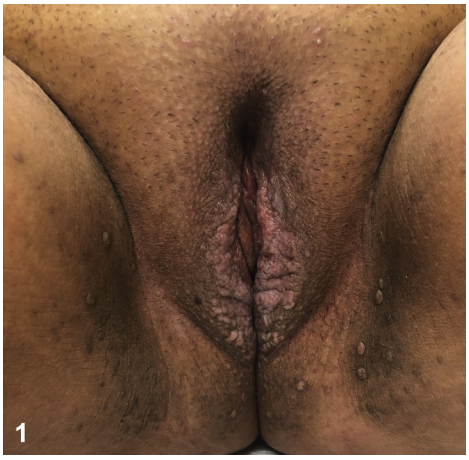
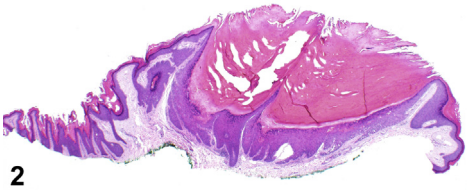
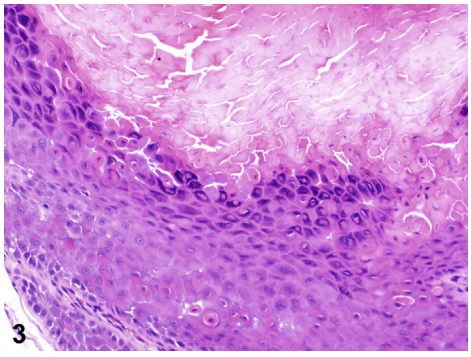
Eruption on the vulva and groin

Jane Harrell, BS,[a] Colton Nielson, MD,[b] Paula Beers, MD,[b] Eric Rudnick, MD,[b] Addie Walker, MD,[b] and Kiran Motaparthi, MD[b]
Gainesville, Florida

Key words: dyskeratosis; genodermatosis; Hailey-Hailey disease; isotretinoin; oral magnesium; papular acantholytic dyskeratosis; vulvar dermatoses.







A 30-year-old woman presented with a spreading papular eruption on the vulva, inguinal, and perianal skin of 9 years' duration. A prior course of prednisone provided temporary resolution. Treatment of recent flares with desonide, mupirocin, and topical tacrolimus were ineffective. Medical history was relevant for herpes simplex labialis treated with acyclovir. A similar eruption was observed in her father and paternal grandmother. Physical examination found agminated papules forming plaques on the labia majora and multiple 2- to 5-mm skin-colored exophytic papules on the inner thighs (Fig 1) and perianal skin. A shave biopsy was obtained from the inner thigh (Figs 2 and 3).

From the Department of Dermatology,[b] University of Florida College of Medicine.[a]
Funding sources: None.
Conflicts of interest: None disclosed.
Correspondence to: Kiran Motaparthi, MD, Department of Dermatology, University of Florida College of Medicine, 4037 NW 86 Terrace, 4 floor, Room 4123 Springhill, Gainesville, FL 32606. E-mail: kmotaparthi@dermatology.med.ufl.edu.

JAAD Case Reports 2020;6:6-8.
2352-5126

https://doi.org/10.1016/j.jdcr.2019.11.003

Question 1: Based on the clinical presentation and histology, what is the most likely diagnosis?

A. Transient acantholytic dermatosis (Grover disease)

B. Segmental follicular dyskeratosis (Darier disease)

C. Segmental Hailey-Hailey disease

D. Papular acantholytic dyskeratosis (PAD) (of the genitocrural folds)

E. Familial dyskeratotic comedones

Answers:

A. Transient acantholytic dermatosis (Grover disease) — Incorrect. Grover disease is a self-limited pruritic papulovesicular condition with predilection for the trunk, neck, and proximal extremities, sparing the genitocrural region. Histology may resemble pemphigus, Darier disease, or Hailey-Hailey disease or be spongiotic.[1]

B. Segmental follicular dyskeratosis (Darier disease) — Incorrect. Darier disease presents in adolescence as greasy, scaly brown papules that may form large verrucous plaques. Histology displays acantholysis with hyperkeratosis and dyskeratotic cells; verrucous epidermal hyperplasia and prominent folliculocentricity are typical. Seborrheic regions are affected with distribution on the trunk, scalp, face and neck in addition to the groin. Nail abnormalities are common.[1] A segmental distribution indicates this form of Darier follows the lines of Blaschko, which is inconsistent with the genitocrural distribution found in this patient.

C. Segmental Hailey-Hailey disease — Incorrect. Histopathology shows dyskeratosis and suprabasilar acantholysis with loss of intercellular bridges, classically described as a *dilapidated brick wall*. The clinical morphology is dissimilar, with painful flaccid vesicles and crusted erosions on intertriginous skin such as the neck, axilla, and groin in a blaschkoid distribution.[1]

D. PAD (of the genitocrural folds) — Correct. Discrete white to skin-colored smooth or verrucous papules that coalesce into plaques on the vulva and perineum reflect the morphology of PAD. PAD is a rare chronic acantholytic dermatosis that presents in young women with asymptomatic but persistent lesions limited to the genital, inguinal, and perineal skin. PAD occurs less frequently in men and can involve the penis, scrotum, perineum, or thighs. Histology shows overlapping features of Hailey-Hailey and Darier disease, including suprabasilar acantholysis, parakeratosis, and dyskeratosis. Verrucous epidermal hyperplasia is also typical.[1]

E. Familial dyskeratotic comedones — Incorrect. Although the clinical morphology includes discrete asymptomatic hyperkeratotic papules, comedones are the principal lesions. The trunk, extremities, face, and groin are involved. Histology shows dilated infundibula filled with keratin and dyskeratosis; acantholysis is occasionally observed.[2]

Question 2: If the patient does not improve with topical medications, a reasonable option would be:

A. Acitretin

B. Methotrexate

C. Chronic high potency topical steroids

D. Combination oral magnesium, low-dose naltrexone, and isotretinoin

E. Systemic corticosteroids

Answers:

A. Acitretin — Incorrect. Acitretin is not recommended in a woman of childbearing age unless disease is severe and unresponsive to other therapies.

B. Methotrexate — Incorrect. Methotrexate has been reported to be used successfully at doses of 7.5-15 mg weekly but would not be considered first-line treatment in a woman of childbearing age unless disease is severe and unresponsive to other therapies.[3]

C. Chronic high-potency topical steroids — Incorrect. Short-term use of high-potency topical steroids in these anatomic sites is acceptable, but prolonged use should be avoided to avoid atrophy and striae.

D. Combination oral magnesium, low-dose naltrexone, and isotretinoin — Correct. There is no standard treatment for papular acantholytic dyskeratosis that has not responded to topical therapy; however, oral retinoids have successfully induced remission in extensive disease.[1] Oral magnesium may be a useful adjunct, as disease resolution has been observed in Hailey-Hailey disease.[4] Low-dose naltrexone can be added in patients with refractory disease; however, treatment response to naltrexone alone is variable, and relapses may occur.[5]

E. Systemic corticosteroids — Incorrect. Oral corticosteroids have been used to treat severe flares or as maintenance therapy at low doses. However, adverse effects and worsening disease upon discontinuation limit their use.[3]

Question 3: Which genetic mutation has been implicated in the pathogenesis of this disease?

A. ATP7A

B. ATP2A

C. ATP2C1

D. Postzygotic somatic mutation

E. Loss of heterozygosity mutation

Answers:

A. ATP7A — Incorrect. ATP7A or Menkes protein is a copper-transporting ATPase that is mutated in Menkes disease. Progressive neurodegeneration and connective tissue dysfunction are seen, including the characteristic finding of depigmented "kinky" hair.[6]

B. ATP2A2 — Incorrect. ATP2A2 encodes sarcoplasmic/endoplasmic reticulum ATPase type 2 that is mutated in segmental follicular dyskeratosis (Darier disease).[7]

C. ATP2C1 — Correct. Historically, PAD was considered to be a separate entity from Hailey-Hailey disease, occurring sporadically in patients without family history. However, evidence of mutations in the ATP2C1 gene suggests a relation to Hailey-Hailey disease.[1] ATP2C1 encodes a calcium-dependent Golgi apparatus ATPase involved in desmosome protein function.

D. Postzygotic somatic mutation — Incorrect. Segmental forms of Darier disease and Hailey-Hailey disease can be caused by postzygotic spontaneous somatic mutations.[7]

E. Loss of heterozygosity mutation — Incorrect. Loss of heterozygosity has been posited as a cause of segmental Darier disease type 2.[7]

Abbreviation used:

PAD: papular acantholytic dyskeratosis

REFERENCES

1. Al-Muriesh M, Abdul-Fattah B, Wang X, Zhao M, Chen S, Huang C. Papular acantholytic dyskeratosis of the anogenital and genitocrural area: case series and review of the literature. *J Cutan Pathol*. 2016;43:749-758.
2. Maddala RR, Ghorpade A, Polavarpu M, Adulkar SA, Das M. Familial dyskeratotic comedones: a rare entity. *Indian Dermatol Online J*. 2016;7:46-48.
3. Arora H, Bray FN, Cervantes J, Falto Aizpurua LA. Management of familial benign chronic pemphigus. *Clin Cosmet Investig Dermatol*. 2016;9:281-290.
4. Borghi A, Rimessi A, Minghetti S, Corazza M, Pinton P, Virgili A. Efficacy of magnesium chloride in the treatment of Hailey-Hailey disease: from serendipity to evidence of its effect on intracellular Ca(2+) homeostasis. *Int J Dermatol*. 2015;54:543-548.
5. Riquelme-Mc Loughlin C, Riera-Monroig J, Morgado-Carrasco D, et al. Low-dose naltrexone therapy in benign chronic pemphigus (Hailey-Hailey disease): a case series. *J Am Acad Dermatol*. 2019;81:644-646.
6. Tümer Z, Møller LB. Menkes disease. *Eur J Hum Genet*. 2010;18:511-518.
7. Guerra L, Pedicelli C, Proto V, Condorelli AG, Mazzanti C, Castiglia D. A postzygotic ATP2A2 novel mutation identified by next-generation sequencing in mosaic Darier disease. *Acta Derm Venereol*. 2019;99:115-116.