

## Case Report

# Clinical Sign Revisited: Knuckle Hyperpigmentation Associated with Vitamin B12 Deficiency

Monica Gupta<sup>1\*</sup> and Ram Singh<sup>1</sup>

Department of Medicine, Government Medical College and Hospital, India

**\*Corresponding author:** Monica Gupta, Department of Medicine, Government Medical College and Hospital, 1156-C, 32-B, Chandigarh-160030, India**Received:** May 24, 2014; **Accepted:** June 12, 2014;**Published:** June 14, 2014**Abstract**

Pancytopenia due to vitamin B12 deficiency is very common in the predominantly vegetarian population. Here we emphasize the clinical sign of knuckle hyper pigmentation as an important clue towards the etiology of pancytopenia.

**Keywords:** Hyperpigmentation; Vitamin B12; Deficiency**Case Presentation**

A 17-year-old boy presented with three months history of worsening fatigue, dyspnea on exertion and general weakness. There was no history of fever, loose stools, steatorrhea, diabetes mellitus or tuberculosis. He was lacto vegetarian, non-smoker, non-alcoholic with unremarkable past history or drug history. On examination he was extremely pale, had mild icterus, glossitis, lusterless hair and splenomegaly. Romberg's sign was positive and he had bilateral loss of vibration and position sense. Patient had generalized increased skin pigmentation, however characteristically the patient had prominent bilateral knuckle hyperpigmentation (Figure 1).

The investigations revealed severe pancytopenia; the hemoglobin was 1.8 g/dl, total leucocyte count was 3100/mm<sup>3</sup> and the platelets were 42,000/mm<sup>3</sup>. The Mean Corpuscular Volume (MCV) was 124fl and Mean Corpuscular Hemoglobin Concentration (MCHC) was 38g/dl. The reticulocyte count was 0.5%. The peripheral blood film revealed anisocytosis, hypersegmented neutrophils, macrocytes and macroovalocytes. Serum folate levels were 2.9ng/ml (normal 3.6-20ng/ml) and serum cobalamin levels were 72pg/ml (normal 180-900pg/ml). Bone marrow demonstrated severe megaloblastic erythropoiesis. A diagnosis of megaloblastic anemia due to combined cobalamin and folate deficiency was made. Patient was managed with blood transfusions, folic acid tablets, parenteral cobalamin supplementation and nutritional counseling. The pancytopenia improved with therapy in two weeks and hyperpigmentation partially improved over the next three months.

**Discussion**

Megaloblastic pancytopenia due to cobalamin and folate deficiency occurs usually in the age group of 10-30 years with female preponderance. The predominant symptoms are fatigue, anorexia and gastritis, low grade fever, shortness of breath, palpitations and mild jaundice [1]. Common physical findings include pallor (85%), glossitis (29%), and mild icterus (25%) and generalized hyper pigmentation (18%) [1]. Although commonly encountered in clinical practice, knuckle hyper pigmentation has been rarely reported as the presenting manifestation of vitamin B12 deficiency. Hyperpigmentation of the extremities especially over the dorsum of the hands and feet, with accentuation over the inter-phalangeal joints

and terminal phalanges associated with pigmentation of oral mucosa is characteristic of vitamin B12 deficiency [2].

Besides vitamin B12 deficiency, knuckle hyper pigmentation may be a part of the generalized hyper pigmentation as seen in certain ethnic groups, Addison's disease, thyroid disease, hemochromatosis and rarely homocystinuria. The generally accepted mechanism of this pigmentation is an increase in the melanin synthesis [3]. The other hypothesis proposed are 1) Deficiency of vitamin B12 decreases the level of reduced glutathione, which activate tyrosinase and thus leads to transfer to melanosomes. 2) Defect in the melanin transfer between melanocytes and keratinocytes, resulting in pigmentary incontinence [3].

The main source of vitamin B12 (cobalamin) in humans is the consumption of meat, poultry and dairy products. The recommended dietary allowance for a standard adult is 2.4µg/day. Generally vitamin B12 deficiency is seen in nutritionally poor diet in low socio-economic groups, vegans and vegetarians, pernicious anemia, chronic drug intake (e.g. phenytoin and acid-suppressing medication), increased requirements during growth and pregnancy and in malabsorption syndromes [1]. It is also observed in patients with eating disorders

**Figure 1:** Clinical picture showing bilateral knuckle hyperpigmentation

like anorexia nervosa, bulimia nervosa, pica or other psychiatric disorders.

Knuckle hyperpigmentation associated with vitamin B12 deficiency may have additional features of myeloneuropathy of posterior and lateral columns, white matter demyelination and cognitive impairment, cranial and peripheral or autonomic neuropathy. Other cutaneous changes observed with B12 deficiency include atrophic glossitis, brittle hair, dermatitis and recurrent angular stomatitis and cheilosis and uncommonly vitiligo [3].

In our patient, combined folate and cobalamin deficiency was present, and although the typical hyperpigmentation was attributable to cobalamin deficiency, the contribution of folate deficiency cannot be completely ignored. Indeed, rarely hyper pigmentation may be associated with isolated folate deficiency; very few such cases have been reported in alcoholics and pregnant women.

### Learning points

Vitamin B12 deficiency is very common in the general population. Its manifestations range from subtle signs to grave neurological features. Hyperpigmentation is typically seen in many vitamin B12 deficient individuals. Nutritional counseling and supplementation is very important to arrest the progression of the disease.

### References

1. Khanduri U, Sharma A. Megaloblastic anemia: prevalence and causative factors. *Natl Med J India* 2007; 4: 172-175.
2. Agrawala RK, Sahoo SK, Choudhury AK, Mohanty BK, Baliarsingha AK. Pigmentation in vitamin B12 deficiency masquerading Addison's pigmentation: A rare presentation. *Indian J Endocr Metab* 2013; 17: 254-256.
3. Mori K, Ando I, Kukita A. Generalized hyperpigmentation of the skin due to vitamin B12 deficiency. *J Dermatol* 2001; 28: 282-285.