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CASE REPORT

Necrobiosis lipoidica associated with Hashimoto's thyroiditis and positive detection of ANA and ASMA autoantibodies

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Key Clinical Message

Necrobiosis lipoidica (NL) is a rare idiopathic cutaneous condition exceptionally associated with autoimmune thyroiditis. We describe the first case of NL, Hashimoto's thyroiditis and positive detection of autoantibodies. Appropriate screening for NL in patients with autoimmune thyroiditis may clarify its real incidence and the existence of a common pathogenetic pathway.

Keywords

Autoantibodies, diabetes mellitus, Hashimoto's thyroiditis, necrobiosis lipoidica, photodynamic therapy.

Introduction

Necrobiosis lipoidica (NL) is a rare idiopathic cutaneous condition strongly, but not exclusively, associated with diabetes mellitus (DM). NL lesions appear as yellowish-brown telangiectatic plaques usually localized on the pretibial skin of young adults or middle-aged subjects, with a female-to-male ratio of 3:1. Lesions are typically bilateral and asymptomatic; ulceration, often induced by trauma, may occur in 35% of cases, sometimes leading to severe painful forms, refractory to therapy. The course of the illness is chronic, with a slow extension of the lesions over many years [1]. NL has been considered as a complication of DM, even if relatively uncommon; however, NL lesions are not pathognomonic of DM, being also very rarely associated with thyroid autoimmune disorders [2]. Here we report the first case of NL associated with Hashimoto's thyroiditis and a positive detection of antinuclear antibodies (ANA) and anti–smooth muscle antibodies (ASMA) in a nondiabetic patient.

Case report

A 44-year-old woman was referred to our dermatological outpatient clinic in July 2012 for the presence of slowly growing patches of 2 years duration, located on her legs. Family history was positive for dyslipidemia, obesity, and cerebrovascular disease, and negative for cardiovascular, endocrine, or neoplastic disorders, as well as for type 1 or type 2 DM. Her past medical history revealed allergy to environmental agents, and Hashimoto's thyroiditis diagnosed 3 years before; the patient was not taking any medication at the time of our observation. Physical examination revealed two symptomless red-yellowish plaques of 5 and 1.5 cm in diameter on the pretibial region of both legs, with a central atrophic area with prominent telangiectatic vessels and erythematous borders (Fig. 1A and B). Histologic examination of biopsy specimen confirmed the diagnosis of NL. General physical examination was normal, with anthropometric measures such as body mass index (BMI: 25.7 kg/m^2), blood pressure, and heart rate within the normal ranges. Baseline chemistry, blood cell count, white blood cells, lipids, hepatic, and renal function tests were all within the normal laboratory ranges, as well as glucose, insulin, and C-peptide concentrations at 0, 30, 60, 90, and 120 min in course of Oral Glucose Tolerance Test. Furthermore, both the $HOMA_{IR}$ calculation (0.45), an indirect index for insulin resistance, and the insulinogenic index (1.18), a surrogate but accurate index

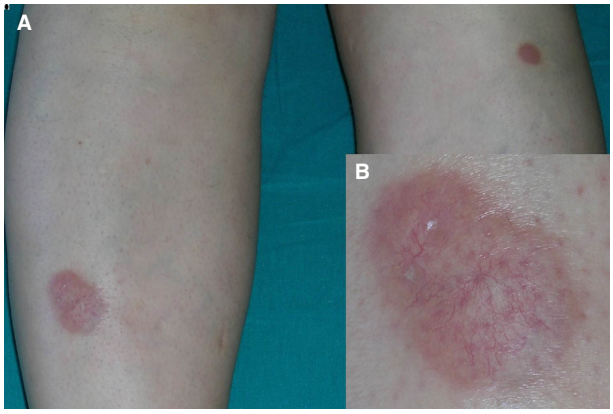

Figure 1. (A) Two red-yellowish plaques of 5 and 1.5 cm in diameter, localized, respectively, on the right and left pretibial regions. (B) Close-up view of the lesion on the right leg.

of insulin secretion, did not reveal insulin resistance or any defect in insulin secretion.

Serum levels of thyroid stimulating hormone (TSH) (0.880 mU/L; normal range 0.270–4.2 mU/L), free triiodothyronine (FT3, 4.43 pmol/L; normal range 3.0–6.7 pmol/L), and free thyroxine (FT4, 14.13 pmol/L; normal range 12.00–22.00 pmol/L) were within the normal values, whereas serum levels of both anti-thyreoglobulin antibodies (ABTg, >4000 UI/mL; normal range 0.00–115.00 UI/mL) and anti-peroxidase antibodies (ABTPO, 1183.00 UI/mL; normal range 0.00–34.00 UI/mL) were increased. TSH-receptor antibodies (TRAb) were negative (<0.1 UI/L; negative if ≤1.0). Thyroid ultrasound (US) examination showed a modestly increased gland size, with a slight predominance of the right lobe (right lobe: 52 × 24 × 20 mm; left lobe: 50 × 23 × 18 mm, isthmus 3.4 mm). Thyroid's echotexture was diffusely heterogeneous, with an overall decreased echogenicity and, sometimes, pseudo-nodular appearance, due to the presence of millimetric hypo-echogenic areas. A better defined hypoechogenic nodular area of 8 × 5 mm was detected in the right lobe, and a slightly hyperechoic area of 5 mm in diameter was detected in the median region of the left lobe. Both thyroid function tests and thyroid US examination confirmed the diagnosis of Hashimoto's thyroiditis. Circulating levels of other organ-specific and nonorgan-specific autoimmune markers were then specifically measured. Islet cell cytoplasmic autoantibodies (ICA), antibodies to glutamic acid decarboxylase (GADA), extractable nuclear antigens (ENA), antimitochondrial antibodies (AMA), antinative DNA antibodies (nDNA), antiparietal cell antibodies (APCA), antineutrophil cytoplasmic antibodies (ANCA), anti-liver kidney microsomal type 1 (LKM-1) were all undetectable. Conversely, both ANA and ASMA were positive, with a titer of 1:320. Liver US was also performed, but it did not show any pathological sign. The cutaneous lesions were treated with photodynamic therapy, based on topical application of a cream containing aminolevulinic acid (ALA) 10%, followed by exposure to appropriate light source (red light at 630 nm) for a total amount of 10 min (75 J/cm^2). The application was repeated every 4 weeks for 6 times, with moderate clinical improvement after 6 months.

Discussion

The pathogenesis of NL remains still unknown. Because of its association with DM, some authors suggested that NL could be one of the clinical manifestations of microangiopathy; however, mounting evidences suggest that NL may be caused by an immunological mechanism, in which either an immune complex disease or autoantibodies directed again st vessel wall tissue antigens are the initiating events. This hypothesis is corroborated by the detection of immunoglobulins and complement factor deposits, principally IgM, C3, and fibrin, in vessel walls and at the dermal–epidermal junction in the involved skin [3]. An immune-mediated process is also suggested by the stronger association with type 1 DM rather than with type 2 DM. The paucity of epidemiological data on NL in other immune-mediated pathologies may at least in part depend on the lack of an appropriate clinical screening of this skin disorder, which has been considered for a long time a DM-specific manifestation. Furthermore, most of the cohort studies present in the literature investigated therapeutical rather than epidemiological aspects. A recent multicentric retrospective study, examining data from 52 patients with NL of the lower legs, revealed a prevalence of thyroid function disorders of 13% versus 5.5% in the general population, with only one case of autoimmune thyroiditis [4]. Patients with chronic thyroiditis have high incidence of other associated autoimmune diseases; furthermore, nonthyroid autoantibodies may also be higher than normal in these patients. Notably, in our patient, Hashimoto's thyroiditis was associated with high titers of both ANA and ASMA. ANA are autoantibodies directed against a variety of nuclear antigens, and their detection is a diagnostic marker for several systemic autoimmune pathologies; ASMA represent a more heterogeneous group of antibodies that may be specifically high in patients with chronic active hepatitis and primary biliary cirrhosis. In this regard, no liver disease was detected in our patient. However, both the prevalence and clinical significance of nonorgan-specific autoantibodies in the serum of patients with autoimmune thyroid diseases are not well established yet [5]. Their presence may be related to a cross-reactivity phenomenon or it may reflect a common etiologic pathway among different

autoimmune diseases. On the basis of these considerations, it may be useful to perform a screening for NL in patients affected by autoimmune thyroiditis, in order to evaluate its real incidence, until now probably underestimated, and to investigate the existence of a pathogenetic link, especially in those with detectable serum markers of autoimmunity.

Conflict of Interest

None declared.

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