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A case report of therapeutically challenging chronic actinic dermatitis

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Abstract

Chronic actinic dermatitis is a difficult to treat photodermatitis. Treatment is not standardized and involves topical corticosteroids and immunomodulators, and systemic immunosuppressive agents. We present a case with partial response to dupilumab, a monoclonal antibody approved for atopic dermatitis. In recalcitrant cases, systemic agents such as methotrexate, azathioprine, mycophenolate mofetil, and thalidomide, extracorpeal electrophoresis, and low-dose psoralen and ultraviolet A can also be considered.

Keywords

Chronic actinic dermatitis, photosensitivity dermatitis, photodermatosis, dupilumab, thalidomide

Introduction

Chronic actinic dermatitis (CAD) is a rare, immunologically mediated photodermatosis resulting in an eczematous eruption to ultraviolet (UV) rays.[1] Management includes behavioural modification and topical agents, with systemic agents in recalcitrant cases.[2]

The case below showcases a therapeutically challenging case of severe CAD.

Case report

A 54-year-old male presented with a long-standing severe photodistributed eczematous eruption on his face, neck, chest, back, and extremities (Figure 1). His past medical history was significant for severe atopic dermatitis (AD), allergic rhinitis, alopecia universalis, hypertension, and dyslipidemia. His medications included levothyroxine, amlodipine, and atorvastatin.

Diagnostic evaluation included phototesting, patch-testing to the North American Contact Dermatitis Group (NACDG) Standard Series (allergEAZE, SmartPractice, Phoenix, AZ), the Chemotechnique Plant Series (Chemotechnique MB Diagnostics AB, Malmö, Sweden), some of his own products and photopatch-testing to the NACDG Photo Series (allergEAZE, SmartPractice, Phoenix, AZ), in duplicate; one set of allergens was irradiated with 5 J/cm^2 of ultraviolet A (UVA) at 24 h.[3,4] Phototesting revealed a minimal erythema dose (MED) to UVA of 5 J/cm^2 and a MED to ultraviolet B (UVB) of 0.05 J/cm^2. Methods for patch testing, evaluation of reactions, and data recording followed the NACDG protocol.[3,4] Haptens were applied using FINN chambers (Smartpractice, Phoenix, AZ) for the NACDG standard and photoseries and IQ Chambers (Dormer Labs, Chemotechnique Diagnostics, Toronto, ON, Canada) were used for the plant series with Scanpor tape (Norgesplaster Alpharma AS, Vennesla, Norway). Patch test results were positive to lanolin, carba, bacitracin, chloroxylenol, and chlorocresol. Photopatch-testing revealed an equally positive reaction on both non-irradiated and irradiated sites to oxybenzone and ethylhexyl methoxycinnamate suggesting the patient had allergic contact dermatitis (ACD), not photo ACD.

Further investigations were performed prior to initiation of systemic therapy including blood chemistry, hepatitis screen, chest x-ray, tuberculin (TB) skin test, and QuantiFERON gold. All testing was negative except for positive induration of 10 mm on TB skin testing due to previous bacille Calmette–Guerin (BCG) vaccine.

Initial management included sun avoidance, photo-protective clothing, UV protective car window glass, UVA and UVB sunscreen (e.g. Anthelios XL 60, La Roche-Posay), Heliocare (Cantabria Labs, Madrid, Spain), and beta-carotene 25,000 units daily. Avoidance of agents he was positive to on patch testing did not improve his CAD. He was prescribed triamcinolone acetonide 0.1% (Aristocort, Valeant, Laval, Canada) and tacrolimus 0.1% ointments.

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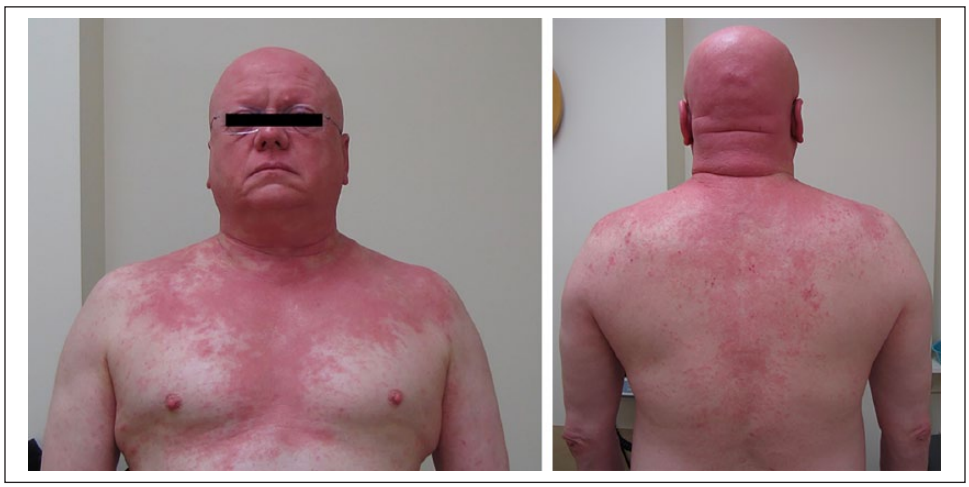

Figure 1. A photodistributed erythematous eczematous eruption affecting the face, neck, and chest (left) and back (right) of a 54-year-old man before starting dupilumab.

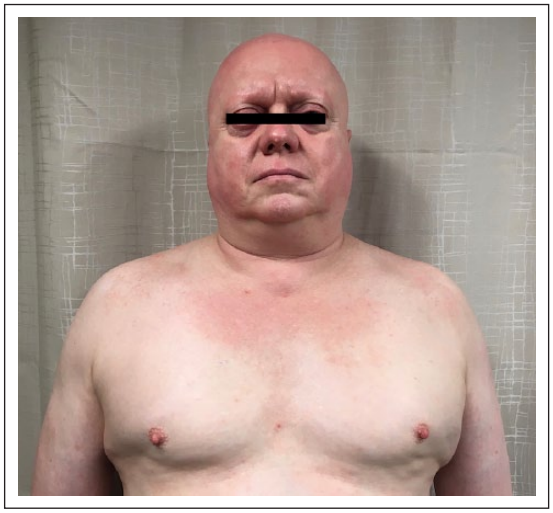

Figure 2. Dramatic partial response after 9 months of treatment with dupilumab.

He was started on methotrexate 15 mg orally once weekly, however, due to gastrointestinal symptoms, not only switched to subcutaneous administration but also discontinued due to extreme fatigue. Mycophenolate mofetil 500 mg twice daily was trialled but discontinued due to elevated liver enzymes. In order, azathioprine 25 mg twice daily (patient was thiopurine methyltransferase heterozygous, therefore, a lower dose was required), hydroxychloroquine 200 mg twice daily, and apremilast 30 mg twice daily were trialled but each discontinued due to inefficacy. He was not able to reach the therapeutic dosage for any of the above agents; therefore, his CAD did not improve.

He was then periodically maintained on cyclosporine 100 mg twice daily (maximum dosage due to elevated blood pressure) until dupilumab became available in Canada, February 2018. He was switched to dupilumab and given a loading dose 600 mg and 300 mg every 2 weeks for maintenance. He partially responded but developed conjunctivitis which was managed with fluorometholone eye drops, dexamethasone ointment, and Refresh tears (Allergan, Unionville, Canada) (Figure 2). To manage periodic flares, he received prednisone over 3–6 weeks.

Due to the patient's partial response to dupliumab, his case was discussed in a joint meeting between the NACDG and International Contact Dermatitis Group (ICDRG) on June 18–19, 2018, in Ottawa, Canada. The recommendations included increasing dupilumab to 300 mg weekly. The use of thalidomide, extracorpeal electrophoresis, and low-dose PUVA (psoralen and UVA) were discussed as potential treatments if symptoms are refractory. Fortunately, this was not necessary.

Discussion

The above case illustrated the range of therapeutic options for CAD. The pathogenesis of CAD is not fully known but likely similar to persistent ACD. This involves a delayed hypersensitivity reaction to antigens in the patient's skin developed from previous UV-mediated molecular alteration.[5] After formation of the antigens, they are presented to T-lymphocytes by Langerhans cells with major histocompatibility complex II. This results in activated T-cells recognizing the antigens at UV exposed areas of the skin, producing skin lesions.[2,5] A summary astutely and expertly stated by world authority Dr John Hawk is as follows: 'CAD appears to be an allergic contact dermatitis-like reaction against UVR-altered DNA or a similar or associated molecule, or more rarely other molecules, perhaps as a result of airborne contact dermatitis-enhanced immune reactivity, or photo-damaged immunosuppressive activity, or both, in mainly long-standing sunlight and airborne allergen exposed subjects'.[5]

Previous studies have shown that management of CAD consists of avoidance and protection from UV rays through clothing, glass, and sunscreens which block UVB, UVA, and

visible UV light with the application of topical steroids and tacrolimus ointment as adjuncts.[2,6] There is also evidence for Heliocare (*Polypodium Leucotomos* extract) and beta-carotene for their photoprotective properties.[6,7] Flares can be managed with prednisone and cephalexin for secondary infection in our patient's case. In more severe cases, systemic immunomodulation with azathioprine, mycophenolate mofetil, cyclosporine, and low-dose methotrexate can be used with azathioprine.[2,6]

The above therapies were all trialled for our case with little success due to adverse effects or inefficacy, necessitating alternative therapies. Dupilumab, a human monoclonal antibody that inhibits type 2 helper T-cell (Th2) cytokines: interleukin-4 and interleukin-13, received approval by Health Canada in November 2017.[8,9] While initial studies were performed on AD patients, other inflammatory skin conditions such as CAD share a similar pathogenesis. Initial studies with dupilumab showed that 85% of patients receiving dupilumab had a 50% reduction in the Eczema Area and Severity Index score compared to 35% in the placebo group.[8] While further studies are needed to determine the direct efficacy of dupilumab on CAD, the similar inflammatory nature of CAD and AD suggests a potential benefit.

Other alternate therapies include thalidomide, which has been successfully used in other photodermatoses including actinic prurigo and lupus erythematosus.[10–12] While the full mechanism of action is unknown, it possesses anti-inflammatory action via inhibiting production of tumour necrosis alpha and, therefore, further T-cell responses. The literature reports one case of recalcitrant CAD successfully managed by low-dose thalidomide (initial dose of 100 mg daily tapered to 50 mg twice weekly).[13] However, further studies are needed to establish the efficacy of thalidomide for CAD.

We conclude that the treatment of CAD is difficult and not standardized. However, the use of systemic agents, duplimumab and thalidomide, can be considered in the management of severe recalcitrant CAD. Further studies assessing the efficacy of duplimumab and thalidomide in CAD are needed.

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Informed consent

Written informed consent for patient information and images published was provided.

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