Oral Glycopyrrolate for the Treatment of Hailey-Hailey Disease

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Hailey-Hailey disease is an autosomal dominant blistering dermatosis due to a mutation in the ATP2C1 gene (OMIM 604384). This gene encodes a calcium ATPase present on the Golgi apparatus contributing to the formation of intercellular adhesions. Disruption of this enzyme results in acantholysis, which is most clinically pronounced in intertriginous areas that are subject to heat, friction, sweating, and bacterial colonization. Hailey-Hailey disease can have spontaneous periods of clinical improvement; however, the disease often has a long-term course and treatment can be challenging. Because there is currently no cure for this condition, most therapies aim to minimize the influence of exacerbating factors.

Report of a Case
A man in his 50s presented with a 30-year history of intermittent flares of pruritic and painful intertriginous lesions. On physical examination, the patient had erythematous, macerated plaques with superficial erosions on the bilateral axillae, inguinal, and crural folds and a few smaller papules on the lateral neck (Figure, A). The patient’s medical history was notable for atrial fibrillation, which was well controlled with digoxin. A skin biopsy revealed acanthosis with elongation of rete ridges and overlying focal parakeratosis. Areas of full and partial thickness acantholysis were noted. The clinical and histopathologic features were consistent with a diagnosis of Hailey-Hailey disease.

Therapeutic Challenge
The patient had been prescribed various topical corticosteroid and antifungal creams as well as oral antibiotics in the past with minimal improvement.

Solution
The patient was started on a combination regimen of topical mometasone ointment, 0.1%, once daily, oral minocycline, 50 mg twice daily, and a trial of oral glycopyrrolate, 1 mg daily, with approval from the patient’s cardiologist. After 1 month of this course of therapy, the patient demonstrated moderate improvement of his lesions but requested a simplified treatment plan. At this point, therapies with minocycline and the topical corticosteroid were discontinued, but glycopyrrolate monotherapy was maintained. Over the next month, the patient’s condition fully cleared, and he has remained symptom-free for 6 months (Figure, B). Prior to this, the patient’s disease course involved numerous flares throughout the year; this relatively long symptom-free period was a substantial improvement. While he did note some mild xerostomia, he has otherwise tolerated glycopyrrolate without any significant adverse effects.

Discussion
The mutation in the ATP2C1 gene in Hailey-Hailey disease produces an abnormal calcium pump on the Golgi bodies of keratinocytes. This
ever, the application of topical steroids is limited by potential adverse effects such as dry mouth, mydriasis, increased intraocular pressure, tachycardia, decreased gastric motility and secretion, constipation, and urinary retention.9,10 and it is contraindicated for patients with myasthenia gravis, paralytic ileus, and pyloric stenosis. Patients with cardiovascular disease, gastroesophageal reflux, bladder obstructions, and glaucoma can use glycopyrrolate but should proceed with treatment cautiously.10 Glycopyrrolate is also relatively inexpensive and on most drug formularies. In our patient, a trial of low-dose glycopyrrolate, 1 mg daily, was initially instituted as part of a combination regimen and was continued as a single agent. Systemic glycopyrrolate was an effective, affordable, and well-tolerated medication, which produced significant improvement and sustained clearance of Hailey-Hailey disease in our patient. While dosing should be titrated to the individual needs of the patient, the currently recommended daily maximum dose of glycopyrrolate is 8 mg. In the future, trials may include the use of topical glycopyrrolate as maintenance therapy, which could provide similar therapeutic benefit with an even milder adverse effect profile. This case demonstrates a novel application for oral glycopyrrolate as a potential adjuvant or single agent maintenance therapy in the management of Hailey-Hailey disease.

ARTICLE INFORMATION

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Accepted for Publication: October 22, 2014.


Conflict of Interest Disclosures: None reported.

REFERENCES


