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CLINICAL INVESTIGATION OF HAILEY HAILEY DISEASE

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ABSTRACT

Hailey-Hailey Disease is a type of rare autosomal dominant hereditary skin disorder. It is generally characterized by blisters and an eruption of vesicles mainly at the site of friction and regions wherein two areas of skin rub each other example axilla region of arm ,anogenital region etc. Formation of brick wall structure and lesions is generally observed when there is detachment of epidermal region. Hailey-Hailey disease (HDD) is also commonly known as Familial benign chronic memphigus. The absence of treatment has led to the progression of the disease. Histopathology is the diagnostic of the disease till date. However, treatment of this disease is far from the satisfactory till today. This article briefly evaluates the discussion and various types of diagnostic and advancements related with Hailey-Hailey disease till date.

Keywords: *Hailry-Hailey disease, Familial benign chronic pemphigus, HHD, ATP2C1 mutation, Rare disease.*

INTRODUCTION

Familial benign chronic pemphigus (Hailey-Hailey disease) is a rare autosomal-dominant genodermatosis, characterized by recurrent skin eruptions mostly in the intertriginous areas. The clinical manifestations consist of closely grouped in small vesicles with a predilection for neck, axillae and groinn areas. The vesicles usually progress to vegetating fissured plaques with bullae and erosions. Familial benign pemphigus differs from other forms of pemphigus in its genetic pattern, as well as by its absence of mouth lesions and absence of intracellular antibodies [1]. Hailey-Hailey disease (Benign familial pemphigus) was first described 1939 by the Hailey brothers [2]. Rare blistering disease is a condition comprising of an autosomal ,inherited and dominant genodermatosis having penetrance of incomplete nature. A positive family history is present in approximately two thirds of patients, while the rest of cases are believed to be new mutations, involving a defect in a calcium ATPase [3]. Reports in the literature note that the underlying pathologic process is acantholysis and that the fragility of epidermis is secondary to a defect in the adhesion complex between desmosomal proteins and tonofilaments. Clinically, the differential diagnosis includes intertrigo, candidiasis, and friction or contact dermatitis [4]. Histologically, a widespread incomplete suprabasal acantholysis is the trademark of Hailey- Hailey disease, causing the well-known "dilapidated brick wall" appearance of the lower epidermis [5].

The onset is mostly between the second and third decade of life and is triggered by friction and excessive sweating [6]. Hailey-Hailey usually appears only after puberty, as

the annex matures [7]. Hailey–Hailey disease (Familial Benign Pemphigus) is autosomal dominantly inherited genodermatosis, caused by mutations in ATP2A2 gene and ATP2C1 respectively [8].

TREATMENTS

The treatment itself is a challenge to this disease while many different thechniques and therapies have been used, ranging from topical and systemic therapy with antibiotics, antifungals, and coticosteroids to dapsone, methotrexate, thalidomide, etretinate and even cyclosporine [3, 5, 9]. Christian and Moy suggested the use of short-pulsed short-dwell carbon dioxide laser for the treatment of Hailey-Hailey disease [9]. Lasers with short pulse durations generally cause less residual thermal damage than the ones with relatively long pulse duration, and are therefore associated with less erythema and faster healing Surgical intervention has been introduced to control difficult cases refractive to medical therapy. The first successful report came in 1966 from Biro and Madday, who performed full-thickness excision of lesional skin followed by split-thickness grafting from the thigh [10]. In 1983 first dermabrasion therapy was suggested by Belhaouari et al [11].

Kirtschig et al. [12] subsequently reported two cases of patients in whom dermabrasion led to a longstanding absence of active skin lesions. Metze et al. [13] performed histological, ultrastractural and histochemical study of lesional and non-lesional skin of 18 patients with Hailey-Hailey disease. They note that none of the adnexal epithelia expressed the intrinsic defect of cell adhesion. The first report of successful carbon dioxide laser abrasion of Hailey-Hailey disease came in 1987 from Don et al. [3], who treated the inner aspect of the left thigh of a 50-year old man.

Recently, the use of carbon dioxide laser emerged as an effective option for treatment of numerous epidermal and dermal lesions along with it serves as therapy for growths of benign or malignant nature, warts ,tattoos, vascular deformities etc [14]. Kartamaa and Reitamo described the use of continuous CO2 laser in six patients with Hailey-Hailey disease, demonstrating substantial improvement of disease-affected areas in most patients post CO2 laser [15].

Initially, intravenous antibiotic therapy was started with flucloxacillin 2 g three times daily and ampicillin 1 g with a daily dose of three times as proven due to superinfection with gram-positive and gram-negative bacteria, also when a test was done as a local therapy using 1% chlorhexidine aqueous solution. This is further proceeded using a topical pacrolimus applied twice in a day and used as a specific therapy which led to fast and effective improvement [16]. When compared to tacrolimus the penetrating power of pimecrolimus is less so less risk of systemic effects, also it has affinity power which is higher for epithelial structure and less to lymphoid structure [17].

Tacrolimus, pimecrolimus and cyclosporin A block calcineurin in the cytoplasm and lead to suppression of T-cell function. Tacrolimus and pimecrolimus achieve these effects through the initial linkage to the cytosolic receptor FKBP-12, designated also as macrophillin 12 [17, 18].

Treatment with systemic retinoids followed by aromatic retinoids was tried, but eczema herpeticum developed in the affected areas

and dissemination of Hailey-Hailey disease ultimately occurred [19].

Botulinum toxin type A (BTA) is a protein that produces chemodenervation when it blocks the liberation of acetylcholine in nerve terminations. Originally it was used in the treatment of neurologic, ophthalmologic and cosmetic diseases for its action in the motor plaque with production of muscularis weakness. Currently, new uses for BTA have been proposed for its blocking action to the cholinergic stimulus in the post ganglial symphathetic innervation and reduction of the production of sweat by the eccrine glands. As such it has also been used for the treatment of palmar and axillary hyperidrosis [20, 21].

Lapiere *et al*. reported the case of a patient who had applications of 50U of BTA in each axilla, having had complete remission of the lesions in these areas [22].

CONCLUSION

With the prevailing scenario, the Hailey-Hailey disease is one of the rare diseases which needs more research to explore the hidden facts. This disease occurs in 1 out of 2,00,000 patients. Hence, even government should support for the conduct of various research and clinical trials so that these sort of diseases can be explored in the days to come.

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