.8 M/uL
Hgb	12.3	13.7-17.5 g/dL
MCV	103.2	83.0-98.0 fL
PLT	104	150-350 k/uL
Total Porphyrin	**441.4**	1.0-5.6 mcg/L
Porphobilinogen 24 Hr Ur	0.125	<0.34 mg/24 hr
Uroporphyrin	laboratory error	–
Hepatitis B PCR	Nonreactive	Nonreactive
Hepatitis C PCR	Nonreactive	Nonreactive
Hereditary Hemochromatosis Genetic Analysis	One copy of the C282Y pathogenic variant in the HFE gene	Negative

Intervention

As the patient had a stable hemoglobin of 12.3 g/dl, he was phlebotomized once. His repeat Hgb was 9.5 g/dl with the intention to not continue phlebotomy. After this though, the patient was then lost to follow up at the office. Attempts are being made to reconnect with the patient for continued diagnostics and treatment. Per CareEverywhere, the patient follows at multiple institutions and sees multiple specialists within the same fields inconsistently. This makes his medical management more difficult.

When the patient is able to be seen for follow up, a repeat urine porphyrin test will be performed to determine heptacarboxylate porphyrin levels which should only be elevated in true PCT [4]. Further hereditary hemochromatosis genetic testing could be considered as well to establish a true diagnosis in the patient if all else is inconclusive include a hepatic MRI for liver iron deposits which would suggest true hereditary hemochromatosis.

Discussion and Conclusion

While the true diagnosis has yet to be confirmed in this patient, it is important to remember that there have been cases of pseudoporphyria caused by ESRD and true cases of PCT in the setting of ESRD. While these true cases of PCT have been associated with iron supplementation and transfusions, these interventions might not be necessary to illicit clinical manifestations of elevates porphyria levels in the setting of hereditary hemochromatosis.

Knowing the true diagnosis is essential for initiating the proper treatment. While both PCT and pseudoporphyria can be treated with phlebotomy, in ESRD the concern for worsening anemia becomes significant. If pseudoporphyria can be diagnosed, alternative treatment methods are available that wouldn't be successful in PCT including N-acetylcysteine, and Vitamin D in combination with photoprotection [8,9]. If the patient is also diagnosed with true hereditary hemochromatosis, this will have implications for his relatives and children as well.

References

1. Singal AK. Porphyria cutanea tarda: Recent update. Mol Genet Metab. 2019;128(3):271-281. doi:10.1016/j.ymgme.2019.01.004
2. Anderson CD, Rossi E, Garcia-Webb P. Porphyrin studies in chronic renal failure patients on maintenance hemodialysis. Photodermatol. 1987;4(1):14-22.
3. Green JJ, Manders SM. Pseudoporphyria. J Am Acad Dermatol. 2001;44(1):100-108. doi:10.1067/mjd.2000.111338
4. Poh-Fitzpatrick MB, Masullo AS, Grossman ME. Porphyria cutanea tarda associated with chronic renal disease and hemodialysis. Arch Dermatol. 1980;116(2):191-195.
5. Schettler V, Wieland E, Methe H, Schuff-Werner P, Müller GA. Oxidative stress during dialysis: effect on free radical scavenging enzyme (FRSE) activities and glutathione (GSH) concentration in granulocytes. Nephrol Dial Transplant. 1998;13(10):2588-2593. doi:10.1093/ndt/13.10.2588
6. McKane W, Green CA, Farrington K. Porphyria cutanea tarda precipitated by intravenous iron in a haemodialysis patient. Nephrol Dial Transplant. 2001;16(9):1936-1938. doi:10.1093/ndt/16.9.1936
7. AlGahtani FH, Stuckey R, Alqahtany FS. Secondary hemosiderosis presented by porphyria cutanea tarda in a kidney dialysis patient: A case report. SAGE Open Med Case Rep. 2020;8:2050313X20907815. Published 2020 Feb 22. doi:10.1177/2050313X20907815
8. Guiotoku MM, Pereira Fde P, Miot HA, Marques ME. Pseudoporphyria induced by dialysis treated with oral N-acetylcysteine. An Bras Dermatol. 2011;86(2):383-385. doi:10.1590/s0365-05962011000200031
9. Pranteda G, Bottoni U, Tayefeh Jafari M, et al. Dialysis-associated pseudoporphyria successfully treated with vitamin D. Report of two cases. G Ital Dermatol Venereol. 2015;150(3):327-329.

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