

Idiopathic orthostatic cyclic edema as a unique etiology for vasomotor flushing in a normal estrogenic woman with normal day 3 follicle stimulating hormone – case report

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Summary

Purpose: To describe a unique cause and therapy for vasomotor flushing.

Methods: Serum follicle stimulating hormone (FSH) and estradiol, renal and liver function studies and urinalysis were performed as well as a water load test.

Results: All laboratory tests were normal but the water load test showed inadequate four-hour urine excretion when she was erect but normal when supine. Complete relief from vasomotor symptoms occurred shortly after treatment with sympathomimetic amines.

Conclusions: Idiopathic orthostatic cyclic edema can cause vasomotor flushing even with normal estrogen and serum FSH, and treatment of the edema state with the drug of choice dextroamphetamine sulfate can effectively control these symptoms.

Key words: Vasomotor flushing; Idiopathic edema; Sympathomimetic amines; Normal gonadotropins.

Introduction

Vasomotor flushing may occur in 10-25% of premenopausal women [1-4]. Most of these occur in the age group close to menopause. When a younger patient experiences these symptoms the first thought is incipient ovarian failure. This may be manifested by elevated day 3 serum follicle stimulating hormone (FSH) even if menstruation still occurs and possibly even regular menses [5].

Sometimes vasomotor flushing can be seen in women with estrogen deficiency with low gonadotropins either from a hypothalamic pituitary etiology or from suppression, e.g., with gonadotropin releasing hormone (GnRH) agonists or antagonists. If however, a young woman with vasomotor flushing and sweating has normal FSH and is not estrogen deficient one has to consider other diagnoses, e.g., thyrotoxicosis, pheochromocytoma or carcinoid syndrome or an infectious cause, e.g., tuberculosis or even Hodgkin's disease.

If these conditions are excluded the label idiopathic is given. The case described below presents a new etiology for vasomotor flushing called idiopathic orthostatic cyclic edema [6]. Furthermore the case demonstrates that the standard treatment for idiopathic orthostatic cyclic edema, the use of sympathomimetic amines, was quite effective for alleviating vasomotor symptoms when idiopathic edema is etiologic.

Case Report

A 29-year-old woman complained of "hot flashes" and sweats especially at night for one year's duration. Though her cycles had been irregular this was corrected by oral contraceptives (placebo) which had been started before these symptoms began. There was no worsening of the symptoms during intake of the placebo pills.

A chest X-ray was negative. There was no lymphadenopathy during the initial exam. Her temperature was not elevated during these vasomotor episodes. Her heart rate was 76 and regular without murmurs, and the abdominal exam was negative. Her CBC showed a normal white blood cell count of $6.1 \times 10^3/\text{ml}$ with a normal differential. Her serum T4 was normal at 5.5 ug/dl (nl 4.5-12.0), T3 uptake normal at 35 (nl 24-39), free thyroxin index normal at 1.9 (nl 1.2-4.9), and the TSH was normal at 1.396 uIU/ml (nl 0.350-5.5). Her 8 a.m. serum cortisol was less than 1 ug/dl following a rapid dexamethasone suppression test. Her p.m. cortisol was 10.7 ug/dl. The prolactin was 9.5 ng/ml and the free testosterone normal at 0.8 pg/ml (nl 0-3.8). Urinalysis was normal as were liver and kidney function based on chemistry tests.

Her third menstrual day serum FSH while on placebo oral contraceptives was only 4 mIU/ml and the serum estradiol was 45 pg/ml.

For her water load test she ingested 1500 cc and in the supine position excreted 1650 cc of urine in four hours compared to only 800 cc erect. Based on the abnormal water load test and the absence of finding any other condition that could cause an abnormal free water clearance she was diagnosed with idiopathic orthostatic cyclic edema [7].

She was treated with dextroamphetamine sulfate sustained release capsules 10 mg in the morning and 10 mg at noon [8-10]. Within two weeks the woman stated that the flushes and sweats were 99.9% gone and they remained absent three months later. She lost 18 pounds during this time.

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Discussion

The treatment of idiopathic edema includes the use of converting enzyme inhibitor spironolactone and diuretics [11-14]. However, sympathomimetic amines have been found to be the most effective therapy by far [10]. Consequently the decision to use dextroamphetamine sulfate was made. Water retention in various tissues can lead to pain symptoms in different places and idiopathic edema can lead to a mistaken diagnosis of arthritis, carpal tunnel syndrome, migraine headaches, and esophagitis [9,15].

A capillary permeability defect in idiopathic edema may allow absorption of toxic substances into tissues leading to chronic urticaria or interstitial cystitis which respond quickly to dextroamphetamine sulfate therapy [16, 17].

Anecdotally we have seen idiopathic edema as a cause of refractory to treatment migraine headaches, premenstrual syndrome, and even one case of dyslexia which all improve greatly and quickly from treatment with dextroamphetamine sulfate. We hypothesize that the etiology of these central nervous symptoms are related to cerebral fluid retention and pressure in certain areas of the brain. The hypothesis continues that the mechanism of action of dextroamphetamine sulfate is correction of an orthostatic capillary permeability defect associated with the condition and thus relieves cerebral pressure. In the case described we suspect the edema caused pressure on the temperature regulation center of the brain.

The purpose of this case report was not only to describe a unique cause and treatment of vasomotor flushes and sweats but to introduce a very common condition in women, idiopathic edema, (10 to 1 female/male frequency), that is for some reason not well known by the medical community. Thinking about idiopathic edema in the differential diagnosis can help solve a lot of morbidity that seems to be refractory to conventional therapy.

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