Acta Dermatovenerol APA

Acta Dermatovenerologica
Alpina, Pannonica et Adriatica

2012;21:55-57
doi: 10.2478/v10162-012-0016-1

Actinic reticuloid imitating Sézary syndrome

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Abstract

Actinic reticuloid is a rare chronic idiopathic photosensitive dermatosis belonging to the spectrum of chronic actinic dermatitis and may be mistaken for cutaneous T-cell lymphoma. We report the case of an erythrodermic patient, initially diagnosed with Sézary syndrome, treated with chlorambucil and prednisolone. Later on, a photobiological study demonstrated photosensitivity to UVB, UVA, and visible light. The clinical picture, histological findings resembling lymphoma, and the results of the photobiological study established the diagnosis of actinic reticuloid. Currently the patient is avoiding sun exposure and being medicated with azathioprine and prednisolone, and is showing sustained improvement.

Received: 12 July 2012 | **Returned for modification:** 13 August 2012 | **Accepted:** 23 October 2012

Introduction

Actinic reticuloid (AR) is a rare chronic idiopathic photosensitive dermatosis, with an estimated incidence of 1 in 6,000, found more frequent in elderly men (1, 2). Photobiological investigation may reveal a decreased Minimal Erythemal Dose (MED) to UVB, but often also to UVA and visible light, as well as a decreased Minimal Edematous Dose (MEdD) (3, 4). Professional occupation and outdoor activities are often described as precipitating factors of AR, the diagnosis and treatment of which represents one of the most difficult challenges facing dermatologists.

Case report

A 74-year-old Caucasian man, phototype III, retired (former milling machine operator), was admitted for evaluation, diagnosis, and management of erythroderma. The patient had developed eczematiform lesions on the backs of the hands 1 year before admission. Although the dermatosis was initially restricted to photo-exposed areas, progressive dissemination to the upper limbs, face, neck, and subsequently to covered areas was observed. The patient showed plantar hyperkeratosis and fissures, dystrophy of the fingernails and toenails, diffuse erythematous patches, and alopecia (Fig. 1a). The patient had left axillary lymphadenopathy with no organomegaly.

Laboratory tests: hemoglobin 12 g/dL (RV = 13–17.5), erythrocyte sedimentation rate at first hour 46 mm (RV < 30), beta 2-microglobulin 4.53 mg/L (RV = 0.8–1.8) and total IgE = 150 SU (RV < 85), Sézary-like cells, corresponding to 4,870 circulating cells/ml. The absolute and relative values of circulating lymphocytes with Sézary-like cell morphology continually oscillated. The lymphocyte subpopulation observed in a peripheral blood smear revealed a decrease in CD4 (1,204.0 cell/µL), 23.7% (RV = 29–59), an increase in CD8 (3,231.1 cell/µL), 63.6% (RV = 19–48) and a CD4:CD8 ratio of 0.4. Biopsy of a left axillary lymph node revealed a pattern of dermopathic lymphadenopathy.

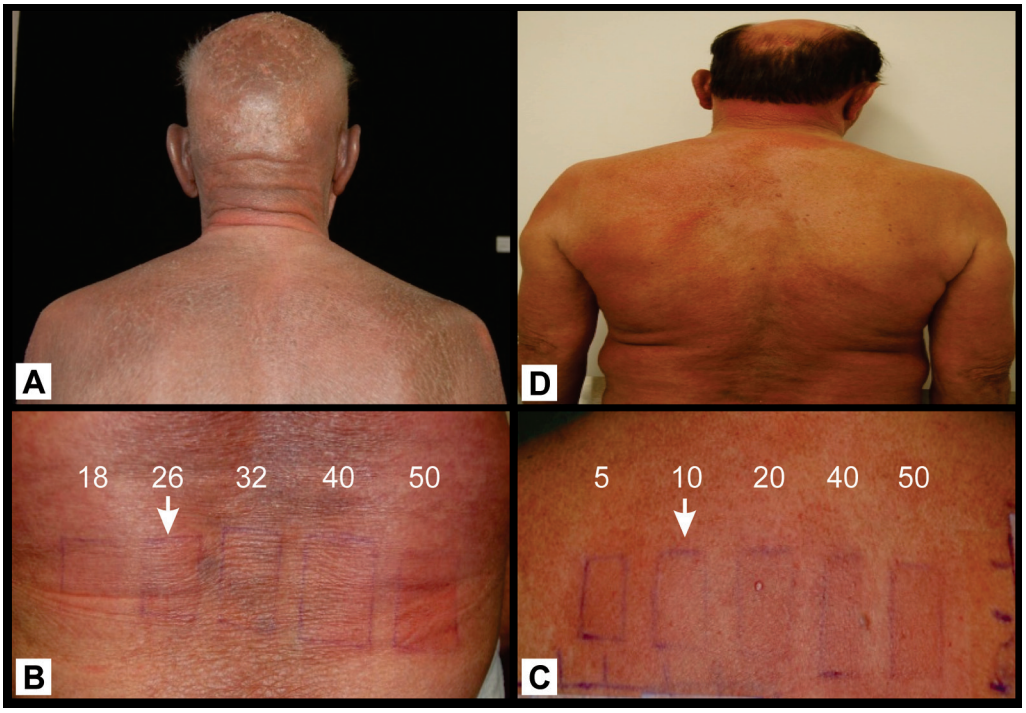

Figure 1 | (A) Clinical features on hospital admission (B) MED UVB: (26 mJ/cm²). (C) MED UVA: (10 J/cm²). (D) Week 8 – Combined immunosuppressive therapy with azathioprine and prednisolone. MED – Minimal Erythematous Dose.

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Bone marrow aspirate showed 10% lymphocyte, 5% plasmocytes without Sézary cells. T-cell clonality studies were performed in the peripheral blood and revealed a genetic rearrangement pattern of the beta chain T-cell receptor (TCR-beta) and abnormal T clone in seven metaphases with loss of Y chromosome. Among the nine skin biopsies performed, only one was compatible with mycosis fungoides, the remaining being suggestive of drug eruption or eczema. Due to the presence of a large number of circulating Sézary-like cells, and after discussing the case with a hematologist, Sézary syndrome was suspected and the patient started chlorambucil plus prednisolone, showing significant improvement after 2 months.

Taking into account that there were still eczematiform patches and lichenification on sun-exposed skin areas, a photobiological study was performed, revealing the following: Minimal Erythematous Dose (MED) for UVB was 26 mJ/cm² (Fig. 1b); MED for UVA was 10 J/cm² (Fig. 1c); epicutaneous testing using the Portuguese Contact Dermatitis Group (PCDG) Standard Series, plants and woods were negative; non-irradiated epicutaneous tests (standard photoallergens) were negative; and irradiated photoepicutaneous tests (standard photoallergens - 5 J/cm²) were globally positive (Table 1). These results supported the diagnosis of AR. The patient was initially treated with azathioprine 50 mg/day and prednisolone 1 mg/kg/day showing sustained improvement after 2 months. Currently the patient is being medicated with azathioprine 100 mg/day and prednisolone has been tapered to 5 mg/day, with clinical improvement (Fig. 1d). Photoprotection with sunscreens and avoidance of UV and artificial radiation from fluorescent lamp exposure was suggested.

Table 1 | **Photo allergen series of the Portuguese Contact Dermatitis Group.**

Photo allergens	After radiation
Tetrachloro salicylanilide	+
Chlorhexidine	+
Triclosan	+
Methylcoumarin	+
Musk ambrette	+
Thiourea	+
Isoamyl p-methoxycinnamate	+
Ethylhexyl p-methoxycinnamate	+
Benzophenone 4	+
Oxybenzone	+
4-tert-butyl-4'-methoxy-dibenzoylmethane	+
Benzydamine	+
Sulfanilamide	+
Chlorpromazine	+
Promethazine	+
Hydrochlorothiazide	+
Carbamazepine	+
Piroxicam	+
Lichen acid mix	+
P-aminobenzoic acid	+

+ = positive irradiated photo-epicutaneous test

Discussion

AR, photosensitive eczema, chronic photosensitive dermatitis, and persistent light reaction are different variants of the same disease, known as chronic actinic dermatitis, defined on the basis of the following criteria: 1) dermatitis of photo-exposed areas; 2) eczema-matched histological appearance (or with lymphoma-like changes); and 3) reduction of MED for UVB (mJ/cm²) and for UVA (J/cm²) (1, 5–7). It was hypothesized that chronic actinic dermatitis may be the final stage of a contact photoallergy, contact eczema, drug photosensitivity, polymorphic light eruption, or endogenous eczema (8).

At the initial stage of AR, erythema is limited to photo-exposed areas. A clinical picture of eczema is gradually established. In the "stationary phase," the clinical picture is marked by lichenification and the presence of infiltrated erythematous pruritic papules. Episodes of edema, vesiculation, and exudation are nonspecific skin signs of phototoxic reactions, either toxic, allergic contact, or photoallergic reactions. The lesions may extend to covered areas and culminate in erythroderma. Lesions will burst after minimum sun exposure and may persist throughout the year, making the photosensitive character difficult to determine (5).

In the end-stage of AR, lesions have a pseudo-lymphomatous appearance, with multiple infiltrated violaceous papules and plaques on photo-exposed areas. Other clinical signs may include lichenoid hyperpigmentation, lichenoid purpuric lesions, palmoplantar hyperkeratosis, onycholysis, and alopecia (9). Histologically, there is a spectrum of changes similar to chronic eczema and mycosis fungoides, as was evidenced in this case report. In the early stage these lesions simulate eczema, and in the chronic stage they resemble a pseudo-lymphoma with flame- or tear-figure exocytosis. The dermal infiltrate is perivascular or band-like. It is usually dense and composed of atypical mononuclear cells with a cerebriform nucleus (1, 7, 9).

Photobiological study is crucial to establish the diagnosis, revealing low MED in several wavelengths, in a broad spectrum between 290 and 430 nm. The average spectrum of the wavelength is found in the UVB. It is usually possible to reproduce the lesions with UVB (3 MED in 3 days) or UVA (total dose of 120 to 150 J/cm²) radiation in 70% of the cases. Photo-patch tests provide one or more positive allergen responses in 75% of cases, the significance of which remains unclear. This phenomenon seems to play a role in photosensitivity maintenance, particularly in cases involving certain classical allergens that have a high phototoallergic potential, such as tetrachloro salicylanilide, musk ambrette, sulfanilamide, lichen acid mix, and P-aminobenzoic acid (5, 9).

In the case of our patient, the diagnosis of Sézary syndrome was excluded because laboratory tests did not confirm the presence of Sézary cells in the peripheral blood smear, only lymphocytes with a similar morphology, whose numbers were continually oscillating. A genetic rearrangement pattern of the TCR-beta was observed (10, 11). This indicates a monoclonal T-lymphocyte proliferation. In this setting, genetic rearrangement study cannot be used as definitive criteria for malignancy because this can also occur in other circumstances, and must therefore be integrated with clinical and laboratory data (10–12).

Several therapeutic regimens have been proposed for AR: light avoidance and use of sunscreens, topical corticosteroids and calcineurin inhibitors, and systemic therapy with corticosteroids and immunosuppressors such as cyclosporine, hidroxyurea, and azathioprine. Ordinary phototherapy with UVA and UVB should be avoided. If used, doses must be lower than usual therapeutic regimens for inflammatory dermatosis (1, 5).

AR is a rare idiopathic photodermatosis that should be considered in patients with a clinical pattern of eczema in photo-exposed areas and in cases of erythroderma with unknown etiology. Early detection of the disease can lead to well-timed therapeutic intervention, better management, and thereby significant improvement.

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