Familial benign chronic pemphigus
(Hailey-Hailey disease) treated with
electron beam radiation

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INTRODUCTION

Hailey-Hailey disease (HHD), or familial benign chronic pemphigus, is an autosomal dominant genodermatosis. In this condition, dysregulation of intracellular calcium homeostasis leads to impaired desmosome function and suprabasilar acantholysis of the epidermis.1 Clinically, this condition presents as intertriginous vesicles, erosions, and weeping, fissured plaques.1 The painful nature of HHD, risk of secondary infection, and malodor can significantly affect a patient’s quality of life. The lesions are often difficult to control with topical steroids and antimicrobials, necessitating more aggressive treatments. In previous case reports, ionizing radiation was found to prolong remission of plaques.2-4 We report the use of electron beam radiation therapy (EBRT) to treat 2 patients with recalcitrant HHD.

CASE REPORT

Patient 1, a 43-year-old woman, presented with a 15-year history of persistent lesions on her back, chest, and groin. Physical examination found extensive, eroded, well-demarcated, erythematous plaques with honey-colored crust scattered over the inframammary folds, lower back, and bilateral inguinal folds (Fig 1). Patient 2, a 67-year-old woman, presented with a long history of persistent lesions on her upper thighs and groin. Physical examination found well-demarcated, erythematous plaques with a “wet tissue paper” appearance in the vulva, bilateral groin, and perianal region.

Patient 1 was treated with local radiation (10 fractions of 2 Gy) to the right inframammary fold and lower back for a total dose of 20 Gy with near complete resolution and no recurrence after 14 weeks (Figs 2 and 3). A second round of local radiation (10 fractions of 2 Gy) is scheduled to treat the left inframammary region. The patient’s residual lesions are being managed with oral glycopyrrolate, magnesium supplements, chlorhexidine wash, and zinc paste.

Patient 2 was treated with local radiation (10 fractions of 2 Gy) to the vulva, bilateral groin, and perianal skin for a total dose of 20 Gy with complete remission of her lesions 4 months after radiation therapy. On 7-month follow-up, the patient had recurrence in approximately 10% of previously irradiated skin, which remained well controlled with oral magnesium supplements, oral glycopyrrolate, topical calcipotriene, and chlorhexidine wash. In both patients, additional relief was obtained with the use of lightweight cotton clothing and avoidance of hot and humid environments.

DISCUSSION

HHD is an autosomal dominant genodermatosis caused by a mutation in the ATP2C1 gene. The resultant loss of cellular adhesion in the epidermis is from abnormal intracellular calcium signaling and suprabasilar acantholysis (Fig 4).1 HHD is

Abbreviations used:

EBRT: electron beam radiation therapy
GRT: Grenz ray therapy
HHD: Hailey-Hailey disease

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characterized by the presence of vesicular and erosive plaques that favor the intertriginous areas of the body. Friction, heat, and sweating tend to exacerbate the disease and minor trauma may induce new lesions (Köebner phenomenon). The clinical course of the disease is hard to predict, but most patients experience waxing and waning severity. Fortunately, there is evidence showing that HHD tends to improve with age, although complete resolution is rare.

Because of the chronicity and recalcitrant nature of this disease, more invasive treatment options have been introduced, including Grenz ray therapy (GRT) and EBRT. Both forms of ionizing radiation alter DNA, therefore, affecting the reproductive integrity of cells. In GRT, low energy x-rays penetrate the superficial epidermis 1 to 2 mm, allowing sufficient energy to reach the site of pathology while sparing the germinative layers. Notably, the photons travel as indefinite waves with continued, although diminished, penetration into deeper tissues, where the absorption of a given dose of radiation may differ based on tissue density. GRT use in HHD was first described in 1956 by Sarkany (200—400 R, 10 kV) on a series of 6 patients with reported remissions lasting from 4 to 14 months. In contrast, EBRT is composed of electron particles and, therefore, exhibits limited...
penetration, stopping suddenly with no exposure beyond a certain depth. Absorption is unaffected by tissue type. For HHD, EBRT is targeted at a depth of 2 to 2.5 mm (epidermal). In 2010, Narbutt et al reported successful EBRT for 3 patients with HHD, achieving remission for 38 months with a cumulative dose of 20 Gy administered in 10 fractions (2 Gy once daily for 5 days per week).

By contrast, one study reported minimal benefit from EBRT. The authors describe 2 cases of HHD treated with a cumulative dose of 20 to 35 Gy that showed initial improvement at the treatment sites with recurrence by 3 to 5 months. The authors reasoned that it was unclear whether the condition improved because of the remitting-relapsing natural history of HHD or from the treatment with electron beam radiation. Even temporary relief can greatly improve quality of life in severe cases like those examined in these reports. This finding was illustrated by a 2008 survey of patients undergoing ionizing radiation therapy for recalcitrant dermatoses, in which most felt radiation treatment was worthwhile, decreasing the discomfort and severity of their conditions.

The favorable results of our study support EBRT as an option for HHD patients that have not responded to more conservative therapies. Lasting effects are likely secondary to direct ionization, resulting in disturbance of intracellular function, immunosuppression and inhibition of excessive epidermal cell proliferation. The adverse effects are limited to transient erythema, hyperpigmentation of the previously irradiated site, and an increased risk of skin cancer development. Importantly, EBRT does not alter the course of systemic disease in non-irradiated sites. Therefore, adjuvant therapy is highly recommended in conjunction with radiation therapy. Symptoms can be managed with topical corticosteroids in combination with topical or oral antibiotics and a gentle cleanser. In 2015, Borgh et al described the use of magnesium chloride in the treatment of HHD. These authors hypothesized that MgCl₂ acts as an inhibitor of the Ca²⁺ pump in keratinocytes, leading to an accumulation of intracellular Ca²⁺ and promoting increased desmosomal assembly. In our cases, we believe that supplementation with MgCl₂ was a contributing factor in the resolution of the lesions. Oral glycopyrrolate has also been reported in helping control exacerbating factors such as increased moisture and sweating in HHD. Patient education on proper techniques to reduce heat and friction is also important. Our results should encourage providers to consider EBRT when designing the multidimensional treatment plan necessary for treating recalcitrant HHD.

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