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B12 Hypovitaminosis Revealed by Melanoderma in an Infant: A Case Report

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Abstract **Case Report**

Vitamin B12 or cobalamin is a micronutrient found mainly in dairy and meat products. It is essential in the synthesis of DNA and RNA. In infants, hypovitaminosis B12 often causes neurological and hematological signs, and skin changes such as melanoderma are an uncommon manifestation. Blood count may not show anemia or macrocytosis, and decreased serum vitamin B12 associated with methylmalonic aciduria or total homocysteine levels confirm the diagnosis. Etiological assessment should also concern the mother. Early replacement treatment with vitamin B12 is the cornerstone of management. We report the case of B12 hypovitaminosis revealed by a delay in psychomotor milestones and stunted growth in height and weight associated with melanoderma, without anemia or macrocytosis on the blood count.

Keywords: Melanoderma, psychomotor developmental delay, B12 hypovitaminosis.

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INTRODUCTION

Vitamin B12 or cobalamin is a micronutrient obtained mainly from dairy and meat products. In combination with folic acid, vitamin B12 acts as a coenzyme in numerous metabolic reactions involved in the synthesis of DNA and RNA 8 [1]. In infants, its deficiency is classically manifested by neurological and hematological disorders and more rarely by dermatological abnormalities. We report a case of melanoderma revealing hypovitaminosis B12 without macrocytic anemia in an infant and reviewed the literature.

CASE REPORT

A 14-month-old infant with delayed psychomotor milestones (inability to sit without support or to stand), with no significant surgical history. Born at term, fed exclusively on breast milk until the age of 6 months when an attempt at dietary diversification proved unsuccessful. The patient was hospitalized for chronic vomiting that had progressed for several months, refusal of food and hyperpigmentation, associated with physical asthenia and observed weight loss. Physical examination noted an apathetic infant, with normal hemodynamic and respiratory exam, afebrile, weight and height were below the 3rd percentile, urine output was 1.3 cc / kg / h, urine dipstick was negative. Conjunctiva were normal in color while a generalized melanoderma was observed (Fig. 1).

Based on this clinical picture we suspected Allgrove syndrome in its incomplete form (without alacrymia) and dysthyroidism. A work-up was done and showed a cortisolemia at 8 0'clock within norms, coupled with the normal ACTH blood levels. Fibroscopy did not reveal achalasia or gastritis and the thyroid hormone levels were within norms. However, the complete blood count ordered showed normal hemoglobin level for age without macrocytosis, profound neutropenia and thrombocytopenia. The myelogram indicated in order to rule out a neoplastic origin showed images of megaloblastosis (Fig. 2) without malignant cells.

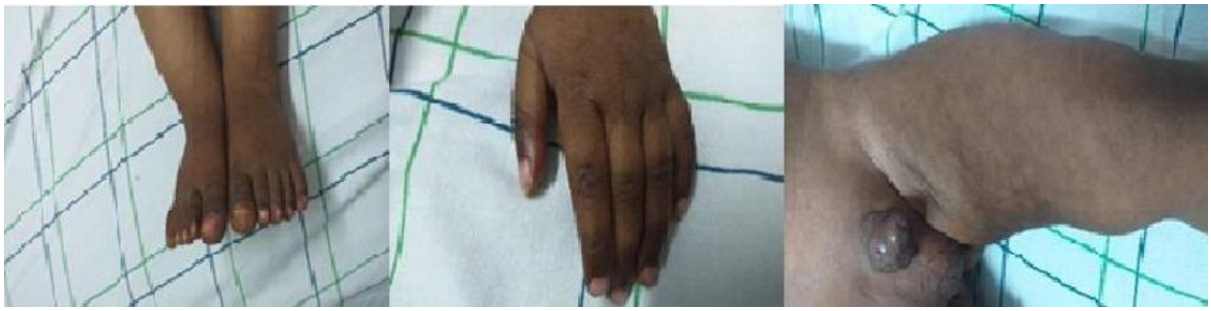
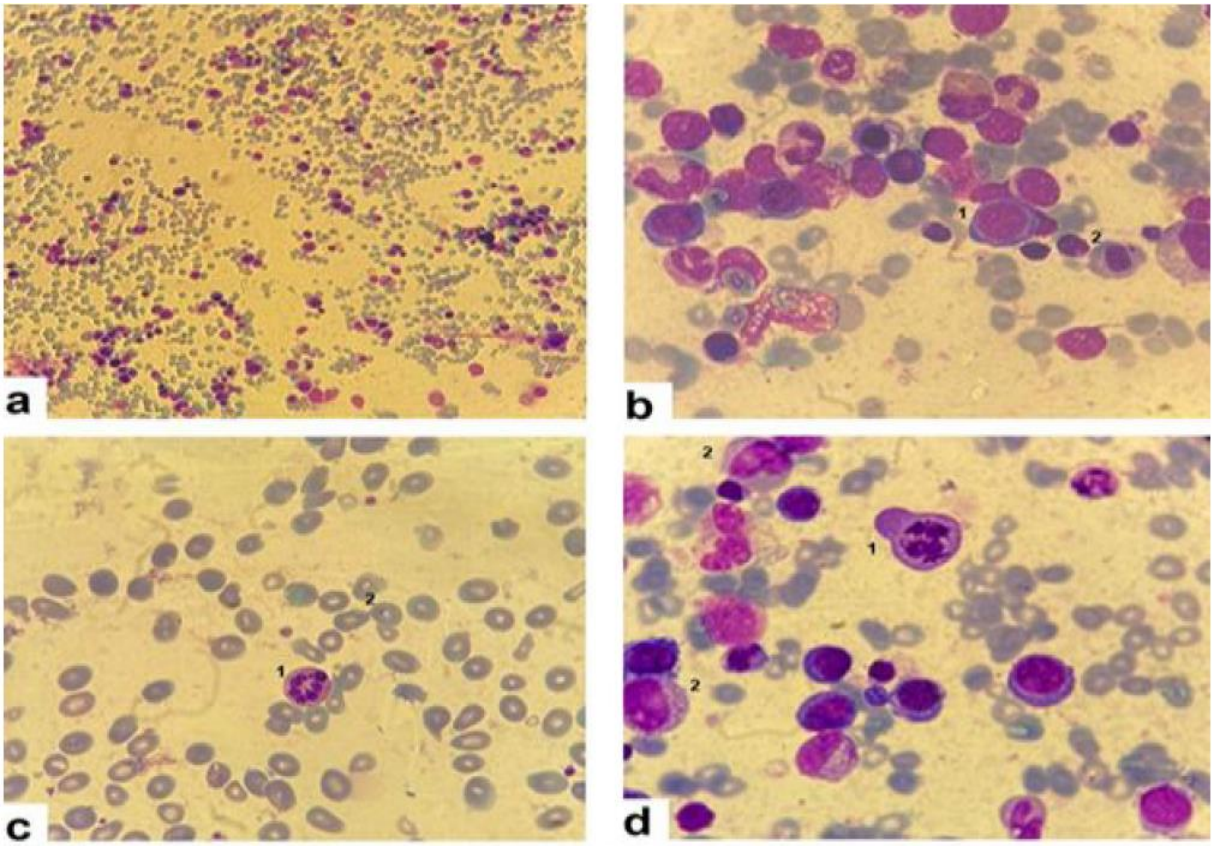


Figure 1: Melanoderma



(a) x20 ; Rich, blue marrow with megaloblasts. (b) x100 ; b1 = Erythroblast with nuclear-cytoplasmic asynchrony: nucleus with fine chromatin nucleolated with basophilic cytoplasm ; b2 = Cytoplasmic basophilic inclusions bodies. (c) x100 ; c1 = Hypersegmented neutrophils with 8 lobes ; c2 = Howell-Jolly bodies. (d) x100 ; d1 = Mitosis ; d2 = Giant myelocyte and metamyelocyte.

Figure 2

The serum vitamin B12 level was down to 100 pg / ml and that of vitamin B9 was normal. Methylmalonic aciduria and homocysteine testing were not performed due to lack of resources.

In view of the above, we concluded that there was B12 hypovitaminosis revealed by melanoderma, growth retardation affecting both height and weight, and delayed psychomotor development. The infant was put on replacement therapy with vitamin B12 at a dose of 1 mg / day for 3 days then 1 mg / week for 1 month then 1 mg/month for 6 months coupled with progressive nutritional rehabilitation. The short-term course was marked by clinical improvement with disappearance of melanoderma, progressive recovery of psychomotor capacities and regain of normal height and weight. A maternal assessment made showed vitamin B9 and B12 levels within the norms, without anemia.

DISCUSSION

Vitamin B12 or cobalamin is a micronutrient mainly from dairy and meat products. In combination with folic acid, vitamin B12 acts as a coenzyme in numerous metabolic reactions involved in the synthesis of DNA and RNA [1]. Vitamin B12, in its reduced form (mono- or divalent cobalt) is an essential coenzyme in two biochemical reactions (Fig. 3) [2].

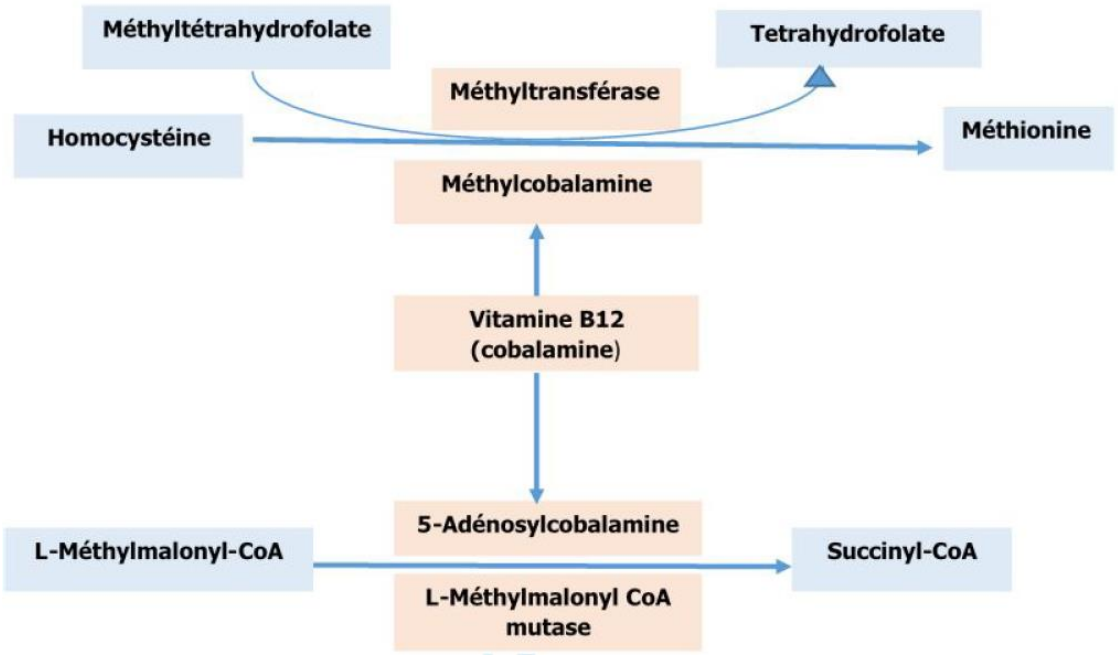


Figure 3: Role of vitamin B12 as a coenzym [2]

The first is the transformation of homocysteine to methionine by methylation in the cytoplasm; the second 1 converts methylmalonyl coenzyme A into succinyl coenzyme A in the mitochondria [3]. Cobalamin acts as a coenzyme essential for two biochemical reactions in the body, thereby reducing the concentration of two potentially toxic substances: homocysteine and methylmalonate, respectively responsible for vascular endothelial damage and metabolic acidosis [2].

The main cause of vitamin B12 deficiency in infants is maternal deficiency. This can be caused by a vegan diet, a low socio-economic level (developing countries with a low-meat diet) or digestive pathologies responsible for a lack of absorption (Helicobacter pylori infection, Biermer's disease , celiac disease or Crohn's disease, taking proton pump inhibitor) [1]. Our patient had a normal digestive tract assessment. Cobalamin delivery to the fetus is transplacental and usually builds up neonatal liver reserves for 6 to 8 months [4]. Maternal deficiencies cause a decrease in neonatal reserves and then a gradual decrease in levels in the months that follow if there is no other intake than breast milk. These situations initially described in children breastfed by malnourished mothers in developing countries such as India [5] can also occur in exclusively breastfeeding mothers when they are strict vegetarians or have Biermer's disease. In our study, the patient was the child of a vitamin B12 deficient mother who almost exclusively breastfed her baby until the age of 14 months due to the failure of dietary diversification.

Symptoms in infants appear between 4 and 8 months when due to antenatal deficiency or between 3 and 18 months when secondary to postnatal depletion of liver reserves [1]. The clinical signs most often at the origin of the diagnosis are pallor, weight loss, psychomotor regression, hypotonia and sleep disturbances [1, 2, 10]. Our patient had presented 30 these symptoms for the first 3 months of life. In infants, the deficiency is classically manifested by neurological and hematological disorders and more rarely by dermatological abnormalities. Among the skin signs, hyperpigmentation, as in our observation, is rare. Only isolated cases or small series have been reported. It is rather rare in children, as it has been reported in the majority of cases in 36 adults [6].

Our patient presented with generalized pseudo-Addisonian hyperpigmentation, as in the majority of cases [6]. Lesions in this form are found more often on photo-exposed regions, the palmar and dorsal surfaces of the feet and hands, the flexion folds, the tongue and the oral mucosa, the palmar folds, the nails and the perineum [7]. The hormonal work-up required to rule out endocrinopathy (Addison's disease and autoimmune dysthyroidism) which could lead to a similar hyperpigmentation was normal in our patient.

The mechanisms behind this hyperpigmentation are unknown. Several hypotheses have been proposed. For some, it is due to an increase in the synthesis of melanin by melanocytes. This would be linked to a disturbance in the action of the enzymes involved in this reaction. There is therefore a reduction in the action of tyrosinase, normally inhibited by glutathione, the intracellular level of which is reduced due to the vitamin B12 deficiency [8]. Besides hyperpigmentation, vitamin B12 deficiency can lead to glossitis which was absent in our patient. Hypotonia and retarded psychomotor development are the most frequently reported signs in infants as in our observation [9-11]. The diagnosis of vitamin B12

deficiency is confirmed by measuring the blood level of this vitamin and its two urinary and blood metabolites (methylmalonic acid and homocysteine), the sensitivity and specificity of which is higher to detect the deficiency [12, 13]. Methylmalonic acid and homocysteine levels were not obtained in our patient for lack.

In a study, Lindenbaum J *et al.*, [13] found that out of 141 consecutive patients with neuropsychiatric abnormalities due to cobalamin deficiency, 40 presented neither anemia nor macrocytosis as in our observation.

The treatment requires vitamin B12 by injection. In the majority of cases, it is prescribed at a dose between 500 and 1000 µg / day [9]. The pigmentation is reversible upon treatment, its disappearance being earlier in children (in 3 to 6 weeks) than in adults (in 2 to 4 months) [6].

CONCLUSION

B12 hypovitaminosis should be considered in any infant who presents with delayed psychomotor milestones, stunted growth and melanoderma even in the absence of anemia or biological macrocytosis. The rapidity of diagnosis and therapy by replacement therapy not only improves or reverses impairments observed but also, and above all, eliminates damage, especially irreversible neurogical damage.

Conflict of Interest: None

Consent for Publication: A written informed consent was obtained from our patient's parents.

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