SAGE Open Medical Case Reports

SAGE Open Medical Case Reports
JCMS Case Reports
SOMCR Volume 6: 1–2

DOI: 10.1177/2050313X18795071
journals.sagepub.com/home/sco
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Treatment of Darier's disease with oral magnesium: a case report

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Abstract

Darier's disease, an autosomal dominant genodermatosis, arises from a mutation in the *ATP2A2* gene that codes for sarco/endoplasmic reticulum Ca^{2+}-ATPase in the endoplasmic reticulum and is characterized by greasy keratotic papules commonly found in seborrheic regions. Conventional treatments, including topical corticosteroids, antibiotics, antifungals and retinoids, often have limited efficacy. The present article reports the novel use of oral magnesium chloride supplementation (300 mg daily) in the treatment of Darier disease. After 5 years of limited improvement using conventional therapies, significant improvements in neck lesions were observed within 1 month of starting oral magnesium chloride. This suggests that oral magnesium chloride may be an effective therapeutic option for Darier disease, although further in vitro and clinical trials are necessary to evaluate its clinical efficacy.

Keywords

Darier's disease, genodermatosis, therapeutics

Introduction

Darier's disease (DD) is an autosomal dominant genodermatosis resulting from a mutation in the *ATP2A2* gene[1] that codes for sarco/endoplasmic reticulum Ca^{2+}-ATPase (SERCA2), a calcium pump, in the endoplasmic reticulum. DD presents a difficult therapeutic challenge as there are no curative treatments. Conventional treatments such as topical corticosteroids, antibiotics, antifungals and retinoids can help manage symptoms but with limited efficacy.[1] Oral retinoids are also effective but may cause many unwanted side effects.[1] Given the recent report of treating Hailey–Hailey disease (HHD)[2] with magnesium chloride, here, we report the novel use of magnesium in the treatment of DD.

Case report

An 11-year-old boy presented in 2012 with small brown papules scattered on his neck, abdomen and inguinal folds and thick malodorous verrucous plaques on his scalp. A skin biopsy revealed an intraepidermal acantholytic dermatosis associated with extensive dyskeratosis. The clinical appearance and histopathologic findings were consistent with DD. He had no family history of DD. Topical antibiotics, mid-potency topical corticosteroids, topical antiseptic treatment and oral doxycycline 100 mg BID were attempted with limited success. Oral systemic retinoids (acitretin) were deferred due to potential adverse effects to his growth. In June 2017, a trial of oral magnesium chloride 300 mg per day was started. Within 1 month, significant improvement was seen in lesions to the neck (Figure 1) and temples but not to the scalp. He did not experience any side effects such as diarrhea, nausea and other gastrointestinal symptoms from magnesium chloride supplementation; however, he discontinued it after 4 months because of its unpleasant taste. One month after discontinuation, he maintained the improvements from the magnesium chloride supplementation. He continued to use Ectosone 0.1% lotion for his scalp lesions.

Discussion

DD is an autosomal dominant disorder that inactivates one ATP2A2 allele resulting in decreased expression of SERCA2.[1] SERCA2 is essential in transporting cytosolic calcium into the endoplasmic reticulum (ER), thus replenishing ER calcium stores.[3] Calcium efflux from ER Ca^{2+} and Golgi Ca^{2+} stores enables keratinocytes to increase intracellular calcium

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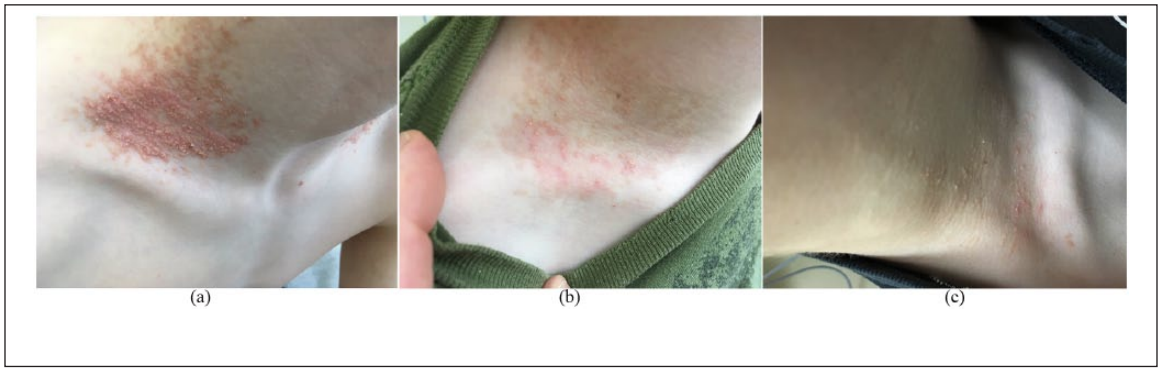

Figure 1. Right lateral neck plaque of a 15-year-old male with Darier's disease (a) before (b) week 6 of treatment and (c) 1 month after a 4-month course of treatment with oral magnesium.

levels in response to increases in extracellular calcium.[2] The transduction of calcium signals is essential in cellular processes that lead to normal keratinocyte differentiation, adhesion and motility.[3,4] In DD, SERCA2 deficiency results in depleted ER calcium stores which affects intracellular calcium homeostasis.[3] This leads to impaired calcium-dependent processes including desmosome assembly[2] and apoptosis[5]—both of which may result in acantholysis and dyskeratosis, two defining clinical features of DD.

HHD is another autosomal dominant genodermatosis that shares similar clinical features and arises due to disrupted intracellular calcium homeostasis.[1] However, HHD is caused by a mutation in the APT2C1 gene that codes for the human secretory pathway calcium-ATPase (hSPCA1) located on the Golgi apparatus.[2] Borghi et al. previously documented the efficacy of a therapeutic regime of oral magnesium (300 mg/day) in treating HHD. In vitro studies demonstrated that $MgCl_2$ decreased calcium efflux of target cells but had no effect on Golgi Ca^{2+} filling,[2] suggesting that the efficacy of Mg^{2+} is not due to the hSPCA1 transporter specific to HHD. Since high Mg^{2+} levels inhibit plasma membrane Ca^{2+} ATPases (PMCA) that allow for calcium efflux,[2] they hypothesized that the observed decrease in calcium efflux may be due to PMCA inhibition. As a result, keratinocytes can regain intracellular Ca^{2+} homeostasis. This enables calcium-dependent processes to occur and could explain the improvement in clinical symptoms observed in both HHD and DD cases.

To date, no studies have investigated the use of magnesium chloride in treating DD. This case supports the hypothesis that oral magnesium chloride may be effective in treating DD. However, the patient's improvement could reflect the natural history of DD and not magnesium chloride supplementation. More extensive in vitro and clinical trials are necessary to assess the mechanism of action and efficacy of oral magnesium chloride in DD treatment.

Declaration of conflicting interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

The author(s) received no financial support for the research, authorship, and/or publication of this article.

Informed consent

The patient's mother provided written permission for publication of this case report and associated images.

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