Photoexposed Rash in an Older Adult

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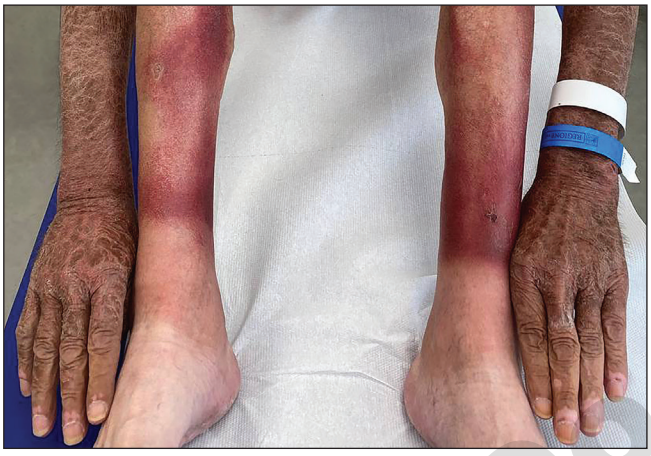

A 66-year-old man presented with an intermittent pruriginous symmetric rash on the dorsal aspects of the arms, legs, and upper chest of 4 months' duration. The patient's hands, forearms, and neck were diffusely hyperpigmented, dry, cracked, and scaling with a ring of peripheral erythema. He also experienced recurrent photosensitivity reactions on the legs. His poor clinical condition including confusion and diarrhea hindered intake of a balanced diet. He also reported a history of excessive alcohol use. The patient's vital signs were normal, and Doppler ultrasonography ruled out deep venous thrombosis of the lower legs. A complete blood cell count showed anemia with decreased hemoglobin levels (117 g/L [reference range, 140–180 g/L]) and increased mean corpuscular volume (107.1 fL [reference range, 80–100 fL]). Additionally, low serum levels of albumin, folate, and vitamin B_{12} were noted. The patient had been taking hydrochlorothiazide and salicylic acid for hypertension with no recent changes in his medication regimen.

WHAT'S YOUR **DIAGNOSIS?**

a. acute cutaneous lupus erythematosus
b. necrolytic migratory erythema
c. pellagra
d. phototoxic reaction
e. porphyria cutanea tarda

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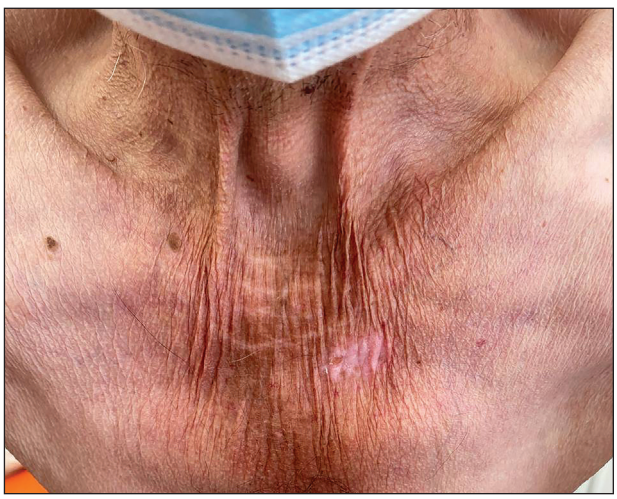
THE **DIAGNOSIS:** Pellagra

The patient was diagnosed with pellagra based on the clinical and laboratory findings. He was discharged with nicotinamide 250 mg and folic acid 5 mg supplementation daily. After 3 months, all symptoms resolved.

Pellagra is a condition usually associated with the 4 Ds: dermatitis; diarrhea; dementia; and, if untreated, death.[1] The word *pellagra* is derived from the Italian terms *pelle* and *agra*, which mean skin and rough, respectively.[2] Spanish physician Gasper Casal first described pellagra in 1762 after observing the disease in poorer peasants in Asturias who mainly relied on maize and rarely consumed fresh meat.[1,2] Joseph Goldberger conducted research in the early 20th century, provoking the disease in jail prisoners by modifying their diets. However, it was not until 1926 that Goldberger discovered the true cause of the illness to be a poor diet and named what would become known as nicotinamide as the pellagra preventative factor.[1,2] Niacin (vitamin B_3), the deficient molecule in pellagra, also is known as nicotinic acid, nicotinamide, or niacinamide. It is a water-soluble vitamin that is converted into nicotinamide-adenine-dinucleotide (NAD) and its phosphate NADP.[1,2] It has been hypothesized that pellagra symptoms arise from insufficient amounts of NAD and NADP, making the body unable to support cellular energy transfer processes.[3]

Pellagra manifests 50 to 60 days after starting a diet low in niacin. Niacin and nicotinamide are absorbed from the digested food to the stomach through a sodium-dependent mechanism, and then nicotinamide may be transformed into nicotinic acid with microsomal deamidation.[3] Niacin may be obtained from one's diet or produced from tryptophan. Foods with the highest amounts of niacin include liver, poultry, fish, eggs, milk, pork, mushrooms, avocados, almonds, and legumes.[1,3] Coffee also contains trigonelline, which may be transformed into nicotinic acid when roasted, increasing the niacin level by 30 times.[3] Approximately 60 mg of dietary tryptophan is needed to produce up to 1 mg of niacin in the presence of B_2 and B_6 vitamins. This mechanism provides approximately half of the needs for niacin.[3] Insufficient dietary intake of niacin or the essential amino acid tryptophan can cause pellagra (primary pellagra), which is a concern in resource-limited countries. Alternatively, the body may not be able to properly utilize niacin for metabolic processes (secondary pellagra), which occurs more frequently in developed countries.[1] Secondary pellagra also may be caused by alcoholism, colitis, cirrhosis, carcinoid tumors, Hartnup disease, or gastrointestinal tuberculosis, as these conditions prevent niacin from being consumed, absorbed, or processed. Certain medications can cause pellagra by interfering with the tryptophan-niacin pathway, including isoniazid, 5-fluorouracil, pyrazinamide, 6-mercaptopurine, hydantoins, ethionamide, phenobarbital, azathioprine, and chloramphenicol.[2]

The clinical manifestations of pellagra are diverse because it affects tissues with high turnover rates. Clinical features of pellagra include symmetric photosensitive skin eruptions, gastrointestinal tract symptoms, and neurologic and mental disorders.[3] The first signs of pellagra may include muscle weakness, digestive concerns, and psychological or emotional discomfort.[2] Pellagra dermatitis manifests as an acute or intermittent, bilaterally symmetrical eruption on sun-exposed areas and is markedly distinct from healthy skin.[3] Some individuals may experience vesiculation and bullae development (wet pellagra). The erythema is first brilliant red then turns into a cinnamon-brown color. Over time, the skin becomes thickened, scaly, cracked, and hyperpigmented.[1] The dryness of the skin likely is due to a remarkable decrease in wax ester and sebaceous gland atrophy seen on histopathology.[4] Pellagra most frequently affects the back of the hands (77%–97% of cases), which can extend upward to create the so-called pellagra glove or gauntlet.[3] It is common to see symmetrical eruptions in the shape of a butterfly following an anatomical pattern innervated by the trigeminal nerve, which resembles lupus erythematosus on the face. Another common manifestation is Casal necklace, a well-marginated eruption frequently seen on the front of the neck (Figure).[2] On the foot, lesions often do not develop close to the malleoli but rather terminate distally on the backs of the toes. Sometimes a boot pattern may form that covers the front and back of the leg.[1-3]



Casal necklace presenting as broad hyperpigmented scaly patches distributed along the neck in a patient with pellagra.

The pathophysiology of photosensitivity in pellagra was hypothesized by Karthikeyan and Thappa.[3] They discovered an excessive synthesis of a phototoxic substance, kynurenic acid, and a deficiency in urocanic acid, which normally protects the skin by absorbing light in the UVB range. Niacin deprivation leads to the production of kynurenic acid through the tryptophan-kynurenine-nicotinic acid pathway and reduces the amount of urocanic acid by affecting the enzyme histidase in the stratum corneum.[1-3] In one-third of patients, pellagra affects the oral mucosa, causing characteristic symptoms such as glossitis, angular stomatitis, and cheilitis.[2] In nearly 50% of patients, poor appetite, nausea, epigastric discomfort, diarrhea, and excessive salivation are present. Most of the gastrointestinal tract is affected by mucosal inflammation and atrophy, which can cause malnutrition and cachexia due to anorexia and malabsorptive diarrhea.[2] Headache, irritability, poor concentration, hallucinations, photophobia, tremor, and depression are some of the neuropsychiatric symptoms. Patients experience delirium and disorientation as pellagra progresses, followed by a comatose state and ultimately death.[2]

The patient's history and physical examination are used to make the diagnosis, with particular attention to the patient's dietary details. The diagnosis is made in part *ex juvantibus* by seeing how the patient responds to higher niacin doses. Anemia, hypoproteinemia, elevated blood calcium, reduced serum potassium and phosphorus, abnormal liver function tests, and elevated serum porphyrin levels also indicate pellagra. Niacin 300 mg in divided doses for up to 4 weeks has been recommended by the World Health Organization to treat pellagra.[5] The flushing seen with niacin administration is not linked to the usage of nicotinamide. The recommended nicotinamide dosage for adults is 100 mg orally every 6 hours until most acute symptoms have disappeared, followed by oral administration of 50 mg every 8 to 12 hours until all skin lesions have healed.[2]

Among the differential diagnoses, necrolytic migratory erythema is characterized by an episodic eruption of crusted, erosive, annular erythematous plaques with blister development, which occurs in 70% of patients with glucagonoma syndrome. The perioral region, perineum, lower belly, thighs, and distal extremities are the usual locations.[6,7] Laboratory test results include elevated fasting serum glucagon (>1000 ng/L) and normocytic anemia, which aided in ruling out this diagnosis in our patient. Generalized acute cutaneous lupus erythematosus may appear as a broad morbilliform eruption. The hands frequently exhibit erythema and edema, especially across the dorsal and interphalangeal regions.[8] Other typical findings of systemic lupus erythematosus such as antinuclear antibody were not seen in our patient, making this diagnosis unlikely. Porphyria cutanea tarda also must be considered in the differential diagnosis. The hepatic deficiency of uroporphyrinogen decarboxylase is the primary cause of this condition. Although it is characterized by blistering lesions, patients more frequently describe increased skin fragility in sun-exposed regions. Hypertrichosis, hyperpigmentation or hypopigmentation, hirsutism, or scarring may appear in the later stage of the disease.[9] Phototoxic reaction was ruled out because the patient spent most of the time at home, and no new drugs had been prescribed in the previous months.

REFERENCES

1. Prabhu D, Dawe RS, Mponda K. Pellagra a review exploring causes and mechanisms, including isoniazid-induced pellagra. *Photodermatol Photoimmunol Photomed*. 2021;37:99-104. doi:10.1111/phpp.12659
2. Hegyi J, Schwartz RA, Hegyi V. Pellagra: dermatitis, dementia, and diarrhea. *Int J Dermatol*. 2004;43:1-5. doi:10.1111/j.1365-4632.2004.01959.x
3. Karthikeyan K, Thappa DM. Pellagra and skin. *Int J Dermatol*. 2002;41:476-481. doi:10.1046/j.1365-4362.2002.01551.x
4. Dogliotti M, Liebowitz M, Downing DT, et al. Nutritional influences of pellagra on sebum composition. *Br J Dermatol*. 1977;97:25-28. doi:10.1111/j.1365-2133.1977.tb15423.x
5. World Health Organization. *Pellagra and Its Prevention and Control in Major Emergencies*. Published February 23, 2000. Accessed February 15, 2024. https://www.who.int/publications/i/item/WHO-NHD-00.10
6. Liu JW, Qian YT, Ma DL. Necrolytic migratory erythema. *JAMA Dermatol*. 2019;155:1180. doi:10.1001/jamadermatol.2019.1658
7. Tolliver S, Graham J, Kaffenberger BH. A review of cutaneous manifestations within glucagonoma syndrome: necrolytic migratory erythema. *Int J Dermatol*. 2018;57:642-645. doi:10.1111/ijd.13947
8. Walling HW, Sontheimer RD. Cutaneous lupus erythematosus: issues in diagnosis and treatment. *Am J Clin Dermatol*. 2009;10:365-381. doi:10.2165/11310780-000000000-00000
9. Singal AK. Porphyria cutanea tarda: recent update. *Mol Genet Metab*. 2019;128:271-281. doi:10.1016/j.ymgme.2019.01.004