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Case report

Reversible generalized cutaneous hyperpigmentation: presenting manifestation of pernicious anemia

Filipa Diamantino[1], MD, Catarina Diamantino[2], MD, Andreia Mascarenhas[3], MD, and Maria João Lopes[1], MD

[1]Department of Dermatology, Hospital dos Capuchos, Centro Hospitalar de Lisboa Central, E.P.E, [2]Department of Pediatrics, Hospital do Espírito Santo, Évora, and [3]Department of Pediatrics, Hospital de Dona Estefânia, Centro Hospitalar de Lisboa Central, E.P.E, Lisbon, Portugal

Correspondence
Filipa Diamantino, MD
Serviço de Dermatologia
Hospital de Santo António dos Capuchos
Alameda Santo António dos Capuchos
1169-050 Lisbon
Portugal
E-mail: filipadiamantino@hotmail.com

Generalized acquired cutaneous hyperpigmentation is a challenging diagnostic problem. Although not frequently cited, hyperpigmentation can occur in patients with megaloblastic anemias from folate or vitamin B12 deficiency.[1–5] We report a patient who had hyperpigmentation as his presenting medical complaint and in whom pernicious anemia was the cause.

Case report

A 16-year-old boy presented with progressive and asymptomatic mottled hyperpigmentation that had been there for four years. The lesions had appeared initially on his arms and extended gradually over the years to involve the trunk, face, and extremities (Fig. 1). The palms and soles were prominently involved, and fingernails showed longitudinal hyperpigmented streaks (Fig. 2). The mucous membranes, teeth, and hair appeared normal. Systemic examination was unremarkable, and routine blood investigations were normal on first presentation. Histopathological examination of a skin biopsy revealed a lymphocytic inflammatory infiltrate in the upper dermis with numerous melanophages. Four months later, the patient began to complain of nausea, decreased appetite, significant weight loss, and worsening of cutaneous hyperpigmentation. Laboratory studies were performed, revealing pancytopenia (hemoglobin 8.0 g/dl, mean corpuscular volume 79, whole blood count 1270/mm^3, platelets 55,000/mm^3). The blood smear demonstrated marked anisocytosis and poikilocytosis, and the bone marrow aspirate showed megaloblastic changes. Vitamin B12 serum level was low (72.5 pg/ml), and folate level was normal. Anti-intrinsic factor antibody and antiparietal cell antibody were positive. Diagnosis of pernicious anemia was established and treatment with intramuscular cyanocobalamin started. The anemia responded dramatically to treatment, and the degree of hyperpigmentation decreased noticeably after nine months (Fig. 3). We conclude that the generalized cutaneous hyperpigmentation was secondary to vitamin B12 deficiency.

Discussion

The association between vitamin B12 deficiency and hyperpigmentation, although unusual, has been described. In most of the reported cases, the hyperpigmentation was confined to the dorsum of the hands and feet, particularly over the interphalangeal joints.[2,3,5] Few cases noted

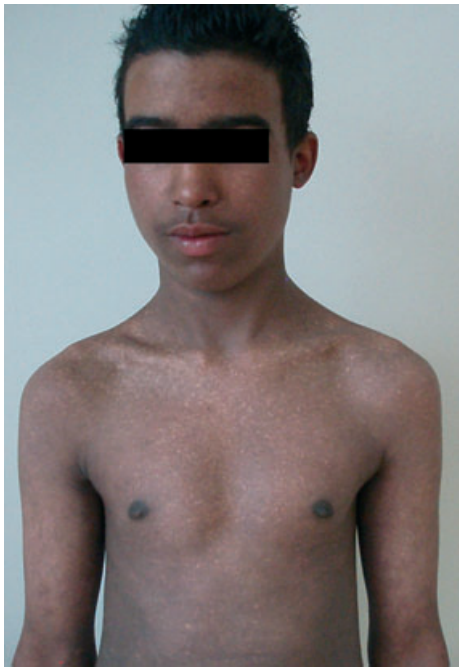

Figure 1 Patient at initial visit: generalized hyperpigmentation

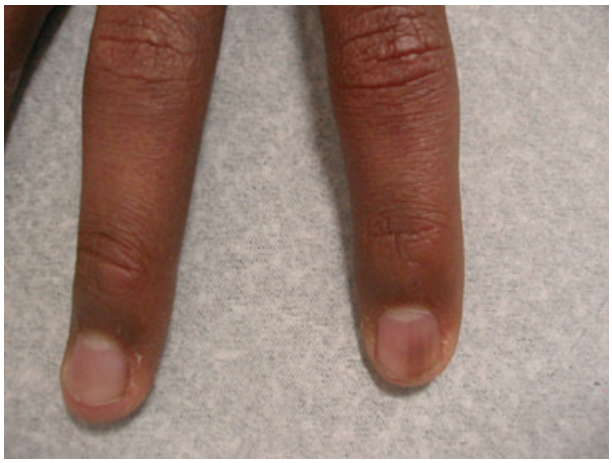

Figure 2 Longitudinal hyperpigmented streaks on the fingernails

generalized hyperpigmentation.[1,4] Nail pigmentation is an uncommon finding.

The mechanism of increased pigmentation in vitamin B12 deficiency is unknown. It has been suggested that the lack of vitamin B12 causes a decrease in intracellular-reduced glutathione levels, which normally inhibits tyrosinase activity in melanogenesis. Lack of this inhibitor would permit an increase in melanogenesis.[4] Another possibility could be a defect in melanin transport and its incorporation into keratinocytes with subsequent incontinence of pigment.[1]

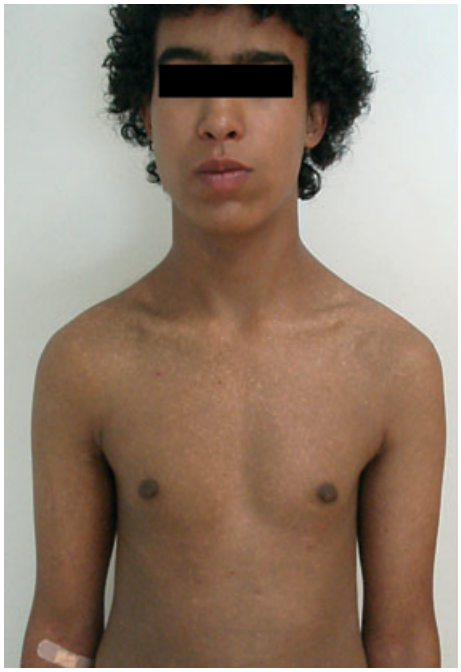

Figure 3 Patient at 9 months after initiation of vitamin B12 therapy showing dilution of skin hyperpigmentation

The most common cause of vitamin B12 deficiency is malabsorption, usually due to pernicious anemia.[5] Pernicious anemia is unusual in the pediatric population. When it occurs, symptoms include macrocytic anemia with megaloblastic bone marrow, neuropsychiatric defects, and gastrointestinal disturbances.[2]

In our patient, hyperpigmentation of the skin was the initial symptom of pernicious anemia, and only after four years did the patient develop anemia.

Our report suggests it may be worthwhile to consider the possibility of pernicious anemia in a patient with unexplained pigmentary changes. Early detection and adequate treatment will prevent partially irreversible neurological manifestations.

With a single exception,[2] there are no other reports of the association between vitamin B12 deficiency and acquired hyperpigmentation in the pediatric literature.

References

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