USE OF LOW-DOSE NALTREXONE IN THE TREATMENT OF SEVERE HAILEY-HAILEY DISEASE: ONE CASE REPORT

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Abstract

Introduction

Hailey-Hailey disease (HHD) or chronic benign familial pemphigus is an autosomal dominant genodermatosis with complete penetrance characterized by painful vesicles, erosions and macerated intertriginous skin.

Case Report

We present a 66-year-old woman with a personal 35-year history of pruritic recurrent vesicles and erosions in both axillae and inguinal folds. HHD was confirmed by cutaneous biopsy.

Past treatments had failed, including topical corticosteroids, antibiotics and oral doxycycline, minocycline, dapsone and acitretin. Phototherapy and intralesional injection of toxin botulinum A was performed in the axillae. The patient was started on naltrexone 6,25mg nightly. Six weeks later, complete clearing was observed.

Discussion

At typical doses, naltrexone blocks μ and δ opiod receptors, thereby blocking the union of β -endorphins at those sites. Paradoxically, at low doses, the partial binding to those receptors leads to a homeostatic increase of opioid receptors and an upregulation of endogenous opioids. Low-dose naltrexone may also exert an anti-inflammatory action through its antagonist effect on toll-like receptor 4 found on macrophages.

Conclusion

We consider that low-dose naltrexone is an effective and safe alternative for the HHD, representing an important progress in the management of this disease with limited therapeutic options.

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Introduction

Hailey-Hailey disease (HHD) or chronic benign familial pemphigus is an autosomal dominant genodermatosis with complete penetrance characterized by painful vesicles, erosions and macerated intertriginous skin. It results from mutations in ATP2C1 gene which encodes a calcium transporter protein in the Golgi apparatus. Defective calcium homeostasis results in abnormal adhesion of keratinocytes and acantholysis (1).

Case Report

Herein, we present a 66-year-old woman, with no known drug allergies, with a family history significant for HHD and a personal 35-year history of pruritic recurrent vesicles and erosions in both axillae and inguinal folds, worsening during the summer. HHD was confirmed by cutaneous biopsy. Direct immunofluorescence was negative.

On physical examination, reddish, fissured, macerated, symmetrical and well-defined plaques were found involving both axillae and inguinal creases (figure 1).

Past treatments had failed, including topical corticosteroids, antibiotics and oral doxycycline, minocycline, dapsone and acitretin. Phototherapy and intralesional injection of toxin botulinum A (50UI per side) was performed in the axillae with a brief clinical improvement followed by an acute flare.

As most of the reported low-dose naltrexone (LDN) dosages in the literature range from 1,5 to 12,5mg per day, the patient was started on naltrexone 6,25mg nightly given the ability to divide the commercially available 50-mg tablets in 8 pieces. After 3 weeks of treatment, erosions began to heal (figure 2). Six weeks later, complete clearing was observed and some hyperpigmented patches remained (figure 3).

The patient continues to have sustained results 8 months into treatment. She denies any adverse effect.

Discussion

A wide range of treatments have been attempted for HHD, being often refractory to many of them.

Naltrexone is an opioid receptor antagonist approved by the UD Food and Drug Administration for the treatment of alcohol, heroin and opioid addiction. LDN has been recently reported effective in 3 inflammatory skin diseases: HHD, lichen planopilaris and scleroderma (2).

At typical doses, naltrexone blocks μ and δ opiod receptors, thereby blocking the union of β -endorphins at those sites. Paradoxically, at low doses, the partial binding to those receptors leads to a homeostatic increase of opioid receptors and an upregulation of endogenous opioids: β -endorphins and methionine-enkephalin. These have effects on pain modulation and mood. Moreover, it has been proved that naloxone inhibits histamine release from basophils causing pruritus relief (2). LDN may also exert an anti-inflammatory action through its antagonist effect on toll-like receptor 4 found on macrophages such as microglia, decreasing the central production of proinflammatory cytokines: substance P, reactive oxygen species and excitatory amino acids (3).

LDN has been used in multiple diseases and its safety has been established. Patients may experience minor adverse effects such as headache, gastrointestinal tract symptoms and vivid dreams (3). Contraindications for its use include opiate addiction, acute hepatitis or liver failure (4).

Conclusion

We consider that low-dose naltrexone is an effective and safe alternative for the HHD, representing an important progress in the management of a disease with limited therapeutic options.

3-50-mg doses have been safely reported for an adequate response (3,5), to our knowledge this is the first case treated with naltrexone 6,25mg per day. If required,

adjunctive agents such as acitretin and systemic antibiotics could be added (5,6). Additional studies are needed to determine optimal dosage regimens and long-term side-effects.

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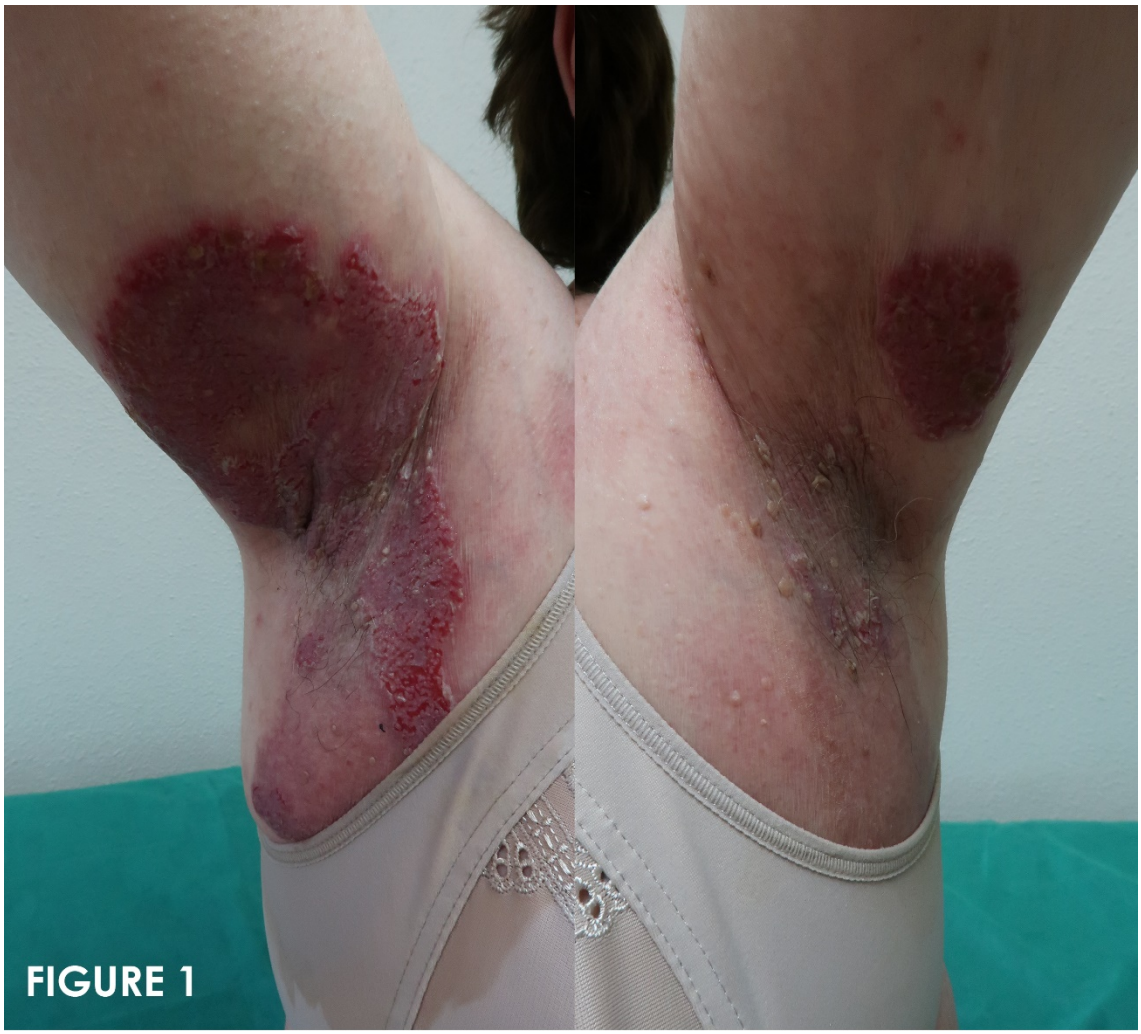

FIGURE 1

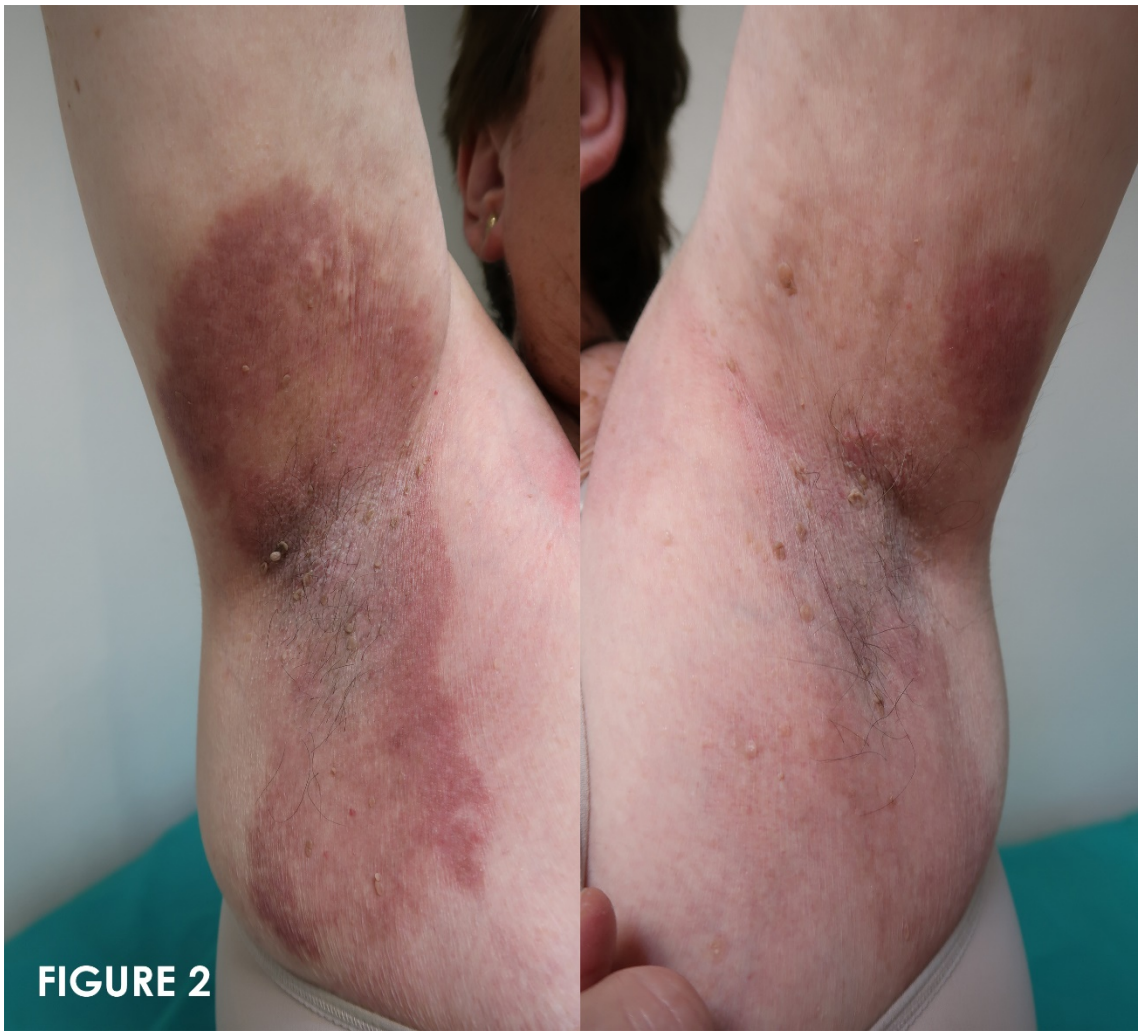

FIGURE 2

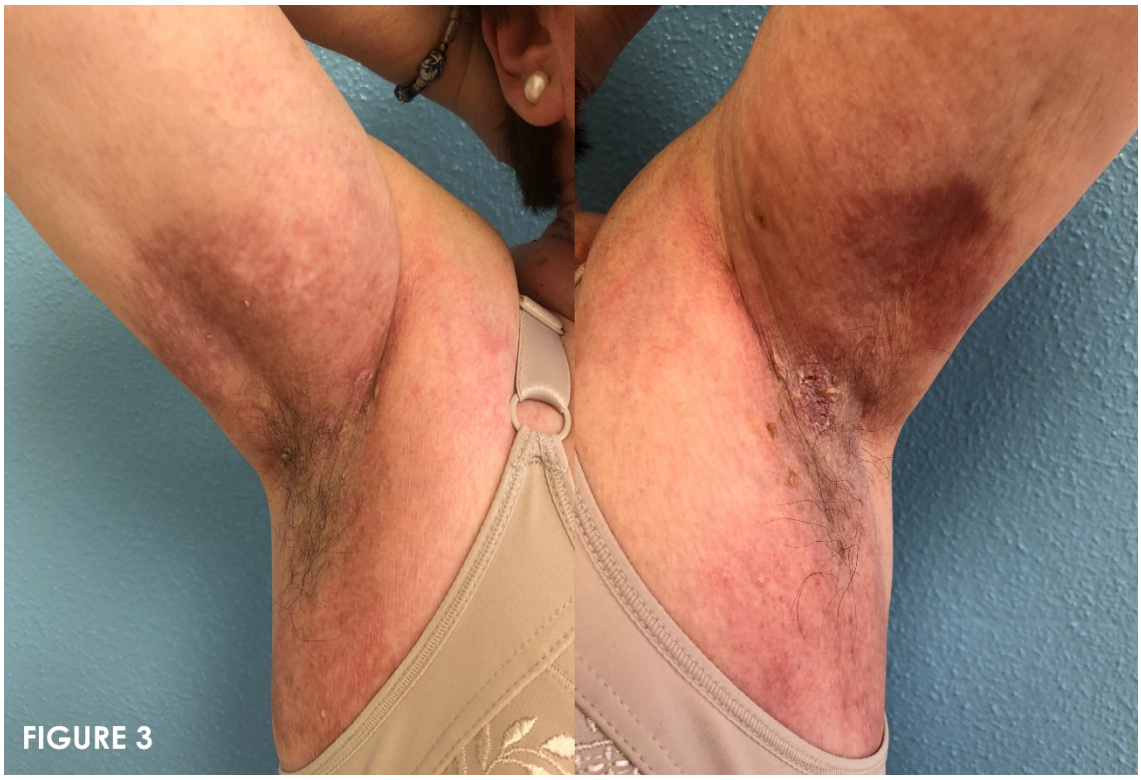

FIGURE 3