Pellagra: A Sporadic Pediatric Case With a Full Triad of Symptoms

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GOAL

To describe a case of pediatric pellagra

OBJECTIVES

Upon completion of this activity, dermatologists and general practitioners should be able to:

1. Identify the underlying vitamin deficiency and foods associated with pellagra.
2. Discuss the causes of pellagra.
3. Describe the clinical presentation and diagnosis of pellagra.

CME Test on page 56.

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Pellagra is clinically manifested by a photosensitive dermatitis, diarrhea, and dementia. The full triad of symptoms is usually not well developed in infants and children. We report a case of a 14-year-old boy with classic symptoms of pellagra. All his symptoms responded to treatment with nicotinic acid.

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Pellagra, a deficiency disease caused mainly by a lack of niacin (nicotinic acid), is rarely seen in developed countries today. It is clinically manifested by the "three Ds": diarrhea, dermatitis, and dementia, and if it is not treated, results in death.[1] The full triad of symptoms occurs in only 22% of patients, and the classic symptoms of pellagra are usually not well developed in infants and children.[2,3] Even the photographs in pediatric textbooks that show

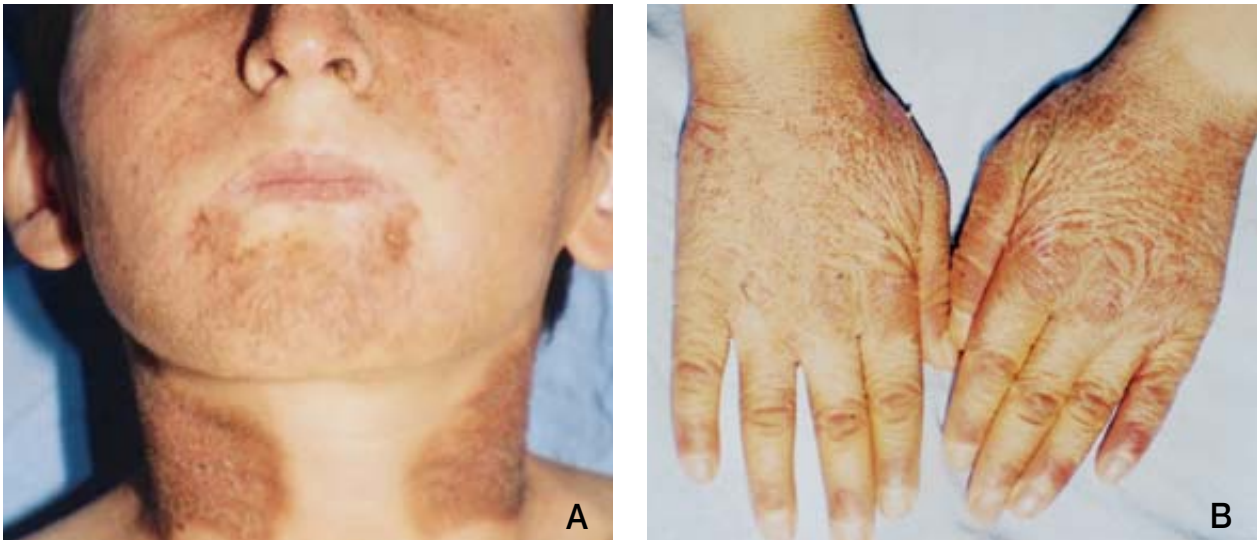

Figure 1. Hyperpigmented skin eruptions with scales on the face, around the neck (A), and on the dorsal aspect of the hands (B).

cutaneous lesions of pellagra are from adult patients.[3] The literature contains reports on many adult cases of pellagra associated with alcoholism, psychiatric disorders, diseases causing cachexia, malabsorption, and some drugs, but to our knowledge, there have been no reported pediatric cases with a full triad of symptoms in the English literature in the last 30 years. We report the case of a 14-year-old boy with pellagra who presented with diarrhea, dermatitis, and dementia, characteristic clinical findings of pellagra.

Case Report

A 14-year-old boy presented with intractable bloody diarrhea of 2 weeks' duration. He had received a 10-day course of metronidazole, but even after the treatment, the illness had not subsided. His mother noted that during the previous 4 years, the diarrhea, fatigue, and dermatitis had recurred during each spring and summer. There was no history of drug use. The patient's development in infancy had been normal, and he had completed a compulsory 5-year education. He had a mentally handicapped older sister; his older brother and 2 younger sisters were completely healthy.

On examination, the patient was depressed, disoriented, and uncooperative. He weighed 31.5 kg, was 140-cm tall, and his weight for height was greater than the fifth quantile (in accordance with the standards of the National Center for Health Statistics). There were symmetric hyperpigmented skin eruptions with scales on his face, around the neck, and on the dorsal surfaces of his hands. The lesions were sharply demarcated from the healthy skin (Figure 1, A and B). Physical examination was otherwise unremarkable.

Laboratory studies revealed a hematocrit level of 34.4%, a hemoglobin level of 12.2 gm/dL, and a white blood cell count of 6000/mm^3. The total serum protein and albumin levels were 5.4 and 3.3 gm/dL, respectively. Blood glucose, serum electrolyte levels, thyroid hormone levels, and chemistry panels were normal. Chromatography of blood and urinary amino acids was normal. The 24-hour urinary 5-hydroxyindoleacetic acid was 3.7 mg/24 h (normal, 2–9 mg/24 h). The stools were unformed and bloody. *Entamoeba histolytica* trophozoites and eggs of *Ascaris lumbricoides* were detected in his stools.

Skin biopsy specimen showed hyperkeratosis, irregular acanthosis, and papillomatosis, with vacuolar degeneration in the basal epidermal cells, as well as edema and perivascular lymphocytic infiltration at the papillary dermis. A diagnosis of pellagra associated with amebiasis and ascariasis was made. Treatment with nicotinic acid (300 mg/d), other members of the B complex vitamins, an adequate nutritional dietary regimen, metronidazole (30 mg/kg per day), diloxanide furoate (20 mg/kg per day), and mebendazole (100 mg twice daily for 3 days) was started. After 2 days of treatment, the patient was more alert, with improved depression and disorientation. All symptoms and findings disappeared within 2 weeks (Figure 2, A and B). Repeated stool examinations for *E histolytica* and *A lumbricoides* after the treatment yielded negative results.

Comment

Niacin forms part of 2 enzymes important in electron transfer and glycolysis: nicotinamide adenine dinucleotide and nicotinamide adenine dinucleotide phosphate. Although dietary tryptophan can partially

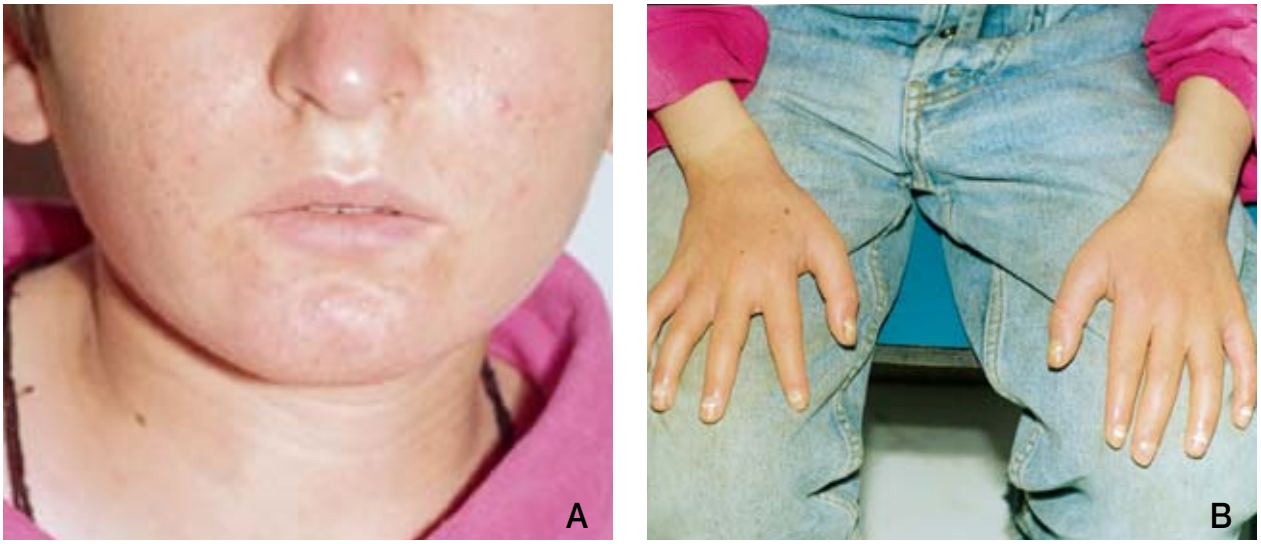

Figure 2. Appearance of the face, neck (A), and hands (B) after 2 weeks of treatment with nicotinic acid.

substitute for niacin, other sources of niacin are necessary. Liver, salmon, poultry, and red meat are good sources, but most cereals contain only small amounts of it. Milk and eggs, which contain little niacin, are good pellagra-preventive foods because of their high content of tryptophan.[3]

Although pellagra was common during the first half of this century in Western society, it is rarely seen in developed countries today.[4] However, it is still endemic among African refugees and in remote underdeveloped areas where cornmeal is the main constituent of the diet and green vegetables and red meat are not regularly available.[5-7] In developed countries, the traditional causes of pellagra, such as famine and malnutrition, have disappeared. Alcoholism, gastrointestinal disorders, psychiatric disorders, malabsorption, and diseases causing cachexia and anorexia nervosa are the current etiologic causes of pellagra in these countries.[8] Pellagra also has been reported in patients receiving isoniazid, pyrazinamide, hydantoin, ethionamide, phenobarbital, azathioprine, 5-fluorouracil, and chloramphenicol. Isoniazid, a structural analog of niacin, can cause suppression of endogenous niacin production; thus, pellagra is a well-recognized complication of isoniazid therapy for tuberculosis.[9] Because 5-fluorouracil inhibits the conversion of tryptophan to nicotinic acid, it may precipitate pellagra.[10] Pellagra also may occur in patients who have carcinoid syndrome, in which tumor cells divert tryptophan toward serotonin, thus depressing endogenous niacin production. Nevertheless, serotonin-producing tumors are rare in children. The diagnosis is usually made by finding increased urinary excretion of 5-hydroxyindoleacetic acid, the end product of serotonin metabolism.[11]

In developing countries, dietary deficiency of niacin still remains an important cause of pellagra.[6] Although Turkey is a developing country, agricultural products are varied and relatively cheap, and diseases directly related to undernutrition are not major public health problems. Vitamin deficiency disorders, such as scurvy, beriberi, and pellagra, are very rare and occur only in limited areas or among disadvantaged people. Our patient lives in a remote mountainous village with limited agriculture, where corn, a poor source of tryptophan, is a basic foodstuff. His family, with 5 children, is too poor to buy high-quality food like meat, milk, and eggs, which supports the finding of low total serum protein and albumin levels of our patient, pointing to a mild general malnutrition. The fact that pellagra developed in 1 of 5 children needs explanation, and the possible answer may be that our patient might be more selective in his diet and taste compared with his siblings.

Cutaneous lesions of disease are the most characteristic manifestations of pellagra.[12] They first appear as symmetric erythema of sun-exposed surfaces that may resemble sunburn and, in mild cases, may escape recognition. The lesions turn rough and scaly in one or more locations. A deficiency in urocanic acid caused by a reduction in histidine and histidase activity has been postulated as a possible mechanism of photosensitivity in pellagra; urocanic acid protects the skin from ultraviolet (UV) wavelengths by absorbing light in the UVB range.[8] Kynurenic acid, a metabolic by-product of the tryptophan-kynurenine-nicotinic pathway, accumulates in pellagra as a result of a deficiency of nicotinamide, which blocks the formation of kynurenic acid. Kynurenic acid induces a phototoxic reaction in skin subjected to long-wave UV radiation ranging from 350 to 380 nm.[8]

Severe disturbances of the digestive tract and

nervous system are late manifestations. Nervous symptoms include depression, disorientation, insomnia, and delirium. Manifestations in children who have parasites, as in our patient, or chronic disorders may be especially severe.[3]

Because vitamin levels are often nondiagnostic, diagnosis is based on clinical signs and symptoms and the patient's response to therapy. Rapid clinical improvement following vitamin substitution frequently confirms the clinical diagnosis.[3,4,12]

The symptomatology and histopathology of Hartnup disease usually resemble pellagra, and like pellagra, respond to treatment with niacin; therefore, pellagra must be distinguished from Hartnup disease. Hartnup disease is a rare autosomal recessive inborn abnormality of renal and intestinal transport involving the neutral amino acids.[13] Most children with Hartnup disease remain asymptomatic. In rare symptomatic patients, intermittent pellagralike photosensitive rash, attacks of cerebellar ataxia, and psychiatric disturbance are characteristic symptoms of this disease.[13] Chromatographic studies of urine show persistent aminoaciduria, particularly of tryptophan and indolic substances derived from tryptophan—a finding that establishes the diagnosis.[13]

Our case is notable for the presence of full-blown clinical pellagra appearing sporadically in a pediatric patient and emphasizes that, even in well-nourished populations, hypovitaminosis can occur in specific environments.

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