

Idiopathic edema, a condition associated with pelvic pain and other symptoms in women, as a remedial cause of chronic cold induced urticaria

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Summary

Purpose: To determine if the treatment of cold induced urticaria refractory to conventional antihistamine-type therapy would respond to treatment with sympathomimetic amines. **Methods:** Dextroamphetamine sulfate (15 mg) extended release capsules were prescribed to be taken daily in the morning. **Results:** The cold-induced urticaria completely disappeared and antihistamine therapy was discontinued. **Conclusions:** Treatment of chronic refractory cold-induced urticaria effectively responds to treatment with sympathomimetic amines similar to other cases of chronic refractory urticaria that are not merely cold induced. Manifestation of idiopathic orthostatic edema, a condition predominantly of women, should always be considered in the differential diagnosis of baffling medical conditions.

Key words:

Introduction

There is a condition involving a defect in the sympathetic nervous system, especially prevalent in women, that is an etiologic factor in a variety of disorders which are refractory to conventional therapy [1]. These various treatment-resistant syndromes respond quickly and effectively to treatment with sympathomimetic amines [1].

Dextroamphetamine sulfate has proven effective for chronic urticaria in women who were not responding to conventional therapy including antihistamines and glucocorticoids [2, 3].

The case described here reports a different type of urticaria, i.e., cold-induced urticaria that was resistant to conventional therapy but responded to treatment with sympathomimetic amines.

Case Report

A 16-year-old female presented with a history of cold urticaria. The problem started one year before her presentation when she developed erythematous papules when she iced her ankles at La Crosse practice. This continued throughout La Crosse season only when she iced her ankles in the spot where the ice touched her skin. However several weeks later when she went swimming she developed hives from her feet to her neck shortly after her body plunged into the somewhat cool water. From that time on whenever she was exposed to cold weather, or cool water, she would break out in hives.

She stated that her symptoms were severe and did not respond to the use of benedryl, loratadine and hydralazine. The laboratory evaluation by her dermatologist showed normal liver and renal function as well as normal serum electrolytes and glucose level. Her complete blood count showed a normal

hemoglobin, hematocrit and platelet count and the white blood cell count was normal at 6.9×10^3 . Her percentage of eosinophils was normal at 3%. The sedimentation rate was normal at 14 (nl ≤ 20 mm/h), the antinuclear antibody screen was negative, the Epstein Barr (EB) virus antibody panel showed EB virus UCA IgM to be 0.00 but EB virus UCA IgG antibody was positive at 5.27 (EIA value positive = ≥ 1.10), and EBV nuclear antigen was > 5.00 (nl > 1.10). Fasting serum glucose was 78 ng/dl (nl 65-99 ng/dl).

Further immune studies showed complement component C3C at 122 ng/dl (nl 90-180), complement C4C at 26 ng/dl (nl 16-47), serum cryoglobulin was negative (normal), the eosinophil count normal at 207 cells/ul (nl = 15-500), and the serum tryptase (a marker for mastocytosis and mast cell degranulation) was 6 ng/ml (nl = 2-10). The immunoglobulin E was slightly increased at 118 ku/l (nl ≤ 118).

Endocrine studies showed the total thyroxin level to be 9.2 mcg/dl (nl - 4.5-12.5 mcg/dl). Thyroid peroxidase antibodies were < 10 IU/ml (nl = < 35 IU/ml). The serum thyroid stimulating hormone (TSH) level was increased to 6.12 mIU/ml. Based on the TSH level the patient was started on L-thyroxin (50 mcg) but did not show improvement in her urticaria after two months of therapy.

She was evaluated for idiopathic orthostatic cyclic edema, a condition sometimes associated with chronic urticaria but she did not have any of the classic symptoms of nocturia, facial and finger edema in the morning, edema of the feet and legs in the evening, unexplained weight gain, abdominal distention or decreased urination while standing.

At the time of the initial visit she had been taking cetirizine, loratadine, montelukast and ranitidine. A water load test was performed where she drank 1500 ml of water over a half hour period on two consecutive days. The first day she measured her urinary output in the supine position over a four-hour period and the next day followed the same instructions but was standing for four hours. The urinary output was 1650 ml supine vs 825 ml standing (normal should be $> 75\%$ of ingested water load in either position) [4].

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She responded very well to dextroamphetamine sulfate XR and was eventually able to discontinue all other therapy. She has remained symptom free for 16 months.

Discussion

The fact that this teenager failed her water load test suggests that her cold urticaria was another manifestation of a condition known as idiopathic orthostatic cyclic edema [5, 6]. This condition is caused by an increase in vascular permeability in the erect position because of a flaw in the sympathetic nervous system. The increase in hydrostatic pressure that occurs with standing would generally result in fluid diffusing from the intravascular to extravascular spaces were it not for a compensatory closure of pre-capillary sphincters through the sympathetic nervous system [6].

Dextroamphetamine sulfate, a sympathomimetic amine, has proven very effective in correcting this defect [4-6]. Whether related to the swelling of interstitial tissues per se or absorption of toxins into tissues related to the increase in vascular permeability the condition has been associated with interstitial cystitis and pelvic pain unresponsive to conventional therapy but yet significantly improves with dextroamphetamine sulfate therapy [7, 8]. Other pain syndromes in women that had been refractory to conventional therapy but respond to dextroamphetamine sulfate therapy include chronic esophageal pain, gastroparesis, arthritis, fibromyalgia, and headaches [1, 9-11].

The previous cases of chronic urticaria that were unresponsive to conventional therapy but responded quickly and efficiently to sympathomimetic amine therapy were hypothesized to be related to the defect in vascular permeability resulting in a release of histamines [2, 3]. When presented with the case of hives only induced by cold it was not clear that the mechanism would be the same as the unusual urticarial condition previously described [2, 3]. This case shows that cold-induced urticaria not responding to antihistamine therapy may show considerable improvement with sympathomimetic amine therapy. Though glucocorticosteroid therapy was not tried, even if it would also prove to be effective, the treatment would be long term and thus a lot less potential complications would be expected from long-term amphetamine therapy vs corticosteroid treatment.

Idiopathic edema is also a cause of inability to lose weight despite dieting and responds well to amphetamine therapy [4]. This young lady did not complain about her weight, maintained the same dietary habits, but a consequence of therapy (in this case beneficial) was weight loss.

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