



Pellagra-Like Dermatitis: To Be or Not to Be?

Oliveira AL^{1*}, Portela J¹, Calixto R¹, Jose Vaz¹, Agostini P² and Calixto M³

¹Department of Internal Medicine, Hospital Jose Joaquim Fernandes, Unidade Local do Baixo Alentejo, R. Dr. Antonio Fernando Covas Lima, Beja, Portugal

²Department of Pathological Anatomy, Hospital do Espírito Santo E.P.E, Largo Senhor da Pobreza 7000, Évora, Portugal

³Department of Dermatology, Hospital das Forças Armadas, Azinhaga Ulmeiros, 1649-020 Lisboa, Portugal

Abstract

Pellagra was first described in Spain in 1795, with outbreaks in Italy and France until it became epidemic in the United States in the early 1900's. Back then, nutritional deficiencies were common as a result of misinformation and famine until it was finally associated to maize, when eaten without being processed to make niacin available in the diet. Nowadays, the wide access to a considerable nutritional variety makes this disease oblivious to most of the medical staff in the current, daily practice. We describe a case of an eighty-five-year-old woman living in a rural isolated area in the southern Portugal, brought to the urgency services of our centre with itchy, edematous dermatological lesions in her face, hands and forearms for the last three days. When observed, the lesions were coarse, ulcerated with serohematic crusts in some areas, strictly delimited in areas of prolonged solar exposure, sparing the rest of the body. The history confirmed a poor intake of nutritional variety. Despite the poor contribution of analytical parameters for the diagnosis, as well as the unspecific dermo pathologic aspects, the clinical history favoured the hypothesis of Pellagra. The patient underwent niacin therapy and hydration with emollient, topic emulsions in the affected areas, with restricted improvement. With this case report we emphasize the importance of the nutritional details in a clinical history in patients with dermatological lesions, focusing as well in the distribution and aspect of those lesions. A careful history taking is essential to suspect such disease and, given its rarity, it is important to carefully consider all the differential diagnosis.

Keywords: Pellagra; Niacin deficiency; Dermopathology; Diagnosis

Introduction

The four 'Ds' that characterize Pellagra (diarrhoea, dermatitis, dementia and, less likely, death) allow an immediate diagnosis, however, in a more realistic scenario, a patient presents solely dermatological lesions, most of them described as hyperpigmented lichenified plaques in photo exposed areas [1,2]. Nowadays, flour is part of the diet, which diminishes the likelihood of finding a case of nutritional deficiency such as pellagra. Besides, factors as alcoholism, malnutrition, malabsorption, haemodialysis, carcinoid syndrome (excess turnover of tryptophan, precursor of niacin, to serotonin) and medications (isoniazid, ethionamide, 6-mercaptopurine and oestrogens) must always be considered [3].

A consistent range of differential diagnosis must be considered, always bearing in mind how unspecific the dermatological lesions are [4]. Bearing in mind all this, Pellagra is a diagnosis that may easily be overlooked if the physician is not aware of the risk groups and the social and behavioural restrictions certain age groups might adopt.

Case Report

An 85-year-old woman was brought to the emergency department complaining of itchy, serous red lesions in forearms, hands and face. The patient lived in a rural area of southern Portugal, living in an isolated area, 10 kilometres apart from the closest village. She was reliable in providing clinical history, informing she was a widow for ten years, living alone with her 42-year-old single daughter, both farm workers subsiding exclusively from agriculture, with regular and unprotected sun exposure. The past medical history was scarce, with no significant information found in the family doctor registration platforms. As far as the dermatological lesions were concerned, the patient informed us those came up in a three-day span, in a worsening fashion, itchy, with occasional serous-hematic discharge and red bruises, aggravated by grazing, scattered all over her forearms and both hand dorsa. The lesions were far less exuberant in her face, mainly reddish and scaly.

Clinical examination revealed normal vital signs, dehydration and a moderate degree of cachexia, otherwise vigilant and cooperative

with coherent speech, glossitis accompanied by extensive lesions in the forearms and hands dorsa one could describe as an ulcerative eczema with serous, hematic crusts with scattered areas of scaly and pigmented skin. The lesions observed corresponded to areas of intense sun exposure over years, with both elbows and arms spared (Figure 1). The face, namely the malar and zygomatic arcs areas, as well as the nasal pyramid were the most affected parts and partially the upper lip. The lesions were also pigmented and scaly but less serous, with no bruises or ulcers. All the other facial areas and the rest of the body were spared.

Clinical follow-up did not reveal signs of underlying infection, only a slight elevation in serum Creatinine caused by dehydration that was promptly corrected with intravenous and oral fluids. Blood tests didn't show anaemia. The patient remained neurologically stable with no gastrointestinal complaints, apart from the constant reluctance in eating. Furthermore, after contacting the patient's daughter, we were informed of her poor dietary intake and variety despite insistence. Confronted with this information, we suspected the characteristic skin lesions found might correspond to pellagra as the most likely diagnosis in a malnourished woman. In order to perform a complete diagnostic work-up, we conducted a blood count, serum protein, calcium, kalium, phosphorous, liver function tests, as well as niacin and plasma porphyrin levels. Urinary assays for determining niacin, tryptophan, N-methylnicotinamide, pyridone, NAD and NADp levels were not available in our centre.

The blood work revealed a hypochromic anemia (Hb 8.6 g/dL, VGM 97.1 fL, normal HGM), normal electrolyte levels (kalium, phosphorus, calcium), liver function tests and serum proteins within normalcy,

***Corresponding author:** Oliveira AL, Department of Medicine, José Joaquim Fernandes Hospital, Local Health Unit of Baixo Alentejo, R. Dr. Antonio Fernando Covas Lima, Beja, Portugal, Tel: +351963378593; E-mail: luisa.oliveira@ulsba.min-saude.pt

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Figure 1: Skin aspect of our patient at the E.R admission. The right cheek is severely damaged, despite the global aspect of the patient's face. In the right hand and forearm, it can be appreciated the ulcerated lesions scattered; a close-up at the ulceration in the left hand, where the biopsy was performed.



Figure 2: Images of the same areas described previously, after treatment. The lesions resolved completely and there was a considerable improvement of the skin aspect and consistency.

but low niacin (<10 microg/mL), as well as low porphyrin levels (6 microg/mL; normal range within 32.5 microg/mL). The histological result described unspecific, acute skin ulceration, no vasculitis, mixt inflammatory infiltrate, solar elastosis with epidermal acanthosis and hyperkeratosis.

The patient underwent a punch skin biopsy of a representative lesion in the left-hand dorsum and the patient started empirical treatment with 100 mg of niacin per os three times a daily, altogether with topic, emollient treatment of the affected areas, with specific indication to avoid sun exposure. Considering the patient was malnourished, we opted to medicate as well with vitamins of the B-complex and specific indication to pursue a high-protein diet.

We scheduled a consultation for clinical and analytical evaluation 4 weeks after the emergency department episode. Clinically, the lesions ameliorated considerably (Figure 2) and there were no signs

of neurological or gastrointestinal complaints. Confronted with such improvement, the patient stopped the niacin supplementation and scheduled another monthly visit, leaving the same indications of topic emollient therapy, solar protection measures and regular hydration and food variety. In the second visit, the lesions were completely resolved, and the patient was discharged from our consultation, with no further relapses and closely monitored nutritionally.

Discussion

Pellagra is a rare diagnostic in nowadays practice, difficult to suspect due to medical unawareness. Despite being well characterized by the typical triad (dermatitis, diarrhea and dementia), most of the cases described in the literature present with dermatologic manifestations, namely photosensitivity associated with lichenified hyperpigmented plaques in photo exposed skin [2], with preferential localization: dorsal side of his hands, lower legs and around the neck [5,6]. This disease

is uncommon in developed countries, diagnosed often in alcoholic patients.

When faced with a patient with skin lesions associated with solar exposure, a series of elements must be investigated despite the dermatological characteristics: history of excessive alcohol intake, anorexia or signs of eating disorder, past history of gastrointestinal malabsorption disorders (coeliac or inflammatory bowel disease) and any patient under medications such as 5-fluorouracil, azathioprine and isoniazid. Then, the localization of the lesions, since in pellagra there is a pattern that usually includes the dorsal side of hands/forearms, lower legs and around the neck 'Casal's necklace', a typical sign that provides a strong clue to the diagnosis [7]. In what concerns the dermatosis, there are several differential diagnostics to consider, namely chronified actinic and photoallergic dermatitis due to solar exposure, chronic hyperpigmentation and skin thickening in bone prominences, chronic lichen simplex, as well as seborrheic dermatitis or sebaceous gland hyperplasia.

In a regular emergency service environment, such differentiation is difficult with generalist specialties, so assistance of Dermatology is necessary. However, a detailed history of the patient is needed to support the level of suspicion, namely if none of the above history elements are present. In the case we described, it was difficult to grasp the nutritional deficiencies the patient had, not before investigating on the patient's lifestyle and feeding habits, which lacked any type of meat, fish, fresh and/or cooked vegetables, eggs or bread. With this information and the type of lesions and its localization, the suspicion became reasonable. After considering likely the diagnosis of Pellagra in our patient, the diagnostic work-up included blood counts, serum proteins, calcium, potassium and phosphorus levels, liver function tests, serum porphyrin levels and serum niacin. As depicted in the case presentation, it was not possible to determine other diagnostic items (tryptophan, NAD, and NADP serum levels and urinary levels of N-methylnicotinamide and pyridone) that would support the diagnosis of pellagra.

The anatomopathological investigation in a dermatological biopsy is controversial, since there is no histological pathognomonic finding to diagnose pellagra. In the literature, the histology describes evident nonspecific dermatitis changes, such as early perivascular lymphohistological infiltrate, mild edema in the papillary dermis, dilatation of capillaries and later dermal fibrosis; epidermal changes include early sub corneal blisters; pallor of the upper epidermis and, later, hyperkeratosis, parakeratosis and epidermal atrophy [8]. The histological description of the biopsy performed in our patient was, as expected, not conclusive, describing acute cutaneous ulceration, dermis with mixed inflammatory infiltrate, solar elastosis and epidermal acantosis and orthoqueratosis. According to Hall [4], the histology of a pellagra lesion is quite unspecific and may exist in other nutritional deficiencies. The histologic description features that might corroborate with the diagnosis are the presence of epidermal hyperkeratosis and acantosis, as well as the presence of dermal mixed inflammatory infiltrate.

However, these are also present in several dermatologic lesions, namely the ones associated with solar exposure and photosensitivity. Our patient had an important history of solar exposure throughout the years, what posed many doubts to our reasoning and diagnostic suspicion, considering also the patient was observed in July (hence, summertime) and a UV index for the area categorized as "high". To discern whether photosensitivity dermatosis are due to pellagra or to another photosensitivity disorder can only be defined with systematic photo testing [2], only available in some centres.

In now-a-days practice, the determination of niacin serum levels is quite appropriate when faced with photosensitive dermatosis associated with a high suspicion of pellagra. Once treated, the condition resolves and there is a complete regression of the lesions: it was the case of our patient, after 4 weeks of treatment with niacin and topic emollient.

We admit that, even though our patient showed an impressive clinical improvement after treated with niacin, supporting our diagnostic suspicion of a pellagra, there are some elements that favour otherwise, making us consider we would probably were facing a burst of eruptions in chronic sun-exposed skin in a malnourished woman, namely: the location of the lesions, that resumed to the dorsal side of hands and forearms and malar areas and the unspecific histological description.

Conclusion

With the description of this case we focus the need of bear in mind that systemic nutritional deficiencies may have an indolent presentation, presenting only with dermatological complaints, what reinforces the awareness of less common diseases, such as pellagra and the importance of a detailed past and present history. Advice of other specialties (namely, dermatology) is necessary to direct the diagnosis and make a correct planning of the patient's diagnostic work-up and treatment.

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