Case Reports

Marked improvement of the autoimmune syndrome associated with autoimmune hepatitis by treatment with sympathomimetic amines

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Summary

Purpose: To evaluate the effect of sympathomimetic amine therapy for a life threatening autoimmune disorder. *Materials and Methods:* Dextroamphetamine sulfate was used to treat edema, myalgia, and chronic fatigue associated with autoimmune hepatitis (AIH). *Results:* Sympathomimetic amine therapy completely abrogated the symptoms associated with AIH. *Conclusions:* AIH should be added to the long list of chronic treatment-refractory conditions that respond quickly and effectively to treatment with sympathomimetic amines.

Key words: Autoimmune hepatitis; Sympathetic hypofunction; Chronic fatigue.

Introduction

Autoimmune hepatitis (AIH) is a chronic, progressive form of hepatitis, characterized by periods of disease flares and remissions. Patients may present with asymptomatic elevated liver enzymes or at the other end of the spectrum with acute liver failure. However, the symptoms are often non-specific and include fatigue, lethargy, loss of appetite, pruritis, and arthralgia. While there is no single diagnostic test for AIH, the typical features are elevated transaminases, autoantibodies including anti-nuclear antibody (ANA) and smooth muscle antibody (SMA), and histological inflammation of the liver. Concurrent autoimmune diseases, most commonly thyroiditis, rheumatoid arthritis, ulcerative colitis, vitiligo, and Sjogren's syndrome, are often present [1].

Immunosuppression with steroids has been extremely effective in reducing flares and progression of disease. Standard therapy is a combination of corticosteroids and azathioprine. Patients with AIH usually respond rapidly to corticosteroid treatment, with a reduction in liver transaminases and repeat biopsies showing varying regression of fibrosis and inflammation [2,3]. However, alternative therapies for patients who do not respond or have unacceptable adverse effects are being explored. These second-line agents include drugs such as budesonide, mycophenolate mofetil, cyclosporine, and tacrolimus among others [2].

The sympathomimetic amine dextroamphetamine sulfate has been shown to treat hypofuntion of the sympathetic nervous system, an etiologic factor for a wide variety of chronic treatment-refractory pathologic disorders associated with pain and fatigue [4]. Diminished sympathetic nervous system activity, partly manifested by increased cellular permeability, allows chemicals and toxins to enter tissues, which cause pain and inflammation [4]. Dextroamphetamine sulfate has also been shown to significantly decrease fluid retention in idiopathic orthostatic edema [5]. Additionally, it has been found to be very effective for chronic fatigue syndrome [6].

The case presented here describes the treatment of a woman diagnosed with AIH suffering from edema, diffuse muscle and joint pains, and very severe chronic fatigue syndrome with sympathomimetic amine therapy.

Case Report

A 36-year-old patient presented with a complex medical history, including autoimmune hepatitis, edema, myalgia, diffuse joint pain, and chronic fatigue syndrome. Past medical history was significant for attention deficit disorder, anemia, acute cholycystitis, endometriosis, pre-eclampsia, and recurrent miscarriages. Past surgical history includes cholycystectomy, multiple exploratory laparotomies with adhesiolysis, and total abdominal hysterectomy. About seven years ago, she began to experience extreme fatigue, causing her to sleep for up to twenty hours a day. In addition, she described generalized swelling, chronic pain, and a butterfly rash on the face and chest. She was initially treated for depression, but her symptoms were not relieved. Laboratory work-up at that time revealed aspartate aminotransferase (AST) and alanine aminotransferace (ALT) greater than 1,000 units/l and increased iron. Antinuclear antibody was negative and anti-SMA was 1:320. Differential diagnosis was thought to include sarcoidosis, acute exacerbation of chronic mononucleosis, and he-

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mochromatosis. A liver biopsy revealed lobular scarring but no portal involvement, and a subsequent diagnosis was made of AIH and possibly lupus erythematosus. The autoimmune hepatitis was thought to potentially have been triggered by a hepatitis B booster vaccine, as the patient had experienced similar symptoms after receiving her first hepatitis B vaccine ten years prior.

She was started on prednisone 60 mg daily upon diagnosis, but after an allergic reaction this was switched to mycophenolate mofetil, which also caused significant side effects. Finally, she was switched to azathioprine 100 mg daily, which has been maintaining AST and ALT within normal range for the past three years.

She sought the authors' opinion because despite the azathioprine keeping her liver enzymes within normal limits and thus controlling the AIH, she was completely incapacitated by the chronic fatigue and joint pain. She was currently taking azathioprine 100 mg daily, furosemide 80 mg daily, spironolactone 25 mg daily, hydrocodone/ibuprofen TID PRN, promethazine 25 mg every six hours PRN, cyclobenzaprine 25 mg TID PRN, aspirin 81 mg daily, potassium chloride 20 mEq BID, estradiol cypionate five mg/ml, one ml IM every two weeks, testosterone cypionate 100 mg/ml, 0.1 ml IM every two weeks, and Vitamin B12 1,000 mcg/ml one ml IM every month.

She was started on dextroamphetamine sulfate 15 mg BID, and almost immediately noticed a decrease in swelling, elimination of pitting edema, and decreased muscle spasms, but no improvement in joint pain. One month later, the dosage was increased to 20 mg BID. This resulted in a decrease in knee and generalized joint pain, as well as increased energy. She was maintained on this dose for 14 months and continued to experience symptom improvement. The dose was recently increased to 25 mg BID and she continues to do so well that, while she had been on complete disability, she has now has resumed working five days a week for ten hours a day as a nurse.

Discussion

The use of dextroamphetamine sulfate has much less potentially long-term pathological consequences than continued immunosuppression. Eventually the authors plan to wean the patient off the azathioprine to see if the dextroamphetamine sulfate which completely abrogated all the other autoimmune symptoms and conditions associated with AIH can also keep the hepatitis under control with monotherapy.

The various syndromes of sympathetic nervous system hypofunction, known as the sympathetic neural hyperalgesia edema syndrome, is most known to gynecologists because sympathetic nervous system hypofunction is the most common and also most remediable cause of chronic pelvic pain including dysmenorrhea, middleschmertz, dyspareunia, vulvovaginitis, interstitial cystitis, and backaches [7-10]. Even if the woman does not ask the opinion of the gynecologist for treatment or diagnosis since the immediate connection is not clear, the patient should reveal other pathologic states to the gynecologist during their annual gyn examination. The gynecologist in turn could offer this potential therapy to the patient or at least consult with her treating specialist.

It is quite possible that this patient's previous pelvic pain resulting in hypersterecomy may have been related to sympathetic nervous system hypofunction and initiation of dextroamphetamine sulfate may have prevented the need for hysterectomy.

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