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Beneficial Effect of Sauna Therapy on Severe Antihistamine-Resistant Chronic Urticaria

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Patients with chronic spontaneous (idiopathic) urticaria are often unsatisfied with the standard treatment since their quality of life is severely impaired. The recent guidelines recommend as a first-line therapy non-sedating H1-antihistamines, increasing their dosage up to fourfold as second-line treatment, and adding a leukotriene antagonist or switching to another antihistamine as the third-line treatment [1]. Although guideline-recommended updosing fourfold increases symptom control in the majority of affected subjects, both our clinical experience and published clinical studies show that in a considerable number of patients the benefit from higher doses of antihistamine is small [2]. We report the case of a patient with severe antihistamine-resistant CIU who responded dramatically to sauna therapy.

PATIENT DESCRIPTION

A 44 year old woman with a 26 week history of recurrent severe urticaria associated with angioedema episodes was seen at our outpatient allergy clinic. The patient was otherwise healthy and did not have a family history of allergic disorders or angioedema. Physical examination was normal, as were chest X-ray examination and blood tests, including complete blood counts, erythrocyte sedimentation rate, antinuclear antibodies, and complement (C3, C4, C1 inhibitor concentration and CH50). Thyroid autoantibodies were negative, and thyroid function was normal. Total serum IgM, IgA, IgG and IgG subclasses levels were within the normal ranges and total serum IgE level was 78 IU/ml.

Helicobacter pylori infection was assessed using the ^{13}C-urea breath test, stool ova and parasite's test and was found to be negative. Skin prick tests with a large series of food allergens were negative, while autologous serum skin test was positive. Physical types of urticaria were excluded using the dermographism test, cold provocation and heat provocation threshold tests, pressure test and intradermal methacholine test for cholinergic urticaria.

Antihistamine therapy (fexofenadine 180 mg once a day) updosing to fourfold did not result in any improvement. Prednisone 60 mg once daily for a week with gradual tapering of the dose for the following 3 weeks effectively suppressed the clinical severity of CIU, but after steroid discontinuation a quick rebound of CIU occurred. All trials of immunomodulation therapy also failed. With the addition of cyclosporine 150 mg/day, there was a substantial reduction in CIU activity score after 3 weeks, but the patient had to stop the medication due to hair loss. A 4 week trial of Dapsone® (Roche Pharmaceutical, Israel) 50 mg/day was without any clinical efficacy and omalizumab treatment was not feasible because of its high cost.

The patient continued on fexofenadine 180 mg twice a day but suffered daily attacks of severe urticaria, until she started sauna therapy in the Finnish steam sauna on the recommendation of her friend. After a single sauna session, severe pruritus and wheals disappeared completely and she decided to take sauna sessions every other day, remaining completely asymptomatic during 2 subsequent weeks. Upon discontinuation of sauna therapy, severe urticaria and pruritus relapsed. The patient renewed the sauna sessions two to three times a week with the similar beneficial effect. She has experienced only very infrequent and mild urticarial eruptions without angioedema for the subsequent 6 months and reduced the dose of fexofenadine to 180 mg once a day.

COMMENT

Sauna therapy has been used for hundreds of years in the Scandinavian countries and Russia. The Finnish steam sauna is a wood-paneled room with a radiant heater that keeps a face level temperature of 80–90°C, while steam is produced by pouring water over heated rocks to create a humidity of 50–60 g H_2O vapor/m^3. The sauna session consists of two to three repeated cycles of 5–15 minutes stay in the sauna, followed by cold bath immersion and a period of room temperature recovery [3]. There is no scientific or medical explanation of the 'cooling' after sauna treatment; it is simply a traditional Finnish custom. Saunas produce thermal stress, activating the sympathetic nervous system, the hypothalamic-pituitary-adrenal axis, and the immune system [3]. In general, sauna bathing is harmless to the skin. It may benefit patients with psoriasis; however,

CIU = chronic spontaneous (idiopathic) urticaria

in patients with atopic dermatitis, heat urticaria and cholinergic urticaria sauna therapy may cause exacerbation of the disease [4]. It is uncertain whether sauna therapy would have a beneficial effect in other cases of CIU, since the observed impressive clinical improvement in our case could be incidental.

The case could be considered autoimmune in origin (chronic autoimmune urticaria) due to positive autoreactivity (by means of a positive autologous serum skin test). It is assumed that whole-body hyperthermia during sauna therapy might have immunoregulatory effects in autoimmune urticaria by reducing the secretion and/or function of histamine-releasing autoantibodies. Whole-body hyperthermia would also attenuate thrombin-induced mast cell degranulation and vascular hyperpermeability in CIU [5].

Our report is notable for two reasons. It represents, to our knowledge, the first documented case of dramatic amelioration of resistant CIU by means of sauna therapy. Second, it illustrates the importance of further investigation of the effect of hyperthermia on cutaneous mast cells and basophils and on the pharmacokinetics of antihistamine medications.

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Capsule

Fas ligand-mediated immune surveillance by T cells is essential for the control of spontaneous B cell lymphomas

Loss of function of the tumor suppressor gene *PRDM1* (also known as *BLIMP1*) or deregulated expression of the oncogene *BCL6* occurs in a large proportion of diffuse large B cell lymphoma (DLBCL) cases. However, targeted mutation of either gene in mice leads to only slow and infrequent development of malignant lymphoma, and despite frequent mutation of *BCL6* in activated B cells of healthy individuals, lymphoma development is rare. Afshar-Sterle and collaborators show that T cells prevent the development of overt lymphoma in mice caused by Blimp1 deficiency or overexpression of Bcl6 in the B cell lineage. Impairment of T cell control results in rapid development of DLBCL-like disease, which can be eradicated by polyclonal $CD8^+$ T cells in a T cell receptor-, CD28- and Fas ligand-dependent manner. Thus, malignant transformation of mature B cells requires mutations that impair intrinsic differentiation processes and permit escape from T cell-mediated tumor surveillance.

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Capsule

Specific and non-hepatotoxic degradation of nuclear hepatitis B virus cccDNA

Current antiviral agents can control but not eliminate hepatitis B virus (HBV), because HBV establishes a stable nuclear covalently closed circular DNA (cccDNA). Interferon-α treatment can clear HBV but is limited by systemic side effects. Lucifora et al. describe how interferon-α can induce specific degradation of the nuclear viral DNA without hepatotoxicity and propose lymphotoxin-β receptor activation as a therapeutic alternative. Interferon-α and lymphotoxin-β receptor activation up-regulated APOBEC3A and APOBEC3B cytidine deaminases, respectively, in HBV-infected cells, primary hepatocytes, and human liver needle biopsies. HBV core protein mediated the interaction with nuclear cccDNA, resulting in cytidine deamination, apurinic/apyrimidinic site formation, and finally cccDNA degradation that prevented HBV reactivation. Genomic DNA was not affected. Thus, inducing nuclear deaminases – for example, by lymphotoxin-β receptor activation – allows the development of new therapeutics that, in combination with existing antivirals, may cure hepatitis B.

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"It is a truism that almost any sect, cult, or religion will legislate its creed into law if it acquires the political power to do so"

Robert A. Heinlein (1907-1988), American science fiction writer. One of the most influential and controversial authors of the genre in his time, he set a standard for scientific and engineering plausibility