Hailey-Hailey disease with lichenoid lesions around the anus

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To the Editor: Hailey-Hailey disease (HHD), first discovered by the brothers Howard and Hugh Hailey,[1] is a genodermatosis at intertriginous sites. Mutation of *ATP2C1* on chromosome 3q21-2 coding a calcium-dependent ATPase gives rise to calcium dysfunction within keratinocytes, resulting in acantholysis due to a signal transduction disorder.[2] It has been suggested that this gene mutation combined with irritation such as frequent friction, cold, and ultraviolet exposure leads to the development of HHD.[3]

A 51-year-old woman diagnosed with pemphigus vulgaris (PV) 1 year previously [Figure 1A] complained of persistent lesions around her anus for 7 months [Figure 1B] despite resolution of all other lesions. Erythema with erosions appeared 7 months previously when she reported consistent mild diarrhea. No family members had similar lesions. Physical examination revealed clustered white or skin-colored, hard, smooth papules of 0.1- to 0.5-cm diameter around the anus. White lichenoid lesions were found in her gluteal sulcus. Antinuclear antibody, extractable nuclear antigen antibody, and ELISA testing of anti-pemphigus antibody were negative. A biopsy specimen was taken from the lesions around the anus [Figure 1C and 1D]. A genetic test for *ATP2C1* showed a heterogeneous mutation: *ATP2C1* c.1504C>T (p. Arg502Ter) [Figure 1E]. She was diagnosed with HHD and treated with topical 0.1% tacrolimus twice daily. The lesions resolved within 2 months [Figure 1F]. No relapse occurred for 1 year after treatment.

After a systematic search of "*ATP2C1* mutation" on PubMed, Embase, and Chinese SinoMed (http://www.sinomed.ac.cn/), we found that *ATP2C1* c.1504C>T (p. Arg502Ter) on exon 16 in chromosome 3 in this patient is a novel mutation site for HHD.

HHD had been misdiagnosed as PV in this patient 1 year previously. Systemic corticosteroid treatment controlled her other lesions well but did not control the perianal lesions. Mild diarrhea was a source of frequent friction that gave rise to the chronic course of HHD and resulted in manifestation of the perianal lesions as papular acantholytic dyskeratosis (PAD).[4] PAD was first described in 1972 as localized papules and lichenoid lesions that histologically show acantholysis and dyskeratosis. More cases of *ATP2C1* mutation have been reported in patients with PAD, suggesting that PAD is allelic to HHD; however, this remains controversial.[5] Localized perianal lichenoid lesions with papules should be clinically differentiated from extramammary Paget disease and bowenoid papulosis. Fungal or virus infection must also be excluded because of the warmth and humidity in the anal area. Histopathologically, PV, PAD, Darier disease,[6] and Grover disease should also be differentiated. This patient was diagnosed with HHD because of typical histopathological features, negative indirect immunofluorescence, *ATP2C1* mutation, and previous extensive lesions.

Treatment of refractory perianal HHD can be challenging due to regular defecation and diarrhea. Diarrhea must be controlled to prevent a chronic course. Previous studies have shown that corticosteroids and topical antiseptics may be employed in mild cases of perianal HHD. Surgical therapy, CO_2 or Er:YAG laser ablation, dermabrasion, and argon plasma coagulation are reportedly useful for extensive perianal lesions of HHD.[7,8] This case has proven that tacrolimus ointment may also be helpful for chronic perianal HHD.

Declaration of patient consent

The authors certify that they have obtained the appropriate patient consent form. In the form, the patient provided her consent for her images and other clinical information to be reported in the journal. The patient understands that her name and initials will not be published and that due efforts will be made to conceal her identity but that anonymity cannot be guaranteed.

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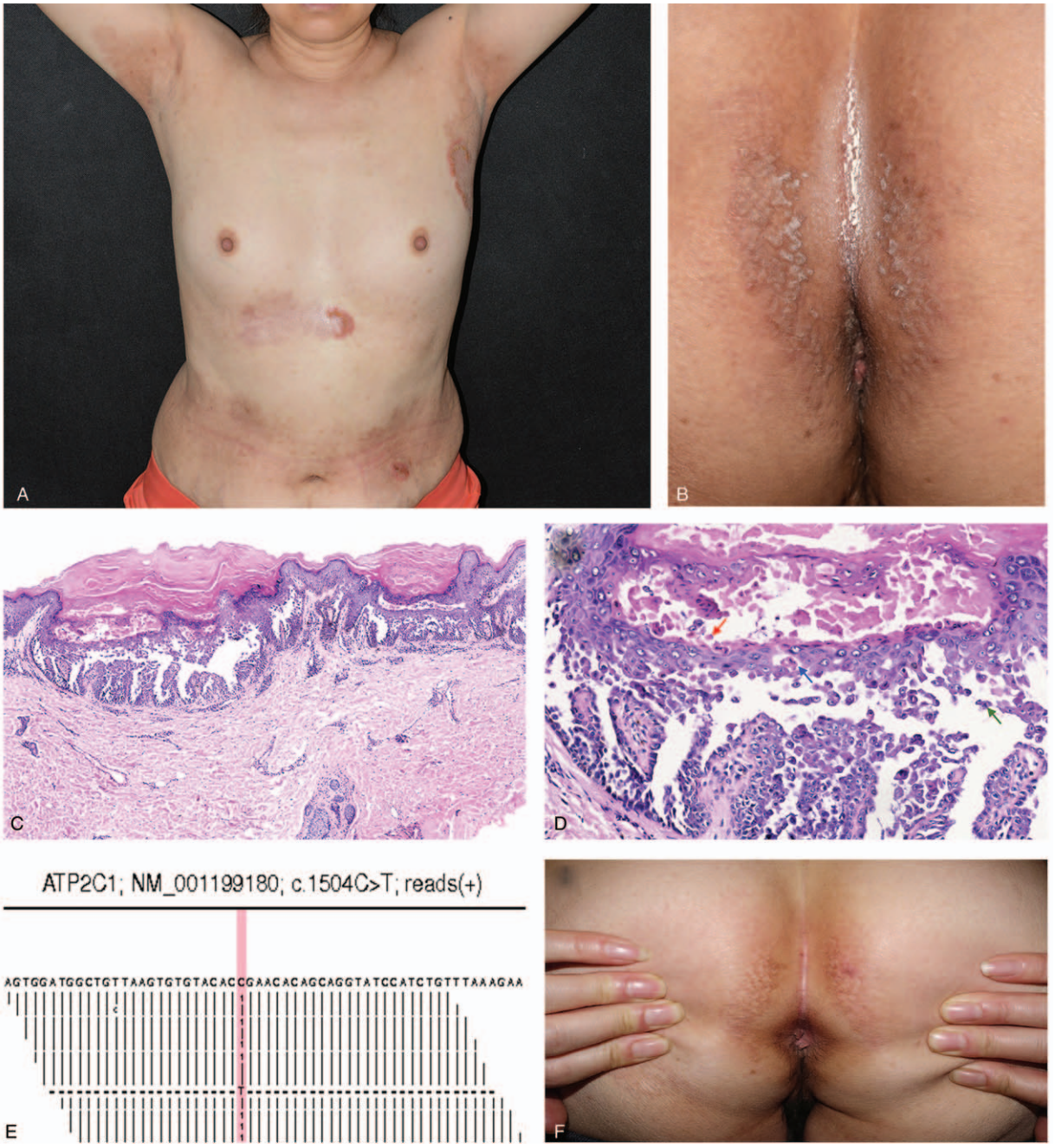

Figure 1: (A) Blisters and erythema on chest, left axilla, and waist. (B) White or skin-colored hard, smooth papules of 0.1- to 0.5-cm diameter around anus. (C) Hyperkeratosis, parakeratosis, and acantholysis (hematoxylin-eosin, original magnification ×25). (D) Acantholytic cells (green arrow), spherical body (red arrow), and grain cell (blue arrow) (hematoxylin-eosin, original magnification ×125). (E) Mutation in *ATP2C1* gene. (F) Resolved lesions.

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Conflicts of interest

None.

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