



Pemphigus Pellagrosus masquerading as cutaneous adverse drug reaction

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Abstract

Pellagra is caused by cellular deficiency of niacin or its precursor amino acid, tryptophan. Niacin, also known as nicotinic acid or vitamin B3 is essential for carbohydrate, fat, protein and alcohol metabolism, detoxification of drugs and reactive oxygen species, cell signaling and DNA repair. Classically characterized by a symmetric photodistributed skin rash, gastrointestinal symptoms, and neurologic and psychiatric disturbances (dermatitis, diarrhea, and dementia), it can lead to death if left untreated. The dermatitis caused by pellagra can present in the acute phase with vesicles and bullae, resembling a sunburn in its early stages (wet pellagra). When pellagra recurs at the same site, blisters may occur (pemphigus pellagrosus). Histopathologic changes in the acute phase can include intra- or subepidermal vesicle formation as a result of spongiosis, ballooning degeneration, and vacuolar alteration of the basal layer. The preferred therapy is with nicotinamide because it does not cause the flushing observed with niacin. Initially Patient was started on injection nicotinamide (200mg) twice daily. Later patient was shifted to oral nicotinamide 50 mg twice daily resulted in significant improvement in tenderness, burning discomfort, and desquamation. It is, therefore, important for dermatologists to be aware of the growing body of literature pertaining to nutrition and skin disease to appropriately inform patients on benefits and harms of specific dietary interventions.

Keywords: Pellagrosus, tryptophan, Pellagra, nicotinamide, pertaining

1. Introduction

Pellagra or niacin (vit B 3) deficiency, is a potentially fatal disease which is now rare in developed world¹. It is characterized by dermatitis, diarrhoea, dementia and eventually death occurring as a result of niacin or its precursor tryptophan deficiency. The classical triad of dermatitis, diarrhea, dementia is not always present. Full triad of symptoms occur only in 22% of patients^[2, 3]. Pellagra cases associated with development of bullae is known as wet pellagra or pemphigus pellagrosus. Pellagra is commonly seen in chronic alcoholics, malabsorption syndrome, and drug toxicity Prolonged therapy with drugs like isoniazid, pyrazinamide, azathioprine, 6-mercaptopurine, sulfonamides, anti convulsants and anti-depressants result in pellagra like symptoms. Skin lesions generally precede other symptoms, and are characteristic and pathognomonic, with symmetric sunburn like eruptions in exposed areas and peeling. Diagnosis is often delayed owing to nonspecific symptoms and low clinical suspicion. Mostly a clinical diagnosis, its treatment includes balanced diet and niacin supplementation. Thus diagnosis is essentially clinical, with a therapeutic trial for confirmation⁴.

Case report

A 25 year old female, known case of pulmonary tuberculosis on Anti-tubercular therapy (ATT) since 2

months presented to casualty with symmetrical, sharply defined, hyper pigmented plaques along with bullae on the neck and dorsal surfaces of the hands, extensor surfaces on forearms and feet, especially on the sun-exposure areas. Patient complained of nausea and erosions of oral cavity and genital mucosa are noted. There was no history of any neuropsychiatric symptoms and no history of any systemic or local application of medication. She was moderately built and nourished with mild pallor and red glossy tongue. Blood and urine investigations are within normal limits. Initially diagnosed as drug reaction and was kept on steroid, later patient did not respond and gastric symptoms increased. Bullae tend to progress day by day and lesions on neck and forearms showed a burnt out picture. Based on characteristic skin lesions involving sun exposed region, development of diarrhea and history of isoniazid usage, diagnosis was revised as Wet pellagra.

Patient was started on injection nicotinamide (200mg) twice daily. Patient showed improvement of symptoms and lesions within 3 days of start of therapy. Diagnosis is confirmed by rapid response to injection nicotinamide. Significant improvement in desquamation and erythema in 10 days. Later patient was shifted to oral nicotinamide 50 mg twice daily was given for a period of 2 months. Post inflammatory hyperpigmentation was only the lesion left after 2 months.



Fig 1: Bullae over dorsum of foot Beefy, red tongue



Fig 2: Burnt out like picture of Hands & Neck



Fig 3

Discussion

Pellagra is common in raw-spirit drinkers of rural populations in the Third World whose staple diet is niacin deficient jawar or maize with inadequate animal protein, fruits and vegetables [5]. Secondary deficiency of niacin occurs in malabsorption and carcinoid syndrome, cirrhosis of liver and Hartnup disease. Prolonged therapy with pyrazinamide, isoniazide, 6-mercaptopurine and 5-fluorouracil may also result in pellagra like syndromes. Pyrazinamide and isonicotinic acid hydrazide (INH) are structural analogues of niacin and can depress endogenous niacin production by feedback inhibition or substrate

competition. INH impairs the functioning of pyridoxine, a cofactor in tryptophan-niacin pathway and inhibits the niacin synthesis leading to pellagra [5]. Nicotinamide is the preferred supplement, as niacin causes flushing and headaches [6,7].

The characteristically described three Ds of pellagra, diarrhea, dementia, and dermatitis are not present in all cases. Skin lesions are classic, characterized by photosensitive eruption, symmetrically distributed on dorsum of hands, forearms, and sometimes feet.

Anorexia, nausea, and diarrhea are the main gastrointestinal complaints. Chelitis, stomatitis, red bald tongue, and

ulcerations can occur in the oral mucosa. The mucosa of the vaginal and perianal regions can be affected ^[10]. Photosensitive skin lesions are due to the deficiency of urocanic acid which acts as an ultraviolet filter ^[8, 10]. In pellagra, nicotinamide adenine dinucleotide (NAD) and nicotinamide adenine dinucleotide phosphate (NADP) levels are inadequate to maintain cellular energy transfer reactions. Tissues with a requirement of high energy like the brain and those with a high turnover of cells like the gastrointestinal tract and skin are particularly affected ^[11]. The recommended daily allowance is 0.66 mg per 1000 Kcal (10–20 mg/day). Since niacin causes unpleasant flushing, itching, burning, or tingling sensations, niacinamide is preferred for therapy and 300–500 mg/day orally in divided doses is recommended. When oral therapy is precluded, 100 mg of niacinamide is injected intramuscularly three times a day. In severe cases with encephalopathy, 1000 mg of niacinamide is recommended

orally in addition to 100–200 mg parenterally. The skin erythema, mucosal lesions, and diarrhea respond in a few days. The skin lesions disappear completely in a few weeks. B complex vitamins, pyridoxine, and riboflavin are needed for the neurological manifestations. Proteins and iron should also be given. A balanced diet should be prescribed ^[12].

Conclusion

Pellagra is seen routinely with characteristic hyper pigmented plaques on sun exposed areas, the development of vesicles and bullae with mucosal erosions is seen only in few cases in this era. If pellagra is early diagnosed and treated appropriately, the prognosis for recovery will be very good as is seen in our patient. This case is probably an isoniazid induced pellagra. Isoniazid is a competitive inhibitor of NAD because of similar structures and also impairs pyridoxine functioning, which is essential for niacin synthesis from tryptophan.

Before treatment



Fig 4

After treatment



Fig 5: Residual Hyperpigmentation

Before treatment**After treatment**

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