Case Report

DIAGNOSIS OF AN UNUSUAL CASE OF PELLAGRA WITH HYPOTHYROIDISM

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ABSTRACT

Niacin deficiency, Pellagra or the 3D´S disease, is a disorder associated with either poor intake of niacin-containing food or secondarily decreased bioavailability of the same. Being an essential component in several co enzymes, its deficiency is also considered a multi-nutritional disorder involving the deficiency of tryptophan and consequently vitamin B2 and B6. The low clinical suspicion of this disease, which may be associated with hypothyroidism, made it a clinical challenge even with the classical triad of symptomatology. A case report of 38 years old woman presented with a 3-month history of progressive erythematous lesions on the dorsum of hands resembling photosensitivity eruptions but lacking the typical Casal necklace sign and preceded by multiple episodes of diarrhea, a paradoxical manifestation to its underlying hypothyroid state.

Key Words: Hypothyroidism, Pellagra, Vitamin B_6

INTRODUCTION

The name pellagra, derived from the Italian word pellagra, sharp, i.e. rough skin, is a disease characterized by dermatitis resembling the photosensitive type, diarrhea that may be present in 50% of the cases, and progressive neuropsychological disorders that may lead to dementia. Without prompt treatment, severe niacin deficiency may lead to death.[1,2] Pellagra was initially described by a Spanish physician Don Gaspar Casal in 1763, who recorded all the clinical features and attribute the disease to the unbalanced diets, based on maize, the reason why it is historically considered a maize-eater's disease.

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Pellagra is caused by deficiency of niacin and or its precursor tryptophan, which is essential for cellular metabolism such as redox reactions, DNA repair, and as a co enzymes in various processes. Thus, clinical manifestations are focused on highly metabolic tissues such as skin, gastrointestinal cells, and CNS. Symptoms of the later two are subtle and nonspecific, thus muco-cutaneous signs should provide diagnostic clues.[3] This case report unveils how a patient with severe niacin deficiency and subclinical hypothyroidism presented to us.

CASE REPORT

A 38 years old woman, came to Medicine I Outpatient department with a one-month history of symmetrical hyperpigmented leathery thickened plaques on the dorsal aspect of both hands that started on the knuckle area. Initially, they were confined to 2/3rd of the dorsum, later it spread up to the wrist joint leaving a sharply demarcated border between affected and unaffected skin. A month back, lesions on hands were erythematous itchy, painful but no treatment was taken for the same. There was no movement restriction or tenderness on hand

joints. The same pattern of lesion started appearing on the patient´s nose and both cheeks, symmetrical in the distribution along with angular stomatitis, glossitis, and vesicle formation in the lower lip causing difficulty in food intake along with odynophagia.

Before the onset of dermatological manifestations, the patient complained of diarrhea for three months, unrelated to food intake, associated with mild to moderate diffuse abdominal pain, with mucus but no blood. (Bristol classification 5-6) and indigestion, dyspepsia, occasional heartburn. She sought medical attention for the same complaint and took multiple medications including antibiotics but symptoms were not relieved. She also had dizziness, palpitations on exertion, and tingling sensation on hands and feet with no specific diurnal, nocturnal variation. Family members of the patient noted behavioral changes such as irritability, weakness, lassitude, and inability to perform normal house activities such as cooking or cleaning.

The patient was diagnosed with pulmonary Tuberculosis in Ghulab Devi Hospital 15 years back, for which she completed a 6-month treatment course. On asking, she was unable to verify the intake of Vitamin B6 during the treatment. She also had a history of 2 pregnancies where there was no vitamin supplementation during the prenatal period. There was no history of similar disease in the family, no history of drug addiction or alcohol intake.

On examination, there was bilateral symmetrical thickened skin on the dorsum of hands, hyperpigmented like leathery parchment, with fissuring and crackling of overlying skin. Same hyperpigmentation was noted over the nose and cheeks in a butterfly pattern. Oral cavity examination revealed multiple erosions on buccal mucosa along with superimposed candidal infection, glossitis with fissuring on the tip of the tongue and lower lip showed vesicles, erosions, and crusted papules. Another systemic examination was unremarkable except for myxedematous swelling on both feet, overall xerotic skin, and periorbital swelling. Neurological examination revealed delayed knee jerk and ankle reflex but power was preserved. The sensory system and autonomic nervous system were intact. Moreover, the patient showed neuropsychiatric symptoms such as apathy, low response, and confusion. Mini-mental examinations were done with a score of 22/30 showing a mild degree of cognitive impairment.

Before treatment:

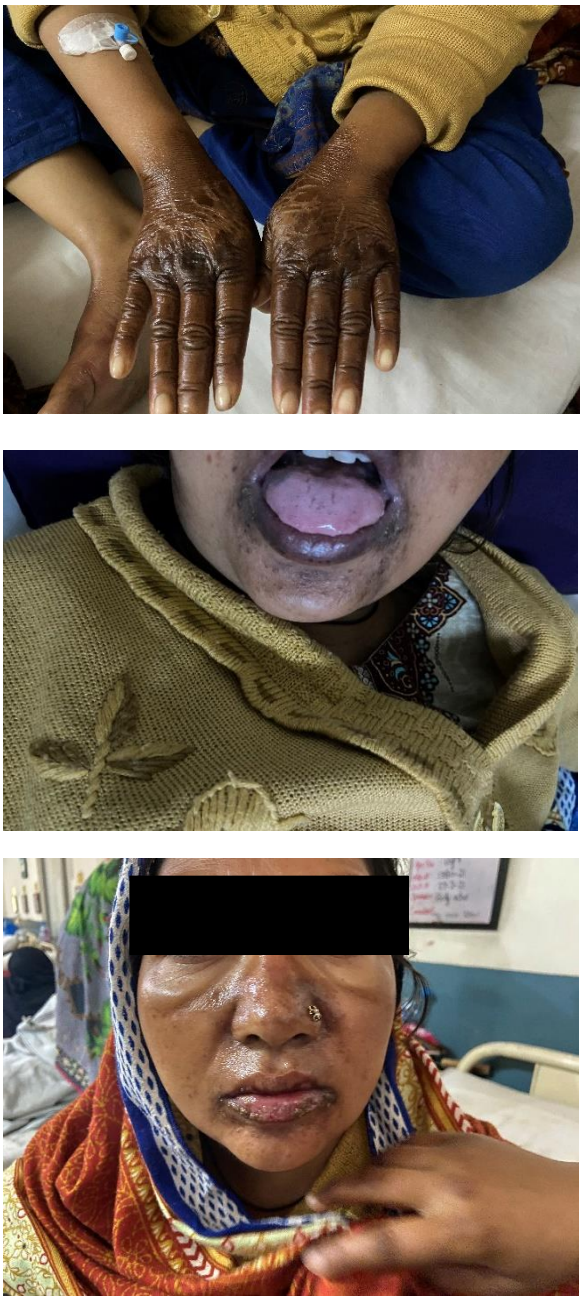
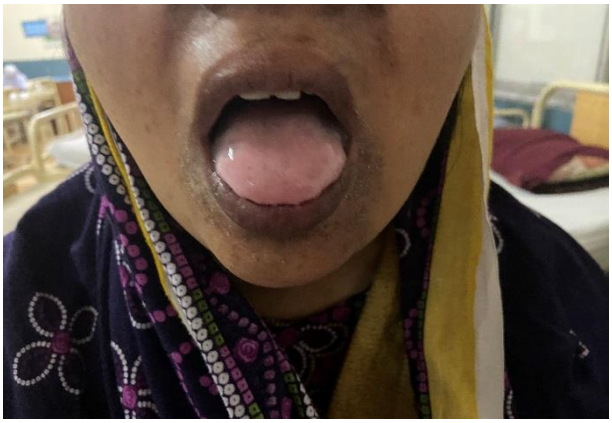


Figure-1: Clinical manifestations before the initiation of treatment

On Laboratory findings, hypochromic normocytic anemia with a Hb of 6.8g/dl, hypokalemia with a value of 2.7 mmol/L, hypocalcemia with 6.9 mg dl was found. CRP was positive and ESR was 102mm 1st hour. Fasting lipid profiles were borderline high with cholesterol 200mg dl and triglycerides 140 mg dl. Thyroid function tests were done and primary hypothyroidism was diagnosed with a TSH level of >100 microIU/ml and T4 levels 0f 0.81 microgram/dl. Serum iron and TIBC were normal. USG abdomen and pelvis showed fatty infiltration of the liver. ECG was low voltage, regular sinus rhythm and echocardiography showed good biventricular function with an ejection fraction of 55-60% and a thin rim of pericardial effusion with approximately 100ml of fluid. The remaining laboratory values were within the normal range.

Niacinamide 500mg in divided doses was started along with multivitamin supplementation, folic acid, and dietary management. She increases caloric intake up to 2400 kilocalories per day focusing on a Niacin-rich diet. The patient's dermatitis, glossitis, and angular stomatitis started improving within the third day of admission, facilitating food intake. By the 8th day of admission, MMSE was repeated and there was an improvement in score from 22 to 24/30 (taking into consideration patient education level) Thyroxine 200 micrograms were started on the 4th day of admission and one blood transfusion was done which brought Hb to 9.0g/dl. The patient´s gastrointestinal symptoms resolved by the time patient was discharged.

After Treatment:



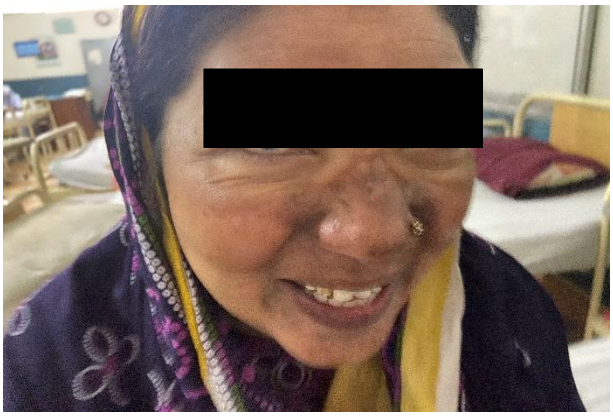


Figure-2: Improvement in clinical signs observed after initiation of treatment

Consent

The authors has produced written counsent of the patient for producing her pictures for academic purpose in Journal.

DISCUSSION

Pellagra is a disorder characterized by the deficiency of the water-soluble vitamin B_3, one of the vital components for various metabolic processes in the body. Pellagra reflects severe malnutrition, as for it to have happened, various other vitamins and amino acids, especially tryptophan, had to be deficient to get a florid manifestation of the disease. Albeit niacinamide can be obtained by tryptophan, the main source of B3 is dietary and storage within the body is minimal, thus a poor suboptimal caloric intake is necessary to cause pellagra. Hence metabolically active cells are the most affected, explaining why the CNS, GIT

system, and skin are the primary target of the disorder resulting in the cardinal features of the disease.[3] Primary pellagra is mainly caused by dietary deficiency, corn-based diets, or eating disorders while secondary pellagra etiology is based on either poor metabolism or poor ability to use niacin within the diet such as in malabsorption syndromes, bypass surgery or subtotal gastrectomy, alcoholism, carcinoid syndrome, Hartnup disease and deficiency of micronutrients use to convert tryptophan to niacin such as riboflavin and pyridoxine.[4] Niacin structural analogs such as isoniazid, 5 fluorouracil, 6 mercaptopurine, and drugs such as anticonvulsants, sulfonamides, chloramphenicol, azathioprine may also lead to pellagra.[5] Nowadays, sporadic cases are reported in rural areas during times of drought and food shortage as well as in food-aid dependent populations during food emergency and refugee programs. Cutaneous findings of pellagra resemble sunburn with papules and occasionally vesicles formation that may exfoliate or may form hyperkeratotic darkly pigmented patches. Facial dermatitis mostly follows the trigeminal nerve distribution and is manifested in a butterfly pattern over the nose and cheeks. Similarly, dermatitis on the neck follows C3 and C4 distribution giving the well-known Cassal´s necklace of Pellagra.[6] In one-third of patients, mucosal surfaces of lips tongue, and oral cavity are involved in the form of glossitis, angular stomatitis, cheilosis, and thrush are seen in niacin deficiency, although these may, in part, be a result of a simultaneous riboflavin deficiency. Inflammation spreads through the gastrointestinal tract, with chronic gastritis and diarrhea typically watery, but it can be mucoid.[3] Neurological symptoms include headache, irritability, poor concentration, anxiety, delusions, hallucinations, fatigue, depression that may progress to confusion, memory loss, and psychosis.[1]

Diagnosis requires a high index of suspicion and is usually done by improvement of symptomatology with the administration of niacinamide. The findings of anemia, low potassium and phosphorus, and higher levels of calcium along with hypoproteinemia may contribute to the diagnosis. Specific tests include Serum niacin levels, tryptophan, NAD, NADP levels, and lower urinary levels of N-methyl nicotinamide and pyridine.[3,4]

A daily average intake of 15–20 mg of niacin prevents pellagra for all age groups. The daily recommended dose is 300 mg of nicotinamide in divided doses, and treatment should be continued for 3–4 weeks.[3] Nicotinamide form is preferable over nicotinic acid because of the side effects such as hot flushing, tachycardia, and itching.[4] Moreover, vitamin B complex preparation, bed rest, and strict dietary management along with photo-protection and emollients should be emphasized during treatment.[3]

CONCLUSION

Our patient presented with the classical symptoms of vitamin B_3 deficiency and primary hypothyroidism. Severe niacin deficiency appeared to unmask the hypothyroid state in our patient. Very few cases have been reported with both concomitant diseases and even though thyroxine may have a role in riboflavin regulation as some case reports showed, there is no evidence of hypothyroid-induced pellagra or pellagra-induced hypothyroidism.[7] Our patient´s dermatitis, diarrhea and neuropsychological symptoms started improving as soon as niacin was administered and diet was improved, however, the complaints attributable to thyroid deficiency, ankle and knee jerk reflexes, and hoarse voice started improving after 2 weeks of thyroxine therapy.

REFERENCES

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MIH: Data Collection
ROF: Data Analysis
IUR: Review Critically
ZIC: Literature review
MS: Drafting the article

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