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Diagnostic Pearls of Vulvar Epidermolytic Acanthoma: Case Report

Navid Farahbakhsh, Colton Nielson, Eric Rudnick, Salma Pothiawala[1], Vincek Vladimir

Department of Dermatology, UF Health Dermatology-Springhill, Gainesville, [1]Riverchase Dermatology, Tampa, FL, United States

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Corresponding Author
Colton Nielson
Department of Dermatology, UF Health Dermatology-Springhill, 4037 NW 86th Terrace, Gainesville, FL 32606, United States
Tel: +1-352-594-1500
Fax: +1-352-594-1501
E-mail: nielsondermatology@gmail.com
https://orcid.org/0000-0003-1663-625X

Epidermolytic acanthomas (EA) are uncommon benign tumors clinically presenting as single to multiple papules. Histologically, EA display hyperkeratosis, hypergranulosis, acanthosis, and epidermal degeneration—also known as epidermolytic hyperkeratosis (EH). EA may be misdiagnosed as condyloma both clinically and histopathologically when located on the genitalia. Thus, this diagnosis carries a significant psychological burden and must remain in the differential when initially considering genital warts. We utilize the case of a 62-year old female referred to dermatology for a 5-year history of multiple pruritic and hypopigmented vulvar papules—misdiagnosed as genital warts—to highlight the impact of differentiating EA from genital warts. This patient was initially misdiagnosed with common genital warts at her gynecologist's office and treated unsuccessfully for years. A shave biopsy was performed and histology revealed EH, consistent with EA.

Keywords: Condylomata acuminata, Epidermolytic acanthoma, Vulvar epidermolytic acanthoma

INTRODUCTION

Epidermolytic acanthomas (EA) are benign tumors of epidermal keratinocytes, which display epidermolytic hyperkeratosis (EH) on histopathology. EH is not specific to EA and can be seen in epidermolytic ichthyosis, epidermolytic palmoplantar keratoderma of Vorner-Unna-Thost, epidermal nevus, and solitary epidermolytic acanthoma[1]. The accurate clinical diagnosis of EA can be difficult as the clinical presentation of multiple vulvar papules can present in many common skin conditions—including condyloma acuminatum (CA). Herein we report an unusual case of a healthy 62-year-old female, with a 5-year history of multiple pruritic EA on the vulva, which was misdiagnosed and treated for what was initially believed to be genital warts.

CASE REPORT

A 62-year-old Caucasian female presented with a 5-year history of slightly pruritic hypopigmented vulvar papules (Fig. 1). The patient denied any prior history of condylomas or abnormal pap smears and no family history of any ichthyosiform disorder. She had initially presented to her gynecologist for

Fig. 1. Multiple skin-colored verrucous papules, some with central umbilication and keratin plugs on the labia majora.

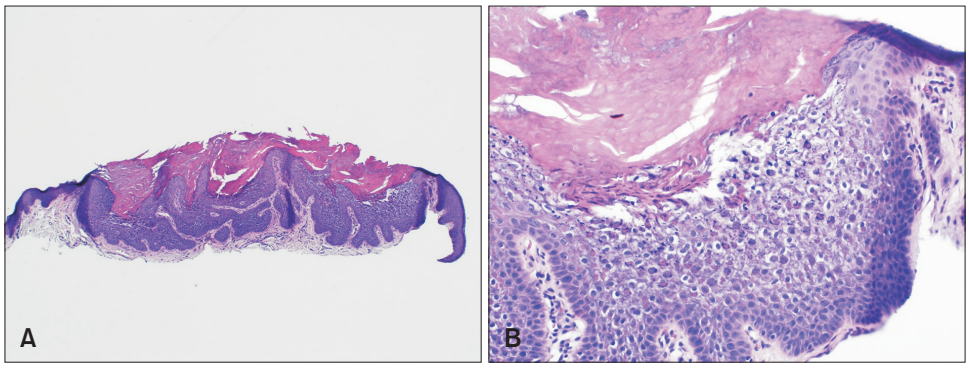

Fig. 2. (A) A cup shaped lesion with hyperkeratosis, acanthosis, and papillomatosis with vacuolation of keratinocytes within the granular layer (H&E, 40×). (B) Large basophilic granules are present in the granular layer and fine eosinophilic granules are present in the granular and spinous layer, representing epidermolysis (H&E, 200×).

evaluation of the papules, one of which was biopsied and reported to be a common wart which was negative for low risk human papillomavirus (HPV). She sought a second opinion at the dermatology clinic shortly after. Prior pathology reports were reviewed and several of the lesions were treated with liquid nitrogen during her initial visit. Sinecatechins ointment was also prescribed. At follow-up patient stated that she did not see an improvement in her lesion count or appearance. The lesions were again treated with liquid nitrogen. Ultimately, a subsequent biopsy was performed of one of the vulvar papules to rule out condyloma.

Shave biopsy of the lesion revealed hyperkeratosis, acanthosis, and papillomatosis with vacuolation of keratinocytes within the granular layer (Fig. 2) and diagnosed as EH (acanthoma). High and low risk HPV stains were negative. The diagnosis was discussed with the patient, and given the noncontagious, benign nature of the lesions, the patient decided to monitor and withhold any further treatments for the time being. We received the patient's consent form about publishing all photographic materials.

DISCUSSION

The first reported cases of solitary EA were described by Shapiro and Baraf in 1970[2] in which they described seven cases of solitary tumors with histopathologic features of granular degeneration. EA are more common in males with increased frequency on the scrotum[3]. In contrast, EA on the female genitalia is rare—as seen in our case with multiple pruritic vulvar papules. A study of 131 EA described 69 male and 62 female with these lesions[4]—only 11.3% (7/62) of the females had lesions on the genitalia, while 39.1% (27/69) of the males had genital lesions[4]. Due to the rarity of vulvar EA, this diagnosis can easily be misdiagnosed. Table 1[1,5-14] reviews the reported cases of vulvar EA and describes the clinician's initial impressions. Of note, over 50.0% of cases (7/14) were initially diagnosed as genital warts.

The etiology of EA remains unclear. EA has previously been suggested to be a local variant of hereditary EH[15]. Keratin 1 (KRT1) and KRT10 mutations are associated with postzygotic somatic mutations in epidermal nevi and EH[5,16,17]. Currently, there have been no conclusive studies correlating mutations in KRT1 and KRT10 with EA[6]. While the etiology of EA is still unknown, immunohistochemical and molecular studies nearly always exclude HPV as a causative factor in EA[4,5] and thus can be used to help differentiate genital warts from EA. Multiple studies on EA have failed to demonstrate the presence of HPV using polymerase chain reaction, and negative staining for both high risk (HPV 16, 18) and low risk (HPV 6, 11) types[4-7]. In our case, high and low risk HPV stains were also negative.

Clinical presentation can vary from asymptomatic to pruritus, burning, and pain[8]. The lesions can present anywhere on the body[4]. The location of these lesions plays a significant role in clinical diagnoses. One study found that extragenital EA lesions were most often confused as seborrheic keratosis, while genital EA lesions were most often confused as CA[4]. Patients with genital lesions typically present with concerns about a sexually transmitted disease[18]. The clinical presentation and distribution of EA can help differentiate it from genital warts. EA are typically discrete and on the vulva, whereas genital warts are generally grouped together and in the perivulvar area[5].

The morphology of EA is described as skin-colored to whitish, smooth hyperkeratotic solitary papules with central keratin plug and umbilication, with genital lesions typically limited to the labia majora or scrotum[7,16]. The keratin plug with um-

Table 1. Cases on vulvar epidermolytic acanthoma

Case	Case study	Age (yr)	Number of lesions	Duration	Initial clinical impression
1	Fletcher et al.[1]	59	Multiple	Several months	Epidermolytic acanthomas
2	Lee and Wu[5]	91	Multiple	1 week	Bowenoid papulosa vs. Condyloma acuminata
3	Lee and Wu[5]	46	Multiple	More than 1 month	Condyloma acuminata
4	Egozi-Reinman et al.[6]	47	Multiple	Not given	Not given
5	Irwin et al.[7]	46	Multiple	Not given	Benign keratosis
6	Irwin et al.[7]	61	Multiple	Several months	Benign keratosis vs genital warts
7	Hijazi et al.[8]	31	Multiple (7 total)	2 years	Multiple epidermolytic acanthoma's
8	Swann et al.[9]	58	Multiple	2 years	Bowenoid papulosa vs. Condyloma acuminata
9	High and Miller[10]	54	Multiple	20 years	Epidermolytic Acanthoma vs. Condyloma acuminata
10	Thomas et al.[11]	50	Multiple	Since early adulthood	Verrucae vs. condyloma acuminata vs. localized Darier's disease vs. inflammatory verrucous epidermal naevus
11	Moulonguet et al.[12]	50	Multiple	Not given	Epidermolytic hyperkeratosis
12	Quinn and Young[13]	75	Multiple	1 year	Not given
13	Russell et al.[14]	69	Multiple	6 week	Fungal skin infection
14	Current case	62	Multiple	5 years	Condyloma acuminata

bilication is a subtle, but reliable clue in the diagnosis of EA. In contrast, CA often present as grouped, dark brown papules of variable size[16]. While the differential diagnosis of multiple vulvar papules is broad –including: CA, molluscum contagiosum, syringomas, papular acantholytic dyskeratosis, calcinosis cutis, verruciform xanthoma and many more[8,19]—the clinical and morphological features listed above can help distinguish EA from other vulvar skin lesions in many cases.

When the clinical diagnosis is unclear, biopsy should be considered, especially when CA is being considered. The histopathological findings of EA display hypergranulosis, hyperkeratosis, perinuclear vacuolization, reticular degeneration in the granular and spinous layers, and EH[2,4,5]. Histology can also help differentiate EA from genital warts. EA presents with ballooning degeneration and keratohyalin clumping, which is not typically seen in genital warts[9]. The absence of koilocytic features and negative HPV genotyping can also help exclude genital warts from the differential[7].

EA typically does not require definitive treatment as these lesions are benign and not transmissible[8,16]. Treatment options include emollients, lactic acid, salicylic acid, tacrolimus, pimecrolimus, curettage, electrodessication, liquid nitrogen therapy, and surgical excision[1,5,8,9]. Some patients decline treatment, once they learn the benign nature of these skin lesions[10,11,18]. In a study on eight patients with multiple EA, five were observed without any treatment, two received cryotherapy, and one received electrocauterization[5]. At 6-month follow-up the number of EA did not change for those untreated and one patient—treated with cryotherapy—had persistent lesions[5]. One report described two patients—with multiple genital EA – treated with liquid nitrogen cryoprobe over the course of multiple cycles, and during 6-month follow-up the lesions resolved without recurrence[20]. In our case the patient was initially treated with liquid nitrogen and sinecatechins ointment without resolution and then finally observed without treatment.

In summary, due to its appearance and presentation on the genitalia, EA can mislead clinicians into misdiagnosing this lesion as CA. The misdiagnosis can increase patients' psychosocial burden, lead to unnecessary treatments, and affect the patient-physician relationship. Helpful clues in the diagnosis of EA include localized presence on the labia majora, papules with a keratin plug and umbilication, absence of koilocytic features, ballooning degeneration and keratohyalin clumping, and negative HPV genotyping[5,7]. Our case highlights the importance of including EA in the differential diagnosis of papular vulvar lesions and highlights several subtle but key differences between the clinical, morphological, and histological features of EA compared to genital warts on the vulva.

CONFLICTS OF INTEREST

The authors have nothing to disclose.

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ORCID

Navid Farahbakhsh, https://orcid.org/0000-0002-2045-2050
Colton Nielson, https://orcid.org/0000-0003-1663-625X
Eric Rudnick, https://orcid.org/0000-0003-3572-0377
Salma Pothiawala, https://orcid.org/0000-0002-2561-6843
Vincek Vladimir, https://orcid.org/0000-0002-1437-4922

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