

Knuckle Pigmentation: A Clue to Systemic Illness

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Received: 29 March 2016 / Accepted: 30 May 2016 / Published online: 4 June 2016
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Description

A 50-year-old female, consuming mixed non-vegetarian diet, presented to our out-patient department with easy fatigability, tiredness and dyspnea of 3 months duration. On examination she had severe pallor but systemic examination of the cardiovascular, respiratory, gastrointestinal and neurological systems were within normal limits. Detailed general examination revealed hyperpigmentation of skin over the knuckles of both hands (Fig. 1). Investigations showed hemoglobin of 73 g/L with mean corpuscular volume (MCV) of 116.7 fL, mean corpuscular hemoglobin of 38.8 pg, mean corpuscular hemoglobin concentration of 38.8 % and red cell distribution width of 30.6 %. She also had mild thrombocytopenia ($137 \times 10^5/\mu\text{L}$). Total leukocyte count was $4100/\mu\text{L}$ and reticulocyte

count was 4 % (Corrected reticulocyte count—1.95 %). Peripheral smear examination showed marked anisopoikilocytosis with macroovalocytes and hypersegmented neutrophils (Fig. 2). Serum lactate dehydrogenase (LDH) was 840 IU/L (normal <480 IU/L). Serum chemistries were within the normal range. Her plasma cyanocobalamin was 144 pg/mL (normal: 187–883 pg/mL). Gastroduodenoscopy and antral biopsy showed features of atrophic gastritis. Her serum tested positive for anti-parietal cell antibody, hence confirming the diagnosis of Addisonian pernicious anemia. She symptomatically improved with parenteral hydroxycobalamine—1000 µg intra muscular (im) injection given every third day for seven injections. Her hemoglobin at 1 month follow up improved to 94 g/day and MCV 100.1 fl with improvement in thrombocytopenia ($256 \times 10^5/\mu\text{L}$). She was put on lifelong vitamin B12 prophylaxis (1000 µg im every month) and asked to follow up yearly with complete blood count and red cell indices.

Vitamin B12 deficiency is under recognized and under diagnosed even though it produces a wide array of pathological manifestations [1]. Reversible knuckle and oral mucosal pigmentation are external markers of vitamin-B12 deficiency in addition to recurrent angular stomatitis, cheilitis and rarely polymorphic cutaneous eruption [2]. This hyperpigmentation was first observed to be associated with macrocytic anemia by Dr. Bramwell Cook in 1944. He also found that both were responsive to crude liver extract [3]. Knuckle hyperpigmentation has been observed to occur in about 19.0 % patients with megaloblastic anemia and sometimes may be the only marker of vitamin-B12 deficiency [4]. It occurs as a result of reduced intracellular glutathione leading to increased melanin synthesis as well as some degree of melanocyte pigmentary incontinence and reverses with supplementation of vitamin-B12 [5].

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Fig. 1 Clinical photograph showing hyperpigmentation of skin over the knuckles of fingers of both hands

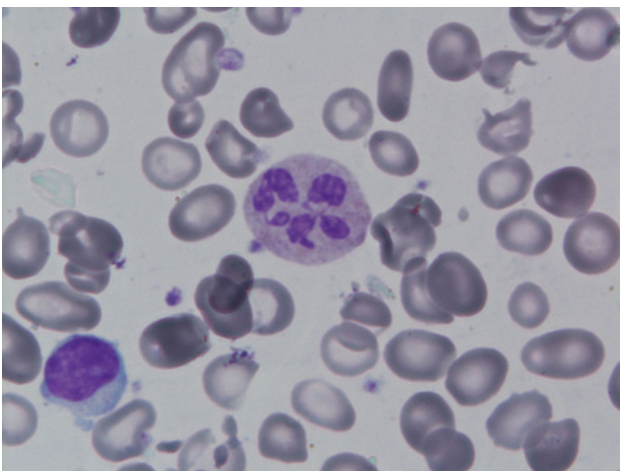


Fig. 2 Photomicrograph of peripheral blood film, showing anisopoikilocytosis with macroovalocytes and a hypersegmented neutrophil in the centre. (magnification $\times 400$)

Careful clinical examination for knuckle hyperpigmentation should be done in any patient, especially elderly individuals presenting with anemia, neurological symptoms and fatigue as it may help to clinch the clinical diagnosis of vitamin B12 deficiency.

Take Home Message

- Vitamin B-12 deficiency is an under recognized, easily correctable cause of anemia, fatigue and neurological symptoms.
- Knuckle hyper pigmentation is an important external marker which gives a clue to the diagnosis of Vitamin B-12 deficiency.
- Careful clinical examination of this subtle and at times only clinical sign is of paramount importance to make a correct diagnosis and instituting proper treatment before serious neurological complications sets in.

Compliance with Ethical Standards

On behalf of all the co-authors (listed above) I would like to state that this work has not been submitted currently elsewhere in any other journal.

Conflict of interest No conflict of interest by any of the authors.

Ethical Approval Conducted study did not involve any animal requiring approval for the same.

Informed Consent Informed Consent was obtained from all individual participants included in the study.

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