Kwashiorkor in Patients With AIDS

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Kwashiorkor, a form of severe protein-energy malnutrition that entails loss of lean body weight, occurs endemically among children in many parts of the world but also has been documented in adults. We report a case of kwashiorkor in an HIV-positive adult male. Cutaneous findings are striking, and skin, hair, and nails are affected. Although kwashiorkor occurs in patients with HIV-AIDS, the skin manifestations have not been emphasized in the dermatologic literature. Indeed, dermatologists may play a vital role in diagnosing this treatable condition.

Severe malnutrition is commonly seen in socially and economically deprived countries but occurs less frequently in the developed nations. Nutritional deprivation in developed urban areas is often considered of secondary importance compared with the patient's other medical problems. However, severe malnutrition can be a life-threatening illness. We report a case of kwashiorkor in an HIV-positive adult male presenting to a tertiary care center in a major urban area. This case illustrates the need for vigilance in identifying and treating potentially fatal nutritional deficiencies, which can occur in populations not historically described as high risk. Early diagnosis of kwashiorkor can be made by dermatologists because of the characteristic constellation of skin findings.

Case Report

A 40-year-old black male was admitted for shortness of breath associated with *Pneumocystis carinii* pneumonia. His medical history included documented HIV infection for 10 years and multiple opportunistic infections, including pulmonary *Mycobacterium tuberculosis*. He was receiving chronic trimethoprim-sulfamethoxazole prophylaxis. This bedridden, cachectic patient admitted alcohol and crack cocaine use.

Skin examination revealed dry, thin, flaccid skin with well-demarcated, hyperpigmented shiny patches and plaques. Confluent areas of superficial desquamation were present on the trunk, extremities, and face (Figures 1 and 2). Desquamation was accentuated in the weight-bearing regions. Linear fissuring was observed in flexures, most prominently over the antecubital and popliteal fossae. Mild tender edema of the lower extremities was noted in the context of overall muscle wasting. The patient displayed perioral hypopigmentation and cheilitis, as well as reddish brown hypopigmentation of the scalp hair, which he reported to be thinner and straighter than before (Figure 3). Oral candidiasis and inguinal lymphadenopathy were present.

Figure 1. The upper left arm shows peeling and erosions resembling "flaky paint."

The patient was alternately agitated and noncommunicative on admission. Lumbar puncture results were normal. Computed tomography of the head revealed moderate cerebral atrophy. Psychiatric evaluation documented a lack of attention and thought disorganization consistent with delirium, which was also confirmed by neurologic evaluation.

Laboratory studies revealed a white blood cell count of 8900 cells/mL, with a hematocrit level of 25.5%.

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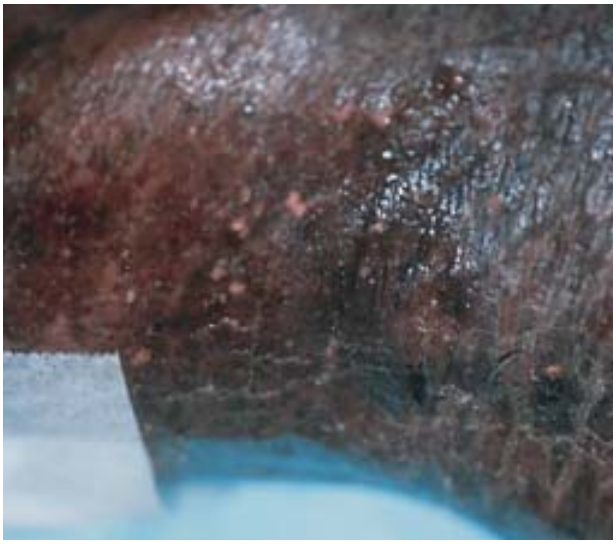

Figure 2. The posterior right thigh shows "crazy pavement" dermatosis, with linear fissuring over weight-bearing areas.

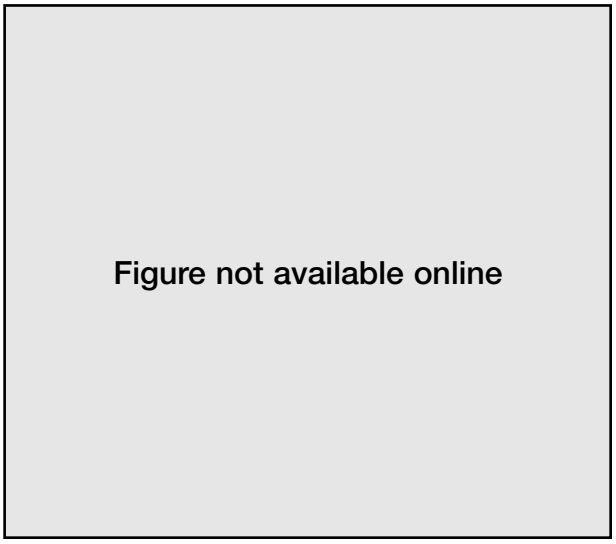

Figure 3. The face is wasted, with hyperpigmented patches and plaques suggesting "enamel paint." The hair shows loss of natural curl.

Thyroid function tests were T_4 of 4.46 μg/dL (normal, 5.41–11.66 μg/dL), T_3 of 14 ng/dL (normal, 76.91–134.7 ng/dL), and thyroid-stimulating hormone of 7.76 μIU/mL (normal, 0.34–4.25 μIU/mL). Morning cortisol was 34 μg/dL (normal, 5.0–25 μg/dL); zinc level was 62 μg/dL (normal, 60–130 μg/dL); and albumin was 3.0 g/dL. Fasting blood glucose was within normal limits, as were other chemistries and liver function tests. Urine toxin screen was positive for cocaine.

Biopsies were obtained from desquamated and nondesquamated areas on the upper and lower extremities and the trunk. Results of 2 of the 4 biopsies showed psoriasiform epidermal hyperplasia, with faint pallor of the upper epidermis (Figure 4A). Scattered necrotic keratinocytes, confluent parakeratosis, and incontinence of melanin were found (Figure 4B). Analysis of plucked hair from the scalp revealed decreased anagen bulbs, which were atrophic, with reduced pigment, shaft diameter, and root sheath thickness (Figure 5).

The patient received liberal lubrication with bland emollients. His nutritional intake remained low, his neurologic status deteriorated, and he died 2 weeks after admission. The family declined autopsy.

Comment

Kwashiorkor was first described in 1935 by Cecily Williams, who also introduced the term.[1-3] Within the general category of protein-energy malnutrition, kwashiorkor is characterized by hypoalbuminemia and edema rather than the carbohydrate depletion and severe cachexia of marasmus. Kwashiorkor usually occurs in children aged 1 through 3 years, whose diet is deficient in protein[4] and whose weight is 60% to 80% of expected levels.[5] Marasmic kwashiorkor is an intermediate stage with edema, accompanied by subcutaneous fat and muscle wasting.[2]

Recent research suggests that kwashiorkor may result not from protein deficiency but rather from a failure of adaptation to metabolic stresses.[6,7] Proposed mechanisms include the action of excess free radicals or of dietary toxins, particularly cyanogens and aflatoxins.[8-11] Efforts are under way to reclassify protein-energy malnutrition as kwashiorkor, marasmus, or various subtypes.[10]

Several tests have been used for the early detection of kwashiorkor. Protein-energy malnutrition can be estimated in a height-to-arm circumference ratio; decreased number of anagen bulbs on the scalp; increased proportion of old cells on mucous membranes; and decreased levels of prealbumin, serum transferrin, and hydroxyproline.[12]

A major skin finding[2,4,13-15] in kwashiorkor is depigmentation, which is more obvious in individuals who have darker skin. Perioral pallor, pretibial hypopigmentation, postinflammatory and postinjury depigmentation, and hypopigmentation preceded by erythema can occur.

Another characteristic skin manifestation of kwashiorkor is the so-called enamel paint appearance, which consists of hyperpigmented patches and plaques at skin sites prone to pressure and exposure to secretions or moisture. Thus, shoulders, elbows, knees, ankles, buttocks, and the trunk are commonly affected. The lesions of kwashiorkor usually spare those areas that are exposed to the sun, such as neck, dorsum of the hands, and forearms—areas that are typically involved in pellagra.

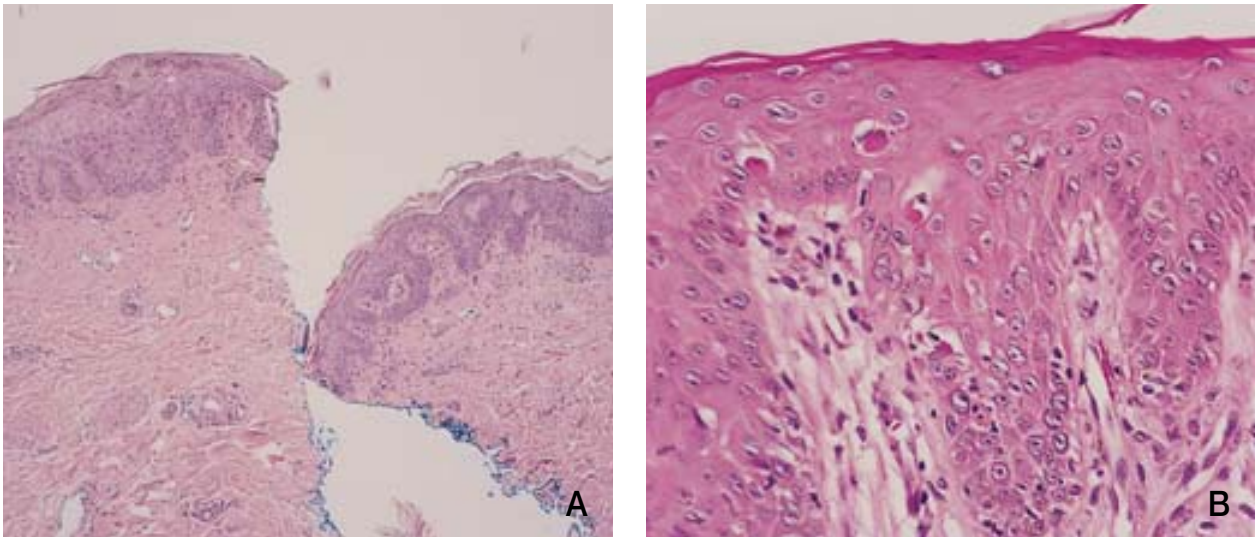

Figure 4. (A) All biopsies showed psoriasiform epidermal hyperplasia. Two of 4 biopsies showed faint pallor of upper epidermis (compare upper epidermis on left with that on right (H&E, original magnification ×40). **(B)** All biopsies showed scattered necrotic keratinocytes, confluent parakeratosis, and incontinence of melanin in addition to psoriasiform hyperplasia, features similar to those seen in pellagra (H&E, original magnification ×250).

Desquamation in kwashiorkor can be merely superficial or consist of severe peeling and erosions, with bulla formation over pressure points. Referred to as *flaky paint* or *crazy pavement dermatosis*, the desquamation can be accompanied by linear fissuring in the flexures. Fissuring is commonly seen at the base of the pinna, over the popliteal and antecubital fossae, in the axilla, between toes, at the foreskin edge, or at the centers or angles of the lips.

Hair changes[16] are characteristic and include diffuse hypopigmentation, reddish discoloration called *hypochromotrichia*, and the "flag sign" of alternating light and dark bands corresponding to periods of adequate and inadequate nutrition. Sparseness of hair; alopecia; loss of natural curl; and a dull, dry, and brittle hair texture are seen. The hair is easily plucked. Since hair changes occur before changes in serum protein and albumin, they may allow early diagnosis.[17] Nails in kwashiorkor are thin and soft.

Mucous membrane changes in kwashiorkor include a smooth, shiny red tongue due to atrophy of the papillae, angular stomatitis, cheilitis, oral ulcers, and perianal and perinasal ulcerations.

Skin findings like those in kwashiorkor are seen in acrodermatitis enteropathica, pellagra, riboflavin deficiency, and glucagonoma. Acrodermatitis enteropathica, which is similar to kwashiorkor from a dermatologic standpoint, is associated with a decreased zinc level; pellagra can be differentiated because of the characteristic photodistributed dermatosis; riboflavin deficiency has a typical angular stomatitis that is heaped up and sodden; and glucagonoma presents with an elevated glucagon level.

Histopathologic changes in kwashiorkor are poorly described, but both skin and hair are affected. On the scalp, anagen bulbs are decreased in number; they are severely atrophic, with reduction in shaft diameter, pigment, and internal and external root sheath thickness.

Skin changes in kwashiorkor are less well-defined. Psoriasiform epidermal hyperplasia can be seen occasionally, with a pallor of the upper epidermis that is similar to changes that can be observed in glucagonoma and other nutritional deficiencies. Necrotic keratinocytes, confluent parakeratosis, and incontinence of pigment are features described for kwashiorkor but also may be seen in pellagra.

Extradermatologic changes in kwashiorkor include growth failure, muscle wasting, diarrhea, edema of the legs and other areas, and an enlarged, fatty liver. Neurologic alterations[18], such as apathy and irritability, are frequent but partially reversible. The endocrine glands modify their function in response to amino acid deficiencies.[5,7,19] Cortisol and growth hormone levels are elevated, thyroxine is decreased, and glucose tolerance is impaired.

Kwashiorkor is generally considered a disease of children in developing countries, but as this case illustrates, it may be found in different populations.[20-21] Our patient was an adult with a history of drug use, urban residence, and AIDS. Yet he presented with the typical dermatologic, neurologic, and hematologic manifestations of kwashiorkor.

The presence of significant muscle wasting and decreased subcutaneous fat in our patient fit the criteria for marasmic kwashiorkor. Our patient also had various conditions that are indicative of a poor

Figure 5. Thin hairs with poorly developed or fragile internal root sheaths and atrophic bulbs are characteristic of kwashiorkor (×100).

prognosis in infant kwashiorkor[2,22]: total protein concentrations less than 3.0 g/dL; severe anemia and hypoxia; intercurrent infection, particularly measles and bronchopneumonia; persistent tachycardia and respiratory difficulty; and coma, stupor, or other changes in mental status.

Kwashiorkor and marasmus are common in patients infected with HIV.[23-30] In 1987, the US Centers for Disease Control and Prevention first classified AIDS as HIV seropositivity with wasting, or specifically, weight loss of greater than 10% over 2 months.[31,32] One study found that 68% of hospitalized patients with AIDS weighed more than 10% below their baseline levels.[33]

Both macronutrients, such as protein and fat, and micronutrients, including vitamins, minerals, and antioxidants, can be depleted in patients with AIDS.[30] The traditional "leaky bucket" metaphor suggests that AIDS patients continually lose both types of nutrients and cannot gain weight without correcting the underlying disease processes responsible.[34] Indeed, HIV-related cachexia is defined as a disproportionate loss of lean body mass that cannot be reversed simply by feeding.[30,35]

Malnutrition in HIV disease is multifactorial[30]: (1) oropharyngeal and esophageal lesions diminish oral intake[36]; (2) increased energy expenditure arises as resting energy expenditure increases at all stages of HIV-AIDS[30]; (3) metabolic alterations such as fasting hypertriglyceridemia are seen; (4) endocrine changes entail high serum cortisol and loss of diurnal rhythms[30]; (5) malabsorption due to enteric protozoal pathogens causes diarrhea[37] and steatorrhea[38] in most patients; and (6) systemic infections prevent weight gain.[36,39]

During a 2-year retrospective study, patients with AIDS averaged 4 nutrition-related complications.[27] HIV wasting also correlates with poor disease prognosis and mortality.[40] Consequently, strenuous efforts have been directed at nutritionally repleting HIV patients. Oral supplementation with micronutrients[41-44] and appetite stimulation with agents like megestrol acetate and dronabinol[30] have been attempted. Complete nutritional support via enteral and parenteral feeding also can be considered.[45] Prospective cohort studies have revealed that a specialized ingredient may be crucial in maintaining adequate nutritional status among patients who have HIV-AIDS.[46]

Protein-energy malnutrition, including both kwashiorkor and marasmus, is a well-recognized feature of AIDS. We believe this is the first paper that attempts to examine the cutaneous features of severe malnutrition in HIV disease. As is apparent, the weight loss experienced by patients with AIDS is consistent mostly with marasmic kwashiorkor, because lean muscle mass decline and its associated protein depletion predominate. In HIV, the standard features of starvation-induced kwashiorkor are complicated by additional metabolic and gastrointestinal effects related to systemic infection and acute immunosuppression. Interestingly, despite the substantial etiologic differences between kwashiorkor due to direct starvation and kwashiorkor due to AIDS wasting, the morphologic and histologic features are largely coincident. Also, in both types, impaired nutritional status predisposes to further morbidity and premature death.

Recognizing the features of kwashiorkor can enable dermatologists to appropriately alert other physicians caring for patients with HIV. Especially in the context of the multiplicity of clinical findings in HIV-AIDS, it is easy for caregivers to miss or misinterpret signs of severe malnutrition, which should be treated expeditiously.

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CONTINUED FROM PAGE 324

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