Letter

Pellagra associated with iron deficiency

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To the Editor

A 50-year-old woman with no previous skin disease presented with a 1-month history of intermittent, itchy, painful erythema and burning sensation on her face, sides of the neck, and anterior chest. Symptoms were aggravated by sun exposure and had recently become persistent, with increasing pigmentation at affected sites. Treatment with hydrocortisone 17-butyrate 0.1% cream was unhelpful. On examination, there was bilateral, well-marginated erythema, scaling, and hyperpigmentation over the face, the sides and back of the neck, and the "V" of the chest in a photoexposed distribution (**Figure 1**).

The patient had previously been prescribed iron supplements for chronic iron deficiency anemia, thought to be a result of dietary inadequacy, but admitted to taking them irregularly. She was otherwise in good health, on no other regular medications, and denied alcohol or substance use.

Pellagra was clinically suspected, prompting a detailed dietary assessment. The patient, who had always avoided red meat, had further restricted her diet in recent years, eliminating all meat, poultry, and fish to lose weight. She had a body mass index of 22.5 kg/m^2 at presentation. She denied diarrhea or other gastrointestinal symptoms, and examination revealed no neuropsychiatric disturbance. Serum vitamin B3 (nicotinamide) level was measured and found to be less than 5.0 µg/L (normal range: 8–100 µg/L). Other causes of cutaneous photosensitivity, including drug-induced reactions, cutaneous lupus erythematosus, dermatomyositis, and primary photodermatoses, were excluded based on history and clinical features. Treatment was initiated with oral nicotinamide 250 mg twice daily, along with dietary counseling. At review 1 month later, there was dramatic improvement, and the skin changes had resolved almost completely (**Figure 2**). Serum vitamin B3 (nicotinamide) level had risen to 19.1 µg/L (normal range: 8–100 µg/L).

Pellagra is a clinical syndrome characterized by the 4 Ds: (1) dermatitis, (2) diarrhea, and (3) dementia, which can lead to (4) death if untreated. However, not all features manifest in every patient. The term "pellagra" originates from the Italian words *pelle*, meaning "skin," and *agra*, meaning "rough" or "harsh," referring to the dry, hard, and cracked skin characteristic of the condition.[1] Skin changes, often the earliest sign, typically appear in spring or summer with an intermittent, pruritic, photosensitive rash affecting exposed areas. In severe cases, vesicles and bullae may form. Over time, the rash can evolve into fixed, sharply demarcated, hyperpigmented, keratotic plaques, particularly around the neck (Casal's collar or necklace) and extremities (pellagrous glove-and-boot). Mucosal involvement may also occur, manifesting as stomatitis, glossitis, cheilitis, or ulcers in the oral and perirectal regions.[1,2]

Pellagra results from insufficient dietary intake of niacin or tryptophan (primary pellagra) or the inability to effectively use these nutrients (secondary pellagra). Approximately half of the body's niacin comes from dietary sources (**Table 1**),[3] while the remainder is synthesized endogenously from tryptophan. Although more common in developing regions owing to limited access to niacin-rich foods, primary pellagra can still arise in developed countries as a result of restrictive diets, including excessive corn-based diets, unbalanced vegan or raw food diets, and ketogenic regimens that exclude fortified grains.[1] Secondary pellagra is more common in developed settings and is associated with chronic alcoholism, certain medications such as isoniazid, gastrointestinal disorders such as Crohn's disease, and malignancies such as carcinoid tumors.[2]

Prevention involves a protein-rich, balanced diet with niacin- and tryptophan-rich foods such as meat, fish, whole grains, and fortified cereals. Daily niacin intake recommendations range from 9 to 13 mg for children, 13 to 20 mg for adults, and 17 to 20 mg for pregnant or lactating women. As a water-soluble vitamin, excess niacin is excreted rather than stored, making regular intake essential.[4] Treatment typically involves 500 mg of nicotinamide or nicotinic acid daily until symptoms re-

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solve, although skin manifestations may take weeks to subside completely. Nicotinamide is preferred over nicotinic acid to minimize side effects such as flushing and headaches.[1]

A notable aspect of this case was the patient's iron deficiency, with a ferritin level of 6 ng/mL (normal range: 10–291 ng/mL). Ferritin, the main protein responsible for iron storage, is the most reliable early marker of iron deficiency, even before anemia develops, and a level below 15 ng/mL is highly specific (specificity 0.99). Since ferritin also acts as an acute phase reactant, false-normal or elevated levels may occur in the context of inflammation or infection. In such situations, additional blood tests, including transferrin saturation, are useful in assessing iron stores.[5] Our patient had no clinical features suggesting inflammation or infection. Additional investigations could not be pursued owing to financial constraints, as the patient was evaluated at a private clinic and paid for her care out of pocket.

Iron is essential for the enzymatic pathway that synthesizes niacin from tryptophan. Low ferritin levels, reflecting depleted iron stores, may impair this pathway, reducing endogenous niacin production.[3] Additionally, iron deficiency can increase oxidative stress, elevating demand for nicotinamide adenine dinucleotide and nicotinamide adenine dinucleotide phosphate, both derived from niacin, further straining the body's niacin reserves.[6] This case demonstrates the classical cutaneous manifestations of pellagra and the important association with iron deficiency. It underscores that pellagra, although rare, remains a possibility even in developed countries, where nutritional deficiencies can occur, highlighting the importance of ongoing awareness and consideration of this condition.

Potential conflicts of interest

The authors declare no conflicts of interest.

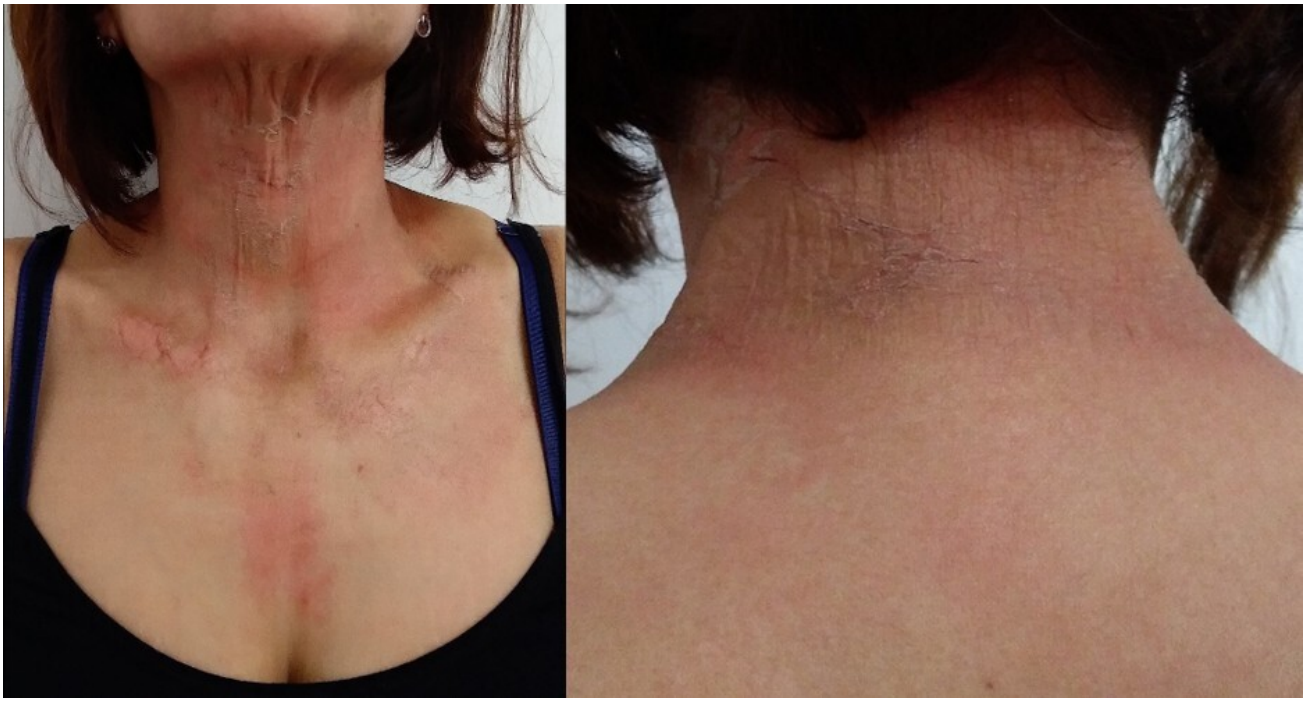

Figure 1. *Well-demarcated scaling, erythema, and hyperpigmentation affecting the photoexposed areas of the neck and upper chest.*

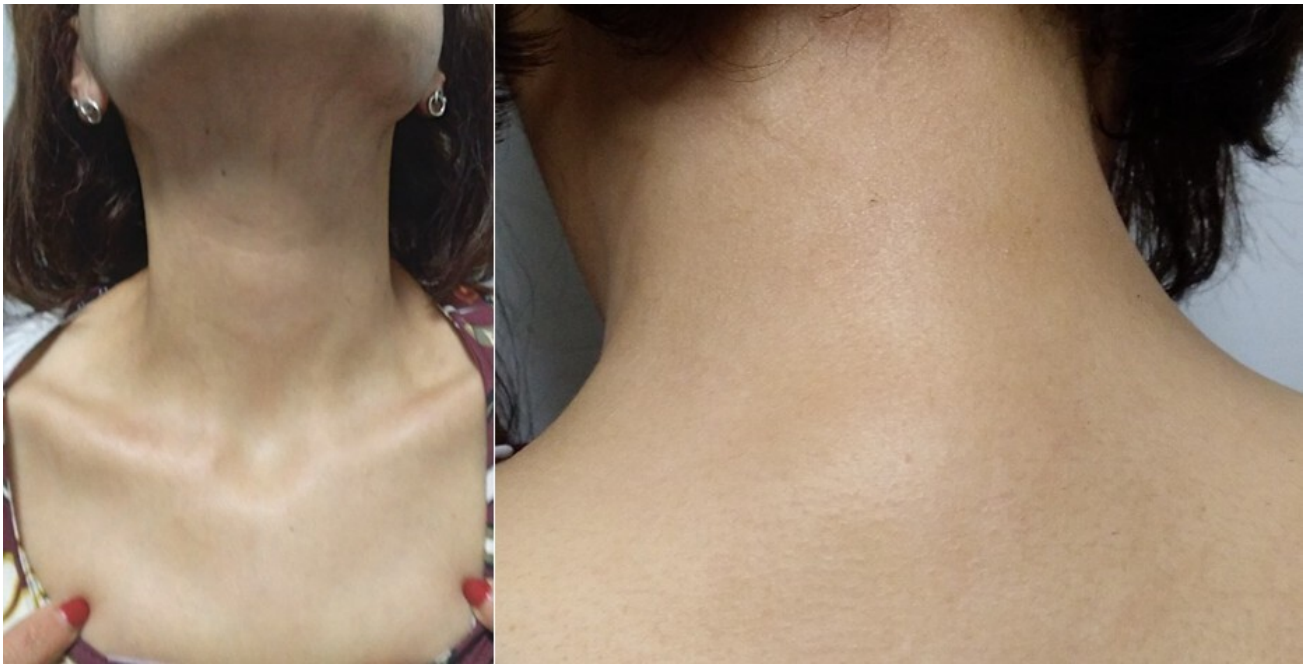

Figure 2. *Resolution of the skin eruption after 1 month of oral nicotinamide.*

Table 1. *Dietary Sources of Vitamin B3 (Niacin) and Their Contribution to Adult Daily Requirements.*

Dietary Source	Serving (g)	Niacin Content (mg)	Daily Requirements (%)	
			Men	Women
Beef liver (cooked)	85	14.7	91	> 100
Tuna (canned in brine)	85	11.3	71	81
Chicken breast (grilled)	85	10.3	64	74
Salmon (cooked)	85	8.5	53	61
Pork (cooked)	85	7.0	44	50
Fortified cereal	30	4.2	26	30
Brown rice (cooked)	1 cup	5.2	33	37
Peanuts (dry roasted)	28	4.1	26	29

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