



## A second case of palmoplantar eczema effectively ameliorated following treatment with the dopamine agonist dextroamphetamine sulfate

### Abstract

Palmoplantar eczema is a skin disorder involving the presence of clear fluid filled intraepidermal vesicles limited to the hands and feet that are very pruritic and painful. Though it presents acutely, it tends to be chronic and recurrent and does not respond very well to standard therapy which is topical or systemic corticosteroids or other immunosuppressives. There has only been one previous case report showing a very positive response to a novel therapy with the dopamine agonist dextroamphetamine. Presented here is a second case showing marked regression of severe palmoplantar eczema in a short time with long lasting relief with dextroamphetamine sulfate treatment. Hopefully with the publication of a second case, this will encourage dermatologists to try this type of therapy on a large series of patients with palmoplantar eczema and corroborate the findings.

**Keywords:** Palmoplantar eczema; Increased cellular permeability syndrome; Dextroamphetamine sulfate; Mucosal barrier.

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### Introduction

Palmoplantar eczema (previously referred to as dyshidrotic eczema related to its usual presentation of clear fluid filled intraepidermal vesicles) typically presents on the hands and the feet. These vesiculobullous lesions sometimes give the appearance of “tapioca pudding” and are typically both pruritic and painful. Another name that has been given is pompholyx [1-4]. Typically, it involves both hands at the same time, especially the lateral aspects of the fingers sometimes extending to the palms.

Though it appears more often acutely, rather than insidiously, it is generally not transient but becomes chronic if not treated with topical steroids or a wide variety of other immunosuppressive agents including systemic monoclonal antibody

type therapy aimed at certain inflammatory cytokines e.g., interleukin 13 [2,5,6]. Unfortunately, frequently these therapies are not fully successful and there is a high rate of recurrence when the treatment is stopped.

Dextroamphetamine sulfate is a sympathomimetic amine which increases the release of biogenic amines from sympathetic nerve fibers including dopamine, epinephrine, and norepinephrine. There have been many case reports of its use for a large variety of seemingly unrelated conditions known as the increased cellular permeability syndrome [7]. Based on studies of the mechanism used by the fetus to establish proper implantation which requires the establishment of an increased presence of cellular immune cells caused by the infiltration of irritants into pelvic tissues which occurs by increasing cellular perme-

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ability by progesterone (P) blocking dopamine. These natural killer cells, macrophages, and cytotoxic T cells strip the thick cellular walls of some of the arteries that dominate during the proliferative phase and are replaced by a thin cell wall of extra villous trophoblast cells. These thin-walled spiral arteries then serve to allow nutrient exchange between mother and fetus [8]. It was found that infusion of more than the normal amount of irritants into pelvic tissues can cause infertility and miscarriage especially in the presence of various types of pelvic pain i.e. dysmenorrhea, dyspareunia, mittelschmerz, and chronic pelvic pain but even in the presence of other autoimmune conditions that are concomitantly present with pelvic pain or exist without pelvic pain [9-14]. The pelvic excessive inflammation related to a defect in the mucosal barrier if it involves the ovaries can cause diminished ovarian reserve or even premature menopause related to inflammatory damage of the ovaries. Thus it is by far the most common cause of egg depletion [15].

Other conditions of pain or dysfunction or other physiological functions even without pelvic pain may have a similar pathophysiology, e.g., increased cellular permeability, as evidenced by marked improvement of the condition mostly from treatment with dextroamphetamine sulfate, a dopamine agonist type of drug (even in males) [16-18].

One could argue that since dextroamphetamine stimulates the release of other biogenic amines from sympathetic nerve fibers, how can one be sure that the beneficial action is from the release of dopamine to theoretically correct the mucosal barrier defect by decreasing cellular permeability rather than from the action of one of the other biogenic amines released from the sympathetic nerve fibers? Evidence to support the dopamine hypothesis is accomplished by the demonstration that some severe treatment refractory condition can be markedly improved by treatment with pure dopamine agonists e.g., cabergoline [19,20].

Though there are many drugs that can provide some improvement of palmoplantar eczema, a search of the literature found only one case of palmoplantar eczema that was completely abrogated following treatment with dextroamphetamine [21]. Presented here is a second case of total eradication of a long persistent treatment refractory case of palmoplantar eczema.

### Case report

The patient presented to our clinic at age 55 to seek possible new treatment for her very severe palmoplantar eczema that not only failed to respond to topical steroids, but the pain was getting worse related to thinning of her skin where she applied the steroid.

The symptoms appeared acutely over a few days in September 2023. It started on the feet and the right foot was the worst. After 2 weeks, it spread to her hands. Because of the busy schedule of dermatologists her first evaluation was in June 2024. She was treated with topical corticosteroids. She had absolutely no improvement with clobetasol. After 6 months of no improvement, and in fact worsening possibly related to thinning of skin from clobetasol she stopped the topical steroid and sought another opinion. She was actually referred by one of our employees who was familiar with one of our patients who seemed to have a similar "tapioca pudding" like vesicular rash on her feet and palms who did respond very well to treatment with dextroamphetamine [21].

At the time of her initial presentation in December 2024 she could barely stand on her feet which compromised her job as a hair stylist. There was significant improvement in both the pruritus and pain, and the skin lesions were starting to dissipate just after 2 days of treatment with amphetamine salts immediate release tablets with 15 mg upon arising and 15 mg at 11 AM. This provided her with 18.8 mg of dextroamphetamine sulfate.

Three months later on 30 mg amphetamine salts, she stated that her pruritus and pain in the feet and hands were completely gone. There was 90% resolution of the vesicular rash in the hands and 75% on the feet. By 6 months of dopamine agonist therapy there was no longer a vesicular rash present and no itching or pain.

It should be noted that the patient had an insidious gain of weight. She could not attribute the increase in weight to a change in dietary habits or exercise. In fact, she tried to lose weight with caloric restriction which slowed the rate of increased weight gain, but weight gain continued despite dieting. When she first presented in December 2024, she weighed 203.6 pounds and was 70 inches tall. After 3 months of treatment with dextroamphetamine sulfate, her weight had dropped to 195.5 lbs., her blood pressure was 104/75 mmHg, and her heart rate was 83 beats/minute. After 6 months of treatment, her weight further decreased to 182.8. Since she was losing weight after 1 month, she stopped dieting, so the 20-pound weight loss was strictly from the dopaminergic therapy.

### Discussion/conclusion

There are many different dermatologic conditions that have been chronic and treatment refractory that have had very good amelioration following treatment with dextroamphetamine sulfate [22-30]. Dextroamphetamine has also successfully treated severe mucosal membrane ulcer disorders e.g., recurrent aphthous stomatitis [31]. Dextroamphetamine sulfate quickly resolved a very severe post-herpetic treatment refractory neuropathy of 5-year duration in an 89-year-old male, i.e., post-herpetic neuralgia [32]. Providing a second case of severe palmoplantar eczema that failed to improve with steroid treatment but quickly responded to treatment with dextroamphetamine sulfate adds more credence to adding palmoplantar eczema to the long list of dermatologic conditions that respond well to a dopamine agonists and lends more support to the concept of the increased cellular permeability syndrome [21].

Dextroamphetamine sulfate had been found to cause significant weight reduction in diet refractory patients [33,34]. The presumed mechanism of the weight increase is related to fluid retention because of the failure to release sufficient dopamine at the capillary level to negate the transudation of intravascular fluid to the interstitial state related to the increase in hydrostatic pressure that occurs in humans when they assume the sitting or standing position [33,34]. The hypothetical mechanism suggests that the beneficial effect of a dopamine agonist that increases release of dopamine from sympathetic fibers innervating the capillaries corrects the permeability defect and thus inhibits the transudation of intravascular fluid to a third space. In a more severe form, the patient may manifest the symptoms of the Postural Orthostatic Tachycardia Syndrome (POTS) and dextroamphetamine has markedly improved a woman with severe treatment refractory POTS of a 25-year duration [35].

There are many more reports of different conditions that respond to dopamine agonists, especially dextroamphetamine

sulfate, but not limited to this drug. Despite its class II narcotic restrictions, it is clear to this author that after treatment of hundreds of patients over 45 years with patients stopping suddenly frequently because of lack of availability, that not only does there not appear to be evidence of addiction when used in the normal pharmacologic dosages but there are no withdrawal symptoms upon sudden cessation.

Because of the “war on opioids” (which this author thinks is definitely a good thing for society) pain management physicians and physicians of other specialties have been putting their patients on dextroamphetamine sulfate and have shared positive experiences. However, just when the widespread use and acceptance of dextroamphetamine was beginning, the major pharmacy chains in the United States seem to be unwilling to not only fill prescriptions for opiates but all class II drugs including dextroamphetamine. The use of dextroamphetamine for the large variety of conditions that failed despite extremely expensive drugs with much greater risk (e.g., the article referring to cases of inflammatory bowel disorders failing to respond to monoclonal antibody therapy costing \$500,000 per year e.g., adalimumab, yet completely responding to dextroamphetamine at a cost of \$500 per year and without the risk of cancer and serious infections imposed by immunotherapy) [12,13]. It is not clear why other drugs used for attention deficit hyperactivity syndrome in addition to dextroamphetamine received a class II narcotic classification. Hopefully, continued demonstration of the efficacy and safety of dextroamphetamine and its multiple uses and the tremendous cost reduction in health care, evidence will be provided that will lead physicians and other medical personnel and patients themselves to get national agencies to remove the class II restriction on these drugs.

In the meantime, it may be necessary to explore the efficacy of other dopamine agonists that have no restrictions (e.g., cabergoline or levodopa/carbidopa) to treat these disorders that may be related to increased cellular permeability, and then determine which dopamine agonist has the most clinical effectiveness, least side effects, and least cost among these dopaminergic drugs. Possibly these case reports will evoke the interest of major pharmaceutical companies to try to create a drug that is superior to dextroamphetamine. Hopefully if such a drug is created it can circumvent a class II narcotic restriction. Dextroamphetamine is not a narcotic!

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