A 27-year-old female presented with complaints of gradually progressive asymptomatic brownish-to-gray colored raised lesions over the genital region and thighs for the last 2 years. Her sexual and family histories were noncontributory. On mucocutaneous examination, there were multiple grouped brownish-to-gray-colored soft papules over the labia majora, inguinal folds, and medial aspect of both thighs [Figure 1]. Few lesions were also present in both inframammary regions [Figure 2]. There were no lesions elsewhere on the body. Biopsy from lesions on the medial aspect of the thigh revealed hyperkeratosis, focal parakeratosis, and papillomatosis along with suprabasal cleft filled with acantholytic cells. Cells with rounded nuclei with perinuclear halo and pale cytoplasm were also seen in the granular layer. Biopsy from the inframammary region showed, in addition, upward proliferation of papillae lined by basal cells (villi) and communication of the clefts with the stratum corneum [Figures 3a and b].

**Question**

What is your diagnosis?
Answer

Papular acantholytic dermatosis.

Discussion

Papular acantholytic dermatosis (PAD) is a rare type of focal acantholytic dyskeratosis clinically characterized by the presence of skin-colored to grayish-white papules localized to anogenital and genitocrural areas. In a review of cases by Al-Muriesh et al., the mean age at the time of presentation was 38.8 years with a male-to-female ratio of 0.8:1. The common types of lesion were papules (55.6% of patients) followed by papuloplaque lesions (25.9% of patients) with a history of pruritis in 59.3% of patients. In females, labia majora is the most common site of involvement. In our patient in addition to the genitocrural area, lesions were also present in the submammary area. Similar site of involvement was reported by Van Joost et al. in a 35-year-old female. Moisture and occlusion had been suggested as contributing factors based on the location of lesions. PAD is clinically confused with genital warts, molluscum contagiosum, eczema, lichen planus, and candidiasis. Histopathologically, it needs to be differentiated from other types of focal acantholytic dyskeratoses, i.e., Hailey–Hailey disease, Darier disease, Grover’s disease, warty dyskeratoma, and acantholytic acanthoma. Both Hailey–Hailey disease and Darier disease are autosomal dominant conditions with a positive family history. In Hailey–Hailey disease, there are moist erosive plaques with linear fissures in intertriginous areas, while Darier disease is characterized by the presence of warty papules in seborrheic distribution along with characteristic nail changes [Table 1]. These were excluded in our patient because of late age of onset, absence of family history, and presence of grayish-brown papules in genitocrural location. Grover’s disease usually presents with transient lesions over the trunk and proximal extremities and is not localized to the genital area. Warty dyskeratoma presents with solitary papule with a keratotic plug.

The histopathology of PAD shows hyperkeratosis, papillomatosis, dyskeratoses, and acantholysis along with variable presence of corps ronds and grains. There have been reports of PAD patients showing ATP2A2 and ATP2C1

| Feature | PAD | Darier disease | Hailey-Hailey disease |
|---------|-----|----------------|-----------------------|
| Etiology | Unknown | Mutation in ATP2A2 gene located on chromosome 12q23-24.1 which encodes the sarcoplasmic/endoplasmic reticulum Ca++ ATP isoform 2 protein (SERCA2) | Mutation in ATP2C1 gene located on chromosome 3q21-24 which encodes the Ca++/Mn++ ATPase (hSPCA1) |
| Family history | Absent | Autosomal dominant | Autosomal dominant |
| Precipitating factors | Moisture and occlusion | Sweating, heat, friction, UVB radiation | Friction, heat, sweating, UV radiation, contact dermatitis, cutaneous infections |
| Onset | Third or fourth decade | Teenage | Third or fourth decade |
| Sites of predilection | Anogenital and genitocrural areas | Seborrhoeic areas | Sites of friction, Flexures: neck, axilla, inframammary area, groins, abdominal folds |
| Cutaneous feature | Grayish white papules | Rough, greasy yellow-brown papules | Flaccid vesicopustules, erosions with fissures |
| Associated features | Absent | Present | Absent |
| Oral mucosa findings | Absent | Uncommon. Can have umbilicated white papules or cobblestone papules and leukoplakia-like lesions | Rarely erosions in oral mucosa |
| Nail changes | Absent | Longitudinal red and white bands, V-shaped nick at the free margin of nail, fragile nails | Longitudinal white bands but without nail fragility |
| Histopathology | Histopathology is similar to Darier disease and Hailey-Hailey disease | Suprabasal cleft, dyskeratosis is prominent, corps ronds and grains are seen | Widespread acantholysis resembling “Dilapidated brick wall” with minimal dyskeratoses |
| Prognosis | Lesions are usually persistent | Chronic relapsing course. May deteriorate or improve in old age | Chronic relapsing and remitting course, may improve in old age |

PAD: Papular acantholytic dermatosis
mutations which are otherwise typically seen in cases of Darier disease and Hailey–Hailey disease, respectively. The above finding in addition to histopathological overlap suggests that PAD may be a mild variant or mosaic form of these diseases.[3,5]

Treatment is usually difficult and disappointing. Topical steroids and topical calcineurin inhibitors provide symptomatic relief in pruritus with no change in lesions. Topical retinoids, oral retinoids, destructive therapies such as electrocautery, cryotherapy, and CO₂ laser are other treatment options which provide a temporary reduction in lesions.[2]

To conclude, proper diagnoses and awareness among the clinicians and pathologists alike about this rare entity are important for pertinent counseling of an anxious patient.

Learning points
- PAD is characterized by the presence of skin colored to grayish-white papules localized to the anogenital and genitocrural areas
- It may mimic venereal diseases such as genital warts and molluscum contagiosum, so its correct identification is important to allay patient anxiety
- The histopathology of PAD shows hyperkeratosis, papillomatosis, dyskeratoses, and acantholysis along with variable presence of corps ronds and grains
- Some cases have shown mutation similar to that of Hailey–Hailey disease and Darier disease. Furthermore, its histopathology overlaps with these diseases; therefore, it may be considered as a mild variant or mosaic form of these diseases.

Declaration of patient consent
The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest
There are no conflicts of interest.

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