Pellagra is a disease characterized by a lack of cellular niacin, generally caused by a dietary insufficiency of nicotinic acid (niacin) or its essential amino acid precursor tryptophan. Historically, systemic complications caused by niacin-deficient diets were of epidemic proportions, though the malady was nearly eradicated once government dietary supplementation programs began fortifying flour with B-vitamins during World War II. Nonetheless, pellagra still remains a threat in various niche patient populations across the developed world. Contemporarily, it is found only in patients with excessive leucine intake, patients who take medicines that inhibit or disrupt vitamin absorption, anorexics, and most often, patients who have malabsorptive gastrointestinal complications caused by a certain illness. We herein report a case of early-stage pellagra induced by chronic alcohol abuse and resolved with niacinamide treatment.

CASE REPORT

A 51-year-old man with a history of chronic alcohol abuse and an alcohol-related cognitive disorder visited our free clinic complaining of an intense pruritic skin rash that had been progressively worsening over the past two months. Upon examination, the primary care physician (PCP) observed “red, coalescing papulovesicular lesions above distribution with crusting” on the patient’s distal extremities. Of note, the patient explained that he had been previously treated with a ceramide-rich hydrating lotion and triamcinolone 0.1% emollience at an outside hospital, but exhibited no improvement or relief. Before referring the patient to the clinic’s staff dermatologist, the patient’s PCP initiated treatment with hydroxyzine 25mg PO TID for itching, suspecting a quetiapine-induced drug flare.

At the one-week follow up with the dermatologist, the patient stated that the hydroxyzine treatment led to only slight improvement of the severe pruritus and had no effect on the progressive eruption. The dermatologist reassessed the patient, noting instead the presence of moderate-to-severe eczematous dermatitis with numerous excoriated papules, some of which were perifollicular (none with evident purpura) on the dorsum of hands and distal extremities, ears, and slightly on the neck. The dermatitis spared protected areas except for waistline where there was involvement. Marginal glossitis was noted as well.

Due to the insidious nature of the skin eruptions and their inception having preceded the initiation of quetiapine treatment, the Seroquel drug-flare hypothesis was considered less likely to account for the cutaneous eruption. The patient’s continued long history of alcohol abuse, malnutrition, memory loss, depression, glossitis, and severe dermatitis were consistent with the causes and symptoms of vitamin B3 deficiency, satisfying the diagnostic criteria for pellagra. Consequently, the dermatologist prescribed niacinamide 500mg QD and OTC multivitamins QD, and discussed dietary management as well as proper sun protection techniques.

At the one-month follow up, the patient displayed a marked decrease of eczematous dermatitis and improved skin...
turgor with less desiccation. The healing excoriations indicated the resolution of pruritus, as well. The patient detailed rapid improvement of the pruritus and skin involvement upon starting niacinamide 500mg and MVI QD, indicating the successful diagnosis and appropriate treatment of vitamin B3 deficiency caused by alcohol-induced pellagra.

After one additional month of daily niacinamide 500mg and MVI, treatment was discontinued, as the clinical manifestations of pellagra were resolved. The patient decided not to attend the subsequent dermatology follow up, indicative of his improved affect post treatment.

**DISCUSSION**

Pellagra can be identified by a number of neurological, gastrointestinal, and integumentary clinical symptoms; however, the classic “Three Ds” of the disease (dementia, dermatitis, and diarrhea) are manifested differently in nearly every patient. Its present-day rarity, compounded with its idiosyncratic nature, makes it a very dangerous case for any physician despite the ease of treatment. In modern-day pellagra, the delay in recognition and treatment is the most dangerous risk factor for sequelae. In this case, an appreciation for the wide range of predisposing factors of the disease allowed an early diagnosis and prompt treatment of an otherwise fatal condition.

The history of epidemic pellagra and the history of vitamin deficient maize-based diets are one in the same. Gaspar Casal recorded the first case in 1735, correlating the disease outbreak with the influx of New World maize consumed by poor populations that could not afford high protein meals. Similarly, pellagra proliferated through the American South at the turn of the twentieth century when poverty stricken families were forced to abandon the costly proteinous parts of their diets with nutrient-poor milled corn. There were more than three million cases and 100,000 pellagra-related deaths in the United States between 1900 and 1940.

Unknown at the time, the shortage of niacin and tryptophan in the maize-based food supply was the culprit. After extensive dietary detective work by Dr. Joseph Goldberger and the expansion of dietary supplementation programs during WWII, pellagra was seemingly overcome. Although outbreaks of the disease are still found during major humanitarian crises in developing countries, diagnoses of pellagra are very scarce. One 2011 study of emergency room patients in Spain estimated that the current annual incidence is approximately only 0.5 pellagra cases per 100,000 patients.

Paradoxically, this past scientific success has now become a burden for our generation of physicians. The contemporary rarity of pellagra has limited the scope of clinical exposure to the illness, resulting in failure to recognize, diagnose, and treat in its early stages. Consequently, it is often mistaken for a vast array of different diseases or as in our case, an atypical, adverse drug reaction. This is due to the inconsistency of the clinical manifestations of dementia, dermatitis, and diarrhea in niacin deficient patients. For example, one hospital did a retrospective analysis of the seven pellagra patients it encountered over an 11-year span, and although all seven displayed a form of skin involvement, only three were diagnosed cor-

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*The common predisposing factors for pellagra are alcohol dependency, anorexia nervosa, excess leucine diets, peculiar food fads diets, and a history of disease or drugs that cause niacin or tryptophan-specific malabsorptive states. If any of these are present simultaneously with a clinical observation of any of the ‘Three D’s,’ pellagra should remain an option within the differential diagnosis process.*

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**Figure 2**

*The Three Ds of Pellagra*

Dementia • Dermatitis • Diarrhea

*These manifest differently in nearly every patient.*
rectly with pellagra initially. Meanwhile, only four displayed a neurological defect and only three experienced diarrhea. In another 42-patient pellagra study in which dermatitis was a prerequisite for diagnosis, only 10 exhibited any form of dementia. In a similar study of 18 patients, just four had the complete triad. Our patient manifested just the symptoms of dermatitis and dementia.

Several reports have commented on the fatal consequence of delaying the diagnosis of pellagra, highlighting the need for physicians to appreciate when the predisposing factors for niacin deficiency correlate with the varying presence of dementia, dermatitis, and diarrhea in any patient. The common predisposing factors for pellagra are alcohol dependency, anorexia nervosa, excess leucine diets, peculiar food fads diets, and a history of disease or drugs that cause niacin or tryptophan-specific malabsorptive states. If any of these are present simultaneously with a clinical observation of any of the “Three Ds,” pellagra should remain an option within the differential diagnosis. In our case, the malnourishment induced by chronic alcohol abuse was first marker for the patient’s niacin deficiency.

Fortunately, the one definitive way to diagnose and treat pellagra is to provide the patient with physiological doses of niacin or equivalent doses of its reciprocal amide, niacinamide. Treatment with these medications is simple, cheap, swift, and relatively harmless. Skin lesions and other clinical manifestations begin to resolve quickly if the diagnosis of pellagra is correct. Furthermore, if there is no sign of improvement, there is little to no risk in providing the patient with the physiological doses of either available form of Vitamin B3.

Of note, some physicians recommend taking 24-hour urine studies or blood samples for detecting abnormally low levels of niacin metabolites to confirm the diagnosis, but our free clinic does not have these capabilities.

Niacinamide, also known as nicotinamide, is very safe at physiological doses and has been frequently used to treat several other inflammatory skin conditions, most commonly necrobiosis lipoidica, bullous pemphigoid, acne vulgaris, rosacea and granuloma annulare. Furthermore, its widespread OTC use as a vitamin or supplement makes it a valuable treatment for uninsured patients who are diagnosed with pellagra, such as our own. The limiting side effects are flushing and plethora, which are less pronounced than with its precursor niacin secondary to the terminal amide substitution. The FDA approved, relatively non-toxic drug is ubiquitously used in cosmetic products with over 30 commercially consumed cosmetic formulations.

CONCLUSION

Pellagra is difficult to diagnose, easy to treat, and extremely important to recognize early to prevent systematic sequelae. In all patients in whom there is reason to suspect illness due to correlation of any of the “Three Ds” and its predisposing factors, a physiological dose of niacin or niacinamide is most likely warranted. Delaying the diagnosis may have much more serious consequences, and the absence of a response to Vitamin B3 replacement therapy will only further the diagnosis process. Patients with a history of chronic alcoholism and dermatis should be considered at-risk for pellagra.

Neither of the authors report any conflicts of interest.

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