CASE REPORT

Pellagra in a patient with primary Sjögren's syndrome

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SUMMARY

A 27-year-old woman presented with persistent dryness of the mouth and eyes. She presented with permanent photodistributed rash involving the face and distal extremities. Laboratory tests showed positive Sjögren's syndrome (SS)-A and SS-B antibodies. Histological examination of minor salivary gland biopsy revealed inflammatory infiltration grade 4 according to Chisholm's classification. Skin biopsy showed acanthosis, hyperkeratosis in the epidermis and little inflammatory infiltrate in the dermis. There was an infiltration of CD4 T lymphocytes in the dermis. Based on the characteristics of the dermatitis and on a rapid response to niacin replacement, the diagnosis of pellagra was carried out. A complete resolution of the dermatological signs was obtained within 2 months. To the best of our knowledge, the association between primary SS and pellagra has never been reported. We emphasise the possible mechanisms of this association.

BACKGROUND

Little progress has been made in our knowledge of pellagra over the past nine decades.¹ In developed countries, pellagra is limited to a small number of at-risk groups (alcoholism and malnutrition).¹ In Tunisia, the disease is extremely rare.²

Sjögren's syndrome (SS) is a non-organ-specific autoimmune disease affecting exocrine glands accompanied by diverse extraglandular manifestations. We report a case of pellagra occurring in a patient with primary SS for the first time, and discuss the possible mechanisms of this association.

CASE PRESENTATION

A 27-year-old woman presented with permanent rash involving the face and distal extremities. She had 3 years history of xerophthalmia and xerostomia. The patient's diet was normal, she did not report any alcohol intake, and there was also no history of diarrhoea.

On physical examination, the skin lesions were characterised by hyperpigmentation and areas of peeling. Lesions of the dorsum of the hands were markedly symmetrical, hyperpigmented, thickened and scaly. There was a clear demarcation zone between skin exposed and unexposed to sunlight (figure 1). The physical examination, and particularly neurological examination, was otherwise unremarkable.

INVESTIGATIONS

Laboratory tests showed positive antinuclear antibodies at a titre of 1:800; a search for anti-SS-A and anti-SS-B antibodies was positive. Serum albumin and calcium levels, as well as haemoglobin levels were normal. Ophthalmological exam revealed keratitis punctata. Minor salivary gland biopsy showed inflammatory infiltration grade 4 according to Chisholm's classification.

Histological examination of skin biopsy specimen revealed acanthosis, hyperkeratosis with focal parakeratosis in the epidermis and little inflammatory infiltrate in the dermis (figure 2).

The immunohistochemical study showed the presence of CD4 T lymphocytes (figure 3A), and rare CD8 T lymphocytes (figure 3B).

The upper gastrointestinal endoscopy and duodenal biopsies were normal.

Figure 1 Photosensitive rash on sun-exposed areas of the face and hands.

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Figure 2 Acanthosis, hyperkeratosis with focal parakeratosis in the epidermis and little inflammatory infiltrate in the dermis (H&E staining $\times 100$).

TREATMENT

Based on the particular characteristics of the dermatitis, a presumptive diagnosis of pellagra was performed. Intravenous multi-vitamins which included niacin (100 mg/day) was started, leading to significant improvement of the skin lesions within 10 days; followed by oral nicotinic acid replacement (50 mg/day).

OUTCOME AND FOLLOW-UP

Complete resolution of the skin lesions was obtained in 2 months (figure 4).

After 2 years of follow-up, the patient has not developed clinical features of another systemic inflammatory rheumatic disease and no digestive sign was noted.

DISCUSSION

Pellagra is a vitamin deficiency disease due to the lack of niacin (vitamin B₃). It is classically characterised by the three D's symptoms (dermatitis, diarrhoea and dementia), but this clinical presentation is becoming rare. The diagnosis of pellagra is usually based on the clinical characteristics of the dermatitis and on the response to treatment.³

SS may present as a primary disease or in association with other autoimmune rheumatic diseases. The diagnosis of primary SS was established according to the American-European Consensus Group (AECG) criteria set.⁴

The histological features of pellagra vary throughout the course of the disease and are non-specific in many cases.⁵ One of the pathological characteristics of primary SS is the infiltration of CD4 T lymphocytes. Interestingly, the immunohistochemical analysis in our case showed the presence of CD4 T lymphocytes infiltrate in the dermis. The interpretation of this finding remains unclear, but may suggest a relationship between primary SS and pellagra in this case.

Exploring tryptophan metabolism could possibly give a clue to the coexistence of pellagra and primary SS in our patient. In autoimmune diseases such as systemic lupus erythematosus⁶ and rheumatoid arthritis,⁷ tryptophan degradation correlates with disease activity and markers of immune activation. In the very late stages, significant acceleration of tryptophan degradation and immune activation is common.⁸

Figure 3 (A) The immunohistochemical study showed CD4 T lymphocytes infiltrate in the dermis ($\times 400$); (B) and CD8 T lymphocytes were rare ($\times 100$).

Figure 4 Complete resolution of the skin lesions after 2 months.

Major depletion in tryptophan levels is reported to cause pellagra in patients with HIV.⁹ Pellagra-like erythemas in Hartnup disease is also explained by tryptophan metabolism abnormalities.

Secondary pellagra could also be caused by malabsorption. Gastrointestinal manifestations in primary SS are diverse and include chronic atrophic gastritis and pancreatic insufficiency. Moreover, coeliac disease is reported to be more prevalent in patients with SS compared with normal controls.¹⁰ However, upper gastrointestinal endoscopy and duodenal biopsies were normal in this case.

Learning points

- ▶ Pellagra is a rare disease caused by a deficiency of niacin. The disease is classically characterised by the three D's symptoms (dermatitis, diarrhoea and dementia), but this clinical pattern is becoming rare, and the diagnosis is usually missed.
- ▶ The histological features in pellagra vary throughout the course of the disease and are non-specific in many cases. The diagnosis of pellagra is usually based on the clinical characteristics of the dermatitis and on the response to treatment.
- ▶ Pellagra is usually reported to be associated with lacking regime, malabsorption, chronic alcoholism and some chemotherapeutic agents. The association of pellagra and autoimmune rheumatic diseases is rarely reported.
- ▶ Exploring tryptophan metabolism could possibly give a clue to the coexistence of pellagra and primary Sjögren's syndrome.

This report broadens our understanding of pellagra and the hypothesis of the possible mechanisms of its association with primary SS. However, on the basis of this single case, it is not possible to say whether this association is causative or coincidental.

Contributors IBG managed the literature searches. NL wrote the first draft of the manuscript. IC and HH revised the manuscript. All authors contributed to and have approved the final manuscript.

Competing interests None.

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