

# Celiac Disease Presenting a Vitamin B12 Deficiency Associated Reversible Hyperpigmentation

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## Abstract

Hyperpigmentation is a known manifestation of Vitamin B12 deficiency but Vitamin B12 deficiency presenting with chief complaint of hyperpigmentation is relatively rare. We report a case of coeliac disease with nutritional anemia (vitamin B12, S. folate, iron) and vitamin B12 deficiency associated hyperpigmentation. Hyperpigmentation in this case was reversible and improved on B12 supplementation.

**Keywords:** Celiac disease; Hyperpigmentation; Vitamin B12 deficiency

## Introduction

Celiac disease, also known as gluten-sensitive enteropathy, can be defined as a permanent intolerance to wheat gliadins and other cereal prolamins in a genetically susceptible individual. There is presence of characteristic, though not specific, lesions in the small intestine leading to impaired absorption of various nutrients. Upon withdrawals of the responsible cereals these lesions improve.

Celiac Disease is associated with a number of autoimmune and inflammatory diseases, implicating a common genetic background. Celiac Disease may be considered an archetype malabsorption syndrome and is a frequent cause of anemia without associated intestinal symptoms. Anemia has frequently been reported as the only manifestation or the most frequent extra-intestinal symptom of Celiac Disease [1]. There are a number of skin manifestations of celiac disease (Table 1).

Skin disorders associated with celiac disease
Acquired ichthyosis
Cutaneous vasculitis
Cutaneous amyloid
Dermatitis herpetiformis
Eczema
Epidermal necrolysis
Nodular prurigo
Pityriasis rubra pilara
Pustular dermatitis

**Table 1:** Skin disorders associated with celiac disease.

Dermatitis herpetiformis is the most common, occurring in up to 24 percent of adult patients with celiac disease [2,3]. A few reports have suggested an association between psoriasis and elevated levels of antibodies to gliadin, reticulin, or tTG, but a strong association between psoriasis and celiac disease has not been documented [4,5]. Similar to celiac disease, anti-tTG antibodies are elevated in patients with dermatitis herpetiformis, confirming the pathogenic similarities between these diseases [6].

Various dermatological manifestations associated with B12 deficiency are skin hyper- or hypopigmentation, angular stomatitis and hair changes [7]. Hyperpigmentation as the primary presenting symptom of B12 deficiency is rarely reported in the literature [8]. Here we present a case of coeliac disease with nutritional anemia (vitamin B12, S. folate, iron) and vitamin B12 deficiency associated hyperpigmentation.

## Case Report

A-20-year old female from Eastern part of India (Saharsa district of Bihar) came to General Medicine OPD of AIIMS Patna (a tertiary care centre at Patna), with progressive blackish discoloration of hands and feet for 1 year. This was associated with gradual loss of weight and generalized weakness. There was no history of any significant illness in past including tuberculosis, jaundice etc.; menstrual history was suggestive of irregular menstrual cycles for past 4-5 months.

On examination Pallor was present but there was no icterus / cyanosis/oedema/lymphadenopathy. Pulse-78/min, BP-Right arm-102/68 mmHg; Left arm-98/66 mmHg. Chest-Bilateral vesicular breath sounds, no added sounds; Cardiovascular-S1, S2 heard, no murmur; Abdomen- Soft, no organomegaly, CNS-WNL.

There was hyperpigmentation present over dorsum of fingers and toes, palmar and plantar aspect of hands and feet, nasal bridge, nasolabial folds. On investigation her hemogram was suggestive of macrocytic anemia with leukocytosis and raised ESR. There was low serum Vitamin B12, folate, iron, ferritin and high TIBC (Table 2).

TLC	13.5 × 109 /L
N- 81/L- 14/E- 02/M- 03/B- 00	
Platelets	214×109 /L
Hb	7.5 g/dl
MCV	112.9 fl
MCH	33.3 pg
MCHC	29.5 g/dl
ESR	70 mm
CRP	0.20 mg/dl (normal)
PBS	Macrocytic hypochromic anemia
ANA	Negative
TSH	2.95 µU/ml
FT4	17.03 pmol/L
Urine R/M	WNL
24 h Urinary Protein	59.8 mg
Serum Vitamin B12	199 mg/dl (low)
Serum folate	4.29 ng/ml (low).
Intrinsic factor IgG antibody	Negative-10.4 U/mL (Normal <12 U/mL)
Iron profile s/o iron deficiency anemia	
S. ferritin	9.4 ng/ml (low)
S. iron	13 µg /dL (low)
TIBC	451 µg/dL (high)
IgA t-TG antibody	Positive (32.14 U/MI)
USG abdomen	Normal study

**Table 2:** Macrocytic anemia with leukocytosis and raised ESR.

Our initial impression was nutritional deficiency of vitamin B12 and folate causing macrocytic anemia and Vitamin B12 deficiency causing hyperpigmentation which improved considerably after injectable Vitamin B12. Associated iron deficiency prompted us to search for malabsorption syndromes.

On enquiry patient said that she has been eating wheat or wheat based food infrequently since long, as she didn't like it and somehow even felt sick after eating them. This prompted us to send IgA t-TG antibody titre which came positive (32.14 U/mL), leading us to the diagnosis of coeliac disease with nutritional anemia (vitamin B12, S. folate and iron deficiency) and Vitamin B12 deficiency associated hyperpigmentation. Though Endoscopic small bowel biopsy was suggested to the patient, for confirmation of our diagnosis of celiac disease, it was not done as she was unwilling. The initial stage of the disease and after 5 days both are shown in Figures 1-3.



**Figure 1:** Initial image.



Figure 2: Initial image.



Figure 3: After 5 days.

## Discussion

Celiac disease is a small bowel disorder characterized by mucosal inflammation, villous atrophy, and crypt hyperplasia upon exposure to dietary gluten. CD is primarily reported from northern India with isolated case reports from the rest of the country [9]. Age-adjusted prevalence of celiac autoantibodies was 1.23% in northern, 0.87% in northeastern part of India [10].

Our case belonged to the Eastern part of India where prevalence of celiac is less than 1%. This part of India eats both wheat and rice as their staple cereal whereas staple cereal for Northern India is wheat and for South India, it is rice. Celiac disease may present with symptoms including typical gastrointestinal symptoms (e.g. diarrhea, steatorrhea, weight loss, bloating, flatulence, abdominal pain) and also non-gastrointestinal abnormalities (e.g. abnormal liver function tests, iron deficiency anemia, bone disease, skin disorder) [11].

Celiac disease is usually detected by serological testing of celiac-specific antibodies [11]. Our patient presented with non-gastrointestinal symptoms of celiac disease like iron deficiency, folate and Vitamin B12 deficiency. Hyperpigmentation related to vitamin B12 deficiency being the presenting complaint. Celiac disease was detected by the presence of IgA t-TG (celiac specific antibody).

The classical findings associated with Vitamin B12 and folate deficiency includes severe macrocytic anemia, yellow skin (anemia +jaundice) and variable neurological abnormalities. [12]. our patient had macrocytic anemia but there was no jaundice or any other neurological manifestation.

Skin hyperpigmentation though associated with vitamin B12 deficiency is not very common [12]. This being the presenting

complaint in our patient makes a rare presentation. Cutaneous pigmentation of Vitamin B12 deficiency is characteristically reversible with administration of Vitamin B12 [13]. In our patient too we found a significant improvement after only five days of parenteral Vitamin B12 administration and a further improvement after about 2 weeks. Pigmentation associated with Vitamin B12 deficiency has been especially noticed in palmar creases, on dorsum of hands and feet, in intertriginous areas, on oral mucosa and in recent scars. In few patients even generalized hyperpigmentation was seen [14].

Our case predominantly had increased pigmentation over knuckles, dorsum of fingers and toes, palmar and plantar aspect of hands and feet, nasal bridge, nasolabial folds. Baker et al. described hyperpigmentation as a sign of Vitamin B12 deficiency [15]. Similar case was also reported in a 65-year-old Korean female by Lee et al. [16] while Ahuja et al. reported presence of Vitamin B12 deficiency related hyperpigmentation in a 10 month old baby [17]. Srivastava et al described a 34-year-old male having reversible hyperpigmentation as the first manifestation of dietary Vitamin B12 deficiency [18]. But in none of the above case, the cause of Vitamin B12 deficiency was celiac disease, thus making this a rare presentation of celiac disease associated Vitamin B12 deficiency.

I could not search any case where hyperpigmentation has been associated with iron deficiency though in few reports its association with folate deficiency has been suggested. In our case we initially gave only vitamin B12 supplementation, resulting in a significant improvement in hyperpigmentation, leading us to assume that the cause of hyperpigmentation in Vitamin B12.

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