CASE STUDY OF PORPHYRIA CUTANEA TARDA IN COMBINATION WITH HEMOCHROMATOSIS IN A COLLEGIATE MALE ATHLETE

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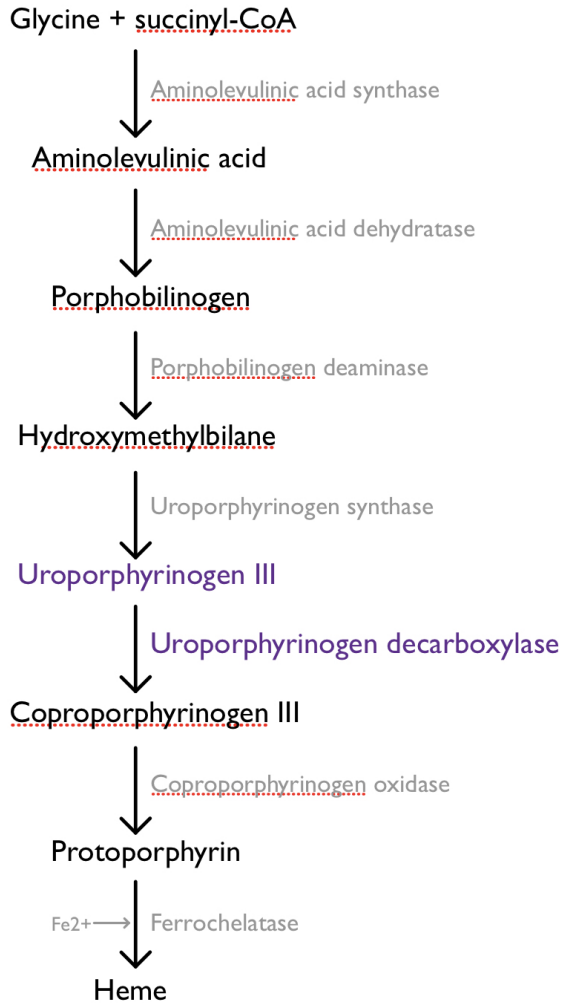
INTRODUCTION- PORPHYRIA CUTANEA TARDA

- PCT- most common form of porphyria
- Characterized as chronic skin blistering and skin friability on sun-exposed areas, especially dorsum of the hand
- Abnormal heme synthesis; Inhibition of uroporphyrinogen decarboxylase by ~80%
  - Mutation of enzyme is only present in a minority of patients
- Clinical disease precipitated by at least two known risk factors

Genetic factors	Acquired factors
Genetic hemochromatosis	Alcohol consumption
Uroporphyrinogen decarboxylase mutation	Tobacco use
	Estrogen use (females)
	Hepatitis C infection
	HIV infection



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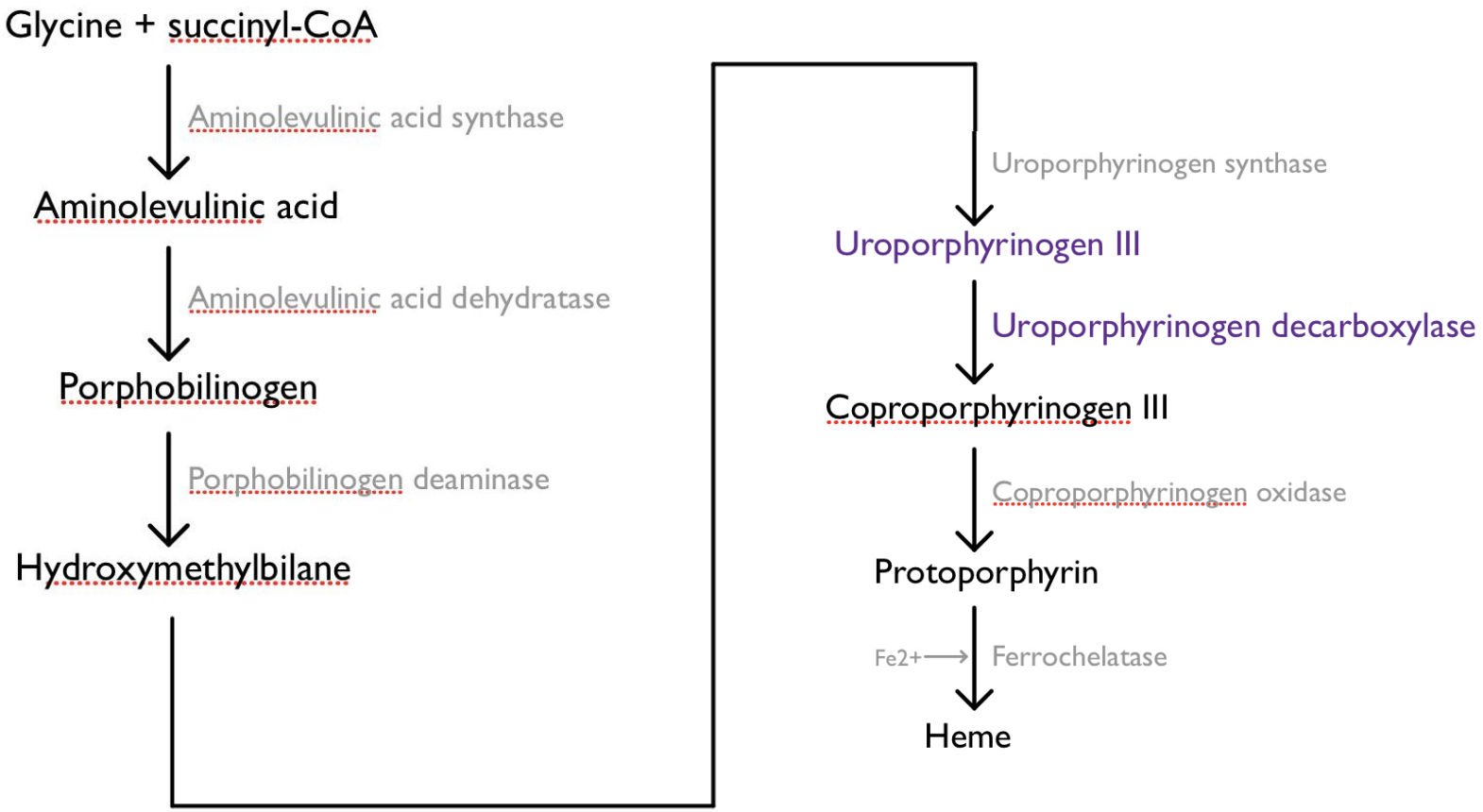
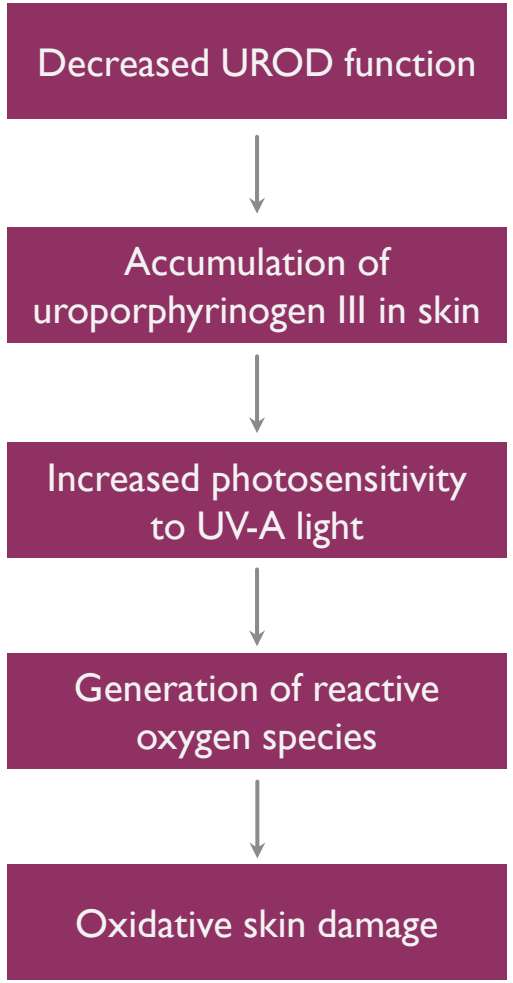


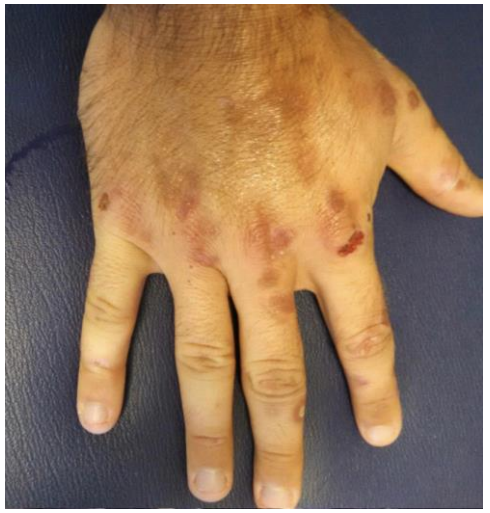


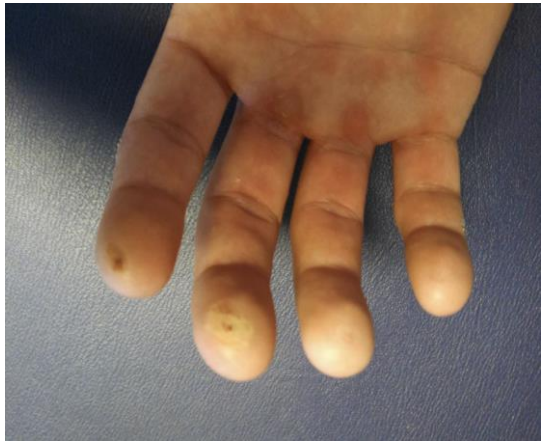
INTRODUCTION- HEMOCHROMATOSIS

- Excessive iron accumulation
- Common clinical presentation: cirrhosis, lethargy, diabetes mellitus, skin pigmentation; typically presents after age 40
- Autosomal recessive disorder
- HFE gene mutation on chromosome 6
  - C282Y mutation and/or H63D mutation
- Disruption of iron sensing via HFE protein
  - Increased intestinal Fe absorption
  - Iron accumulation in organs- liver, pancreas, skin, heart, pituitary, joints
- Complications: restrictive cardiomyopathy, dilated cardiomyopathy, hypogonadism, arthropathy, and hepatocellular carcinoma

PATIENT PRESENTATION AND CHIEF COMPLAINT

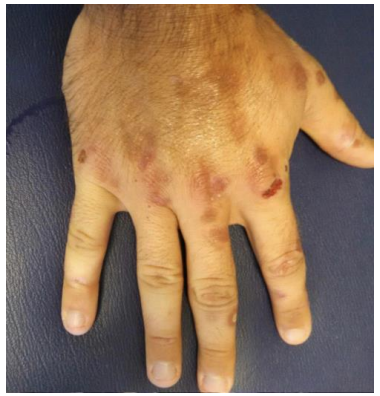
- 23 year old collegiate male quarterback presented with blistering skin lesions on his hands.
- No significant medical history and was returning to football practice after working in construction over the summer.

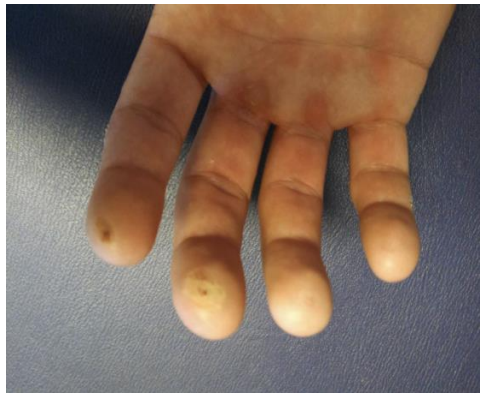




HISTORY OF PRESENT ILLNESS

- Lesions became larger, more tender and fragile. The athlete's hands were so tender he could not catch ball under center.
- Athlete's symptoms progressed to include lesions on both arms and face.
- Dark colored scarring appeared on his hands.
- Denies systemic symptoms.





HISTORY

- Past surgical history- treatment of a fracture
- Past medical history- Cellulitis of right elbow treated with doxycycline 6 weeks before initial workup
- Social history- User of smokeless tobacco products; 7-8 alcoholic drinks twice a week
- Family history- Significant for cancer and hypertension

CURRENT MEDICATIONS AND ALLERGIES

- Medications- None, no supplements
- Allergies- Vancomycin (Red Man Syndrome)

PHYSICAL EXAM

- Vital signs: BP- 128/81, HR- 80 bpm, Temp- 98.8˚F, RR- 18 bpm, BMI 26.7
- Heart, lungs, abdomen and neurologic exam were unremarkable.
- No jaundice was noted on the skin examination. Multiple lesions on both hands, arms and face. Lesions were in various stages of healing along with areas of hyperpigmentation.

LABS

- Initial tests were ordered:
  - Allergy testing
  - Lesion biopsy
- Follow up tests:
  - Comprehensive metabolic panel & CBC with differential
  - Heavy metal panel
  - HCV, HSV, HIV antibody tests
  - Iron studies (Serum Iron, Iron Saturation, Transferrin,)
  - Uroporphyrins
  - Fibroscan
  - Genetic testing

LAB RESULTS- NORMAL

- Allergy testing: negative
- HCV ab: neg
- HIV 1/2: neg
- HSV 1/2: neg
- Mercury: wnl
- Arsenic: wnl
- Lead: wnl

LAB RESULTS- ABNORMAL

- Lesion biopsy: subepidermal blister with rare dyskeratotic keratinocytes, mild lymphocytic infiltrate and red blood cell extravasation
- Liver enzymes:
  - AST: 64 U/L (normal 0-40 U/L)
  - ALT: 158 U/L (0-44 U/L)
- Iron study:
  - Transferrin: 963 mg/dL (200-450 mg/dL)
  - Iron (serum): 204 mcg/dL (38-169 mcg/dL)
  - Iron (transferrin) saturation: 92% (15-55%)
- Uroporphyrins: 1167 nmol/mmol creatinine (<2 nmol/mmol creatinine)
- Fibroscan: 8.5 kPa (2-7 kPa)
- Genetic testing: homozygous C282Y HFE mutation

DIFFERENTIAL DIAGNOSIS

- Allergic Reaction to Chromium
- Hemochromatosis
- Porphyria Cutanea Tarda

WORKING DIAGNOSIS

- Porphyria Cutanea Tarda in combination with Hereditary Hemochromatosis
- Iron overload has been documented to accelerate the inactivation of UROD by affecting the quantity and/or activity level
- Three ideas how this may occur
  1. Iron can catalyze formation of reactive oxygen species and therefore enhance oxidation of uroporphyrinogen to uroporphyrin
  2. Iron can indirectly inhibit UROD actibity by enhancing nonporphyrin products that directly inhibit the enzyme
  3. Iron can induce aminolevulinic acid synthase, increasing production of uroporphyrinogen

Genetic factors	Acquired factors
Genetic hemochromatosis	Alcohol consumption
Uroporphyrinogen decarboxylase mutation	Tobacco use
	Estrogen use (females)
	HCV infection
	HIV infection

TREATMENT OPTIONS/PLAN

- Unsuccessful treatment: allergy shots and steroid injections, minimal improvement
- Successful treatment: phlebotomy every week (remove a total of 30 units of blood) with labs every 2 months, elimination of tobacco and alcohol use

OUTCOMES- IMPACT ON PLAY

- Weekly phlebotomy quickly improved lesions but caused dehydration and fatigue. Impacted athlete's ability to play football. Phlebotomies were decreased to 1-2x's q month, which decreased these symptoms.
- The athlete was a senior quarterback, he was able to return to practice and play in games.
- Modifications included a decrease in the amount of conditioning and lifting in addition to limiting repeated drill practice. He was able to play in all but one game after this diagnosis was made and treatment started.

OUTCOMES- FOLLOW UP APPOINTMENTS

3 month check up

Test	Results
AST	47 U/L
ALT	90 U/L
Transferrin	
Iron (serum)	47 mcg/dL
Iron saturation	17%
Ferritin	57 ng/mL

12 phlebotomies

6 month check up

Test	Results
AST	26 U/L
ALT	36 U/L
Transferrin	251 mcg/dL
Iron (serum)	49 mcg/dL
Iron saturation	20%
Ferritin	50 ng/mL

UPDATES OF PATIENT

- Family members tested for HFE genotype and iron status- sister was also diagnosed with hereditary hemochromatosis, no symptoms
- Patient currently has no restrictions. No longer uses tobacco nor drinks alcohol. He is a regular blood donor giving blood q56 days (minimum of 3x's/year)

CONCLUSIONS

Genetic factors	Acquired factors
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REFERENCES

- Bissell, D. M., Anderson, K. E., & Bonkovsky, H. L. (2017). Porphyria. *New England Journal of Medicine, 377*(9), 862-872. doi:10.1056/nejmra1608634
- Bovenschen, H., & Vissers, W. (2009, June 17). Primary hemochromatosis presented by porphyria cutanea tarda: A case report. *Cases Journal, 2*(7246). doi:10.4076/1757-1626-2-7246
- de Geus, H. R., & Dees, A. (2006). Sporadic porphyria cutanea tarda due to haemochromatosis. *The Netherlands journal of medicine, 64*(8), 307–309.
- Edwards, M.V., Ray, J. M., & Bacon, B. R. (2019). Sporadic Porphyria Cutanea Tarda as the Initial Manifestation of Hereditary Hemochromatosis. *ACG Case Reports Journal, 6*(11). doi:10.14309/crj.0000000000000247
- Fernandes, A., Preza, G. C., Phung, Y., Domenico, I. D., Kaplan, J., Ganz, T., & Nemeth, E. (2009). The molecular basis of hepcidin-resistant hereditary hemochromatosis. *Blood, 114*(2), 437-443. doi:10.1182/blood-2008-03-146134
- Roberts, A. G., Whatley, S. D., Morgan, R. R., Worwood, M., & Elder, G. H. (1997). Increased frequency of the haemochromatosis Cys282Tyr mutation in sporadic porphyria cutanea tarda. *The Lancet, 349*(9048), 321-323. doi:10.1016/s0140-6736(96)09436-6
- Salgia, R. J., & Brown, K. (2015, February 01). Diagnosis and Management of Hereditary Hemochromatosis. *Clinics in Liver Disease, 19*(1), 187-198. doi:10.1016/j.cld.2014.09.011