

## Reticulate pigmentation associated with vitamin B<sub>12</sub> deficiency

Sir,

Vitamin B<sub>12</sub> deficiency is common in India, as a majority of the population is vegetarian.<sup>[1]</sup> Infants of vitamin B<sub>12</sub> deficient mothers are likely to be deficient and they can display various systemic manifestations of vitamin B<sub>12</sub> deficiency. Alterations in skin pigmentation has been described as a clinical manifestation of B<sub>12</sub> deficiency.<sup>[2]</sup> We present a case of a 5-month-old infant who presented with an unusual pattern of cutaneous pigmentation on the extremities associated with vitamin B<sub>12</sub> deficiency.

A 5-month-old-infant was brought to us with reticulate hyperpigmentation of upper and lower limbs of one month duration. Hyperpigmentation started on the lower limbs [Figure 1] and slowly progressed to affect the upper limbs. It was an asymptomatic brownish reticulate pigmentation pattern resembling livedo reticularis. His mother was from a low socioeconomic background and the child was exclusively breastfed. The mother was a pure vegetarian who did not take vitamin B<sub>12</sub> supplement during pregnancy or lactation. His weight was 4.7 kg (50<sup>th</sup> centile) and head circumference was 39 cm (<3<sup>rd</sup> centile). The baby had severe pallor. Systemic examination was unremarkable. He had delay in achieving gross motor and personosocial milestones. On laboratory examination, he had anemia (hemoglobin 5.8 g/dL) and thrombocytopenia (platelet count  $61 \times 10^3/\text{mm}^3$ ). The total leukocyte count (TLC) was normal  $8.2 \times 10^3/\text{mm}^3$

( $6-17.5 \times 10^3/\text{mm}^3$ ). His hematological indices—mean corpuscular volume (MCV) 101 fL (70–86 fL), mean corpuscular hemoglobin 38.8 pg (25–35 pg), mean corpuscular hemoglobin concentration (MCHC) 39.2% (30%–36%)—suggested macrocytic anemia. Vitamin B<sub>12</sub> deficiency was suspected on clinical grounds and hematological data. Blood sample for serum vitamin B<sub>12</sub> was sent. Unfortunately, the sample got hemolysed and as vitamin B<sub>12</sub> supplementation had already been started, a repeat sample could not be sent. The patient was given a single intramuscular injection of 500 µg of vitamin B<sub>12</sub> along with daily supplementation of 5 µg of vitamin B<sub>12</sub>, folic acid 0.5 mg, and ferrous fumarate 100 mg as a syrup formulation (syrup Vitcofol®). At one month followup, cutaneous hyperpigmentation disappeared completely [Figure 2]. His general wellbeing improved. He was playful and had started catching up on his motor milestones. His hematological indices normalized one month after treatment (hemoglobin: 12.2 g/dL; MCV 80.5; MCH 26 pg; MCHC 32.5%; TLC  $9000/\text{mm}^3$ , and platelet count  $188 \times 10^3/\text{mm}^3$ ). The patient was continued on daily supplementation of vitamin B<sub>12</sub> for 3 months and advised dietary management. Although vitamin B<sub>12</sub> levels were not available in this case, circumstantial evidence, based on improvement in hematological picture and disappearance of cutaneous pigmentation after 1 month of vitamin B<sub>12</sub> supplementation, strongly suggests that the cutaneous hyperpigmentation was due to vitamin B<sub>12</sub> deficiency.

Dietary B<sub>12</sub> is obtained mainly from foods of animal origin. Hence childhood vitamin B<sub>12</sub> deficiency is common in some parts of India where people follow strict vegetarian diet. Exclusively breastfed infants of vegetarian mothers are at a higher risk.<sup>[3]</sup> Dermatological manifestations of B<sub>12</sub> deficiency include cutaneous and mucosal hyperpigmentation.<sup>[4]</sup> The pigmentary changes have been described as deep brown or



**Figure 1:** Reticulate hyperpigmentation on lower limb

brownish-black hyperpigmentation predominantly affecting hands and feet (especially the knuckles, periungum, and palmar creases) and oral mucosa.<sup>[4]</sup> Occasionally, hyperpigmentation is accentuated on the pressure points such as elbows, malleoli, and knees.<sup>[5]</sup> Nail changes and premature graying have also been reported.<sup>[6]</sup> The cutaneous hyperpigmentation in our child was present in a reticulate pattern along with typical hematological manifestations of vitamin B<sub>12</sub> deficiency. Furthermore, the dermatological and hematological manifestations improved after vitamin B<sub>12</sub> supplementation. Such a pattern of pigmentation with vitamin B<sub>12</sub> deficiency has not been described earlier. Extracutaneous manifestations of vitamin B<sub>12</sub> deficiency include megaloblastic anemia and an array of neurologic changes, from personality alteration and poor school performance to hypotonia, ataxia, or seizures.<sup>[6]</sup> Our patient had delay in achieving milestones at presentation. He quickly started catching up on milestones after vitamin B<sub>12</sub> supplementation.

Various mechanisms have been suggested to explain hyperpigmentation associated with vitamin B<sub>12</sub> deficiency. According to one hypothesis, the deficiency of vitamin B<sub>12</sub> decreases glutathione levels which in turn activates tyrosinase and leads to increased melanogenesis.<sup>[7]</sup> In another hypothesis, hyperpigmentation has been attributed to a defect in the melanin transfer between melanocytes and keratinocytes, resulting in pigmentary incontinence.<sup>[8]</sup> Appropriate treatment results in dramatic clinical and laboratory response in most patients, particularly, in hematologic and cutaneous changes.<sup>[3]</sup> However, neurologic damage may persist.<sup>[9]</sup> The long-term prognosis of B<sub>12</sub> deficiency is related to the severity and duration of deficiency, underlining the importance of early diagnosis and treatment based on cutaneous findings.

The National Anaemia Prophylaxis Programme in India mandates folic acid and iron (0.5 mg and 100 mg, respectively) supplementation.<sup>[10]</sup> However, vitamin B<sub>12</sub> supplementation for



**Figure 2:** Complete disappearance of pigmentation after one month of treatment

young girls and pregnant women has not been recommended. These guidelines are derived from western data where majority of population is nonvegetarian unlike most Indian women. Since many of the serious consequences of B<sub>12</sub> deficiency could be prevented through proper supplementation, it seems reasonable to recommend that women take supplemental B<sub>12</sub> while they are pregnant or breastfeeding, especially if they are vegetarian. This case highlights the need to review current practices of vitamin supplementation among pregnant Indian women.

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#### Conflicts of interest

There are no conflicts of interest.

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