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High-grade squamous intraepithelial lesion of the oral commissure (bowenoid papulosis). A case and review

Erine A. Kupetsky[1], Carlos A. Charles[2,3], Joan Mones[4]

1 Palisades Medical Center Dermatology, North Bergen, NJ, USA
2 Derma di Colore, New York, NY, USA
3 Department of Dermatology, Weill Medical College of Cornell University, New York, NY, USA
4 Ackerman Academy of Dermatopathology, New York, NY, USA

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Corresponding author: Erine A. Kupetsky, DO, MSc, Palisades Medical Center Dermatology, Graduate Medical Education, 7600 River Road, North Bergen, NJ 07047. Fax. 201 758-2740. Email: eakderm@gmail.com

What is your diagnosis (Figures 1-3)?

A) Verruca vulgaris
B) Actinic keratosis
C) Bowenoid papulosis
D) Seborrheic keratosis
E) Acanthoma

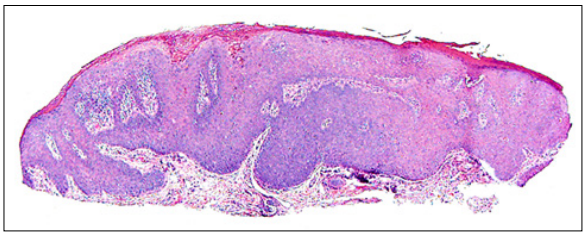

Figure 1. Scanning magnification of the lesion on the oral commissure. [Copyright: ©2015 Kupetsky et al.]

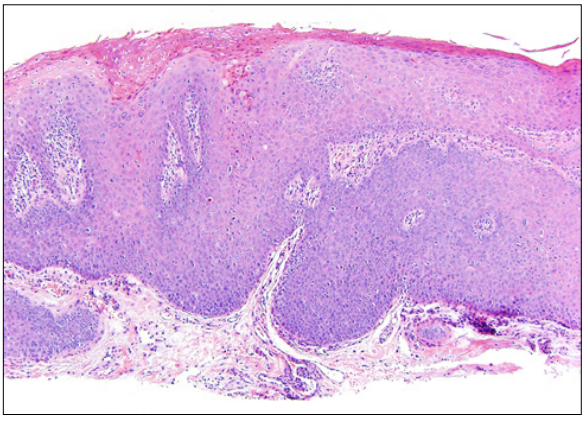

Figure 2. Higher magnification of the oral lesion. [Copyright: ©2015 Kupetsky et al.]

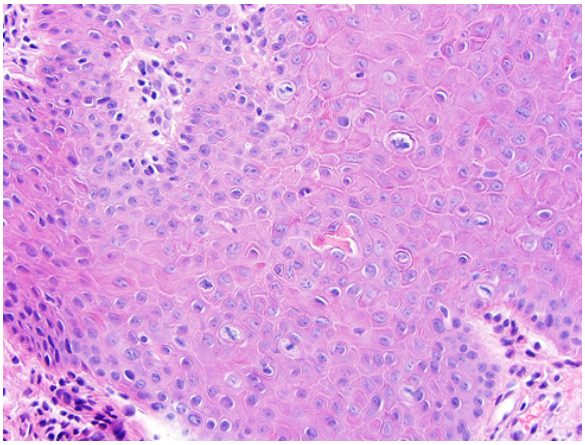

Figure 3. Higher magnification of the slightly verrucous lesion shows hyperplasia with full-thickness atypia of squamous epithelial cells, evidence of loss of polarity, nuclear crowding, nuclear pleomorphism and increased mitotic figures indicative of high-grade squamous intraepithelial lesions. [Copyright: ©2015 Kupetsky et al.]

Answer

C) High-grade squamous intraepithelial lesion of the oral commissure (bowenoid papulosis)

Discussion

Bowenoid papulosis (BP) is characterized clinically by one or more small, verrucous papules usually located on the genitalia or thighs of younger patients [1]. Rarely, BP has been reported on extragenital sites with or without concomitant genital lesions [2,3,4]. On the genitalia, BP clinically resembles condyloma acuminatum or lichen planus; however, histopathologically, BP is indistinguishable from squamous cell carcinoma in situ or Bowen's disease, hence, its designation "bowenoid papulosis," a term coined by Wade, Kopf and Ackerman, in 1978 [1]. BP has been shown to be associated primarily with the high-risk human papillomavirus (HPV) infection subtypes, 16 and 18; however, other high-risk subtypes, such as 31, 32 [5], 33, 35, 39, 53, and 67, have also been reported. Many lesions of BP resolve with or without therapy and behave in a clinically benign fashion despite their malignant histology [7]; however, cases of squamous cell carcinoma in-situ and invasive squamous cell carcinoma have been reported to occur in association with lesions of BP, particularly in immunosuppressed patients [8,9.10]. Risk of penile squamous cell carcinoma in men may be as high as 30% in patients with BP and increases incrementally with the duration of the disease [11]. Patients with BP have also been reported to have concurrent HPV-associated dysplasia of the vulva and uterine cervix, of various degrees, including high-grade dysplasia, VIN 3 and CIN 3, respectively.

Our patient, a 22-year-old man, presented with verrucous papules centrally located within a central lichenified plaque on the oral commissure. The lesion was clinically thought to be a wart or a lesion of lichen simplex chronicus. Histopathologically, the lesion showed full thickness epithelial atypia demonstrating increased numbers of mitotic figures, loss of polarity, and nuclear pleomorphism compatible with squamous cell carcinoma in situ (Figures 1-3). In situ hybridization was positive for the high-risk subtypes 16/18 (Figure 4). p16 immunoperoxidase stain demonstrated strong diffuse staining in the lower portion of the lesion with individually positive cells extending into the upper reaches of the epithelium (Figure 5).

Oral BP is exceeding rare with only nine cases, to our knowledge, reported in the medical literature [11-19]. Men were more commonly affected than women, and the ages ranged from 20 to 40 years. Clinically, reported cases of oral lesions of BP in the medical literature are similar to those occurring on genital sites, namely, small verrucous papules [16]; however, erythematous velvety plaques [20], raised solitary nodules [11], leukoplakia or macules resembling candidiasis [13] have also been described. Histopathologically, lesions of oral BP were indistinguishable from squamous cell carcinoma in situ. A computerized search of the files of the Ackerman Academy of Dermatopathology in New York, NY, from July 1999 through August 31, 2013, yielded 560 biopsies diagnosed as BP; however, only three patients with extragenital BP were identified, including the present case. This finding parallels that of the medical literature and indicates that extragenital BP is exceedingly rare. All three extragenital lesions from the Ackerman Academy were oral: two occurred on the lip and one, the present case, was located on the oral commissure. There were two males and one female, 22, 64 and 40 years of age, respectively. Clinically, the lesions were thought to be lichen simplex chronicus, verruca vulgaris or pemphigus vulgaris, and bowenoid papulosis, respectively. Histopathologically all lesions were indistinguishable from squamous cell carcinoma in situ.

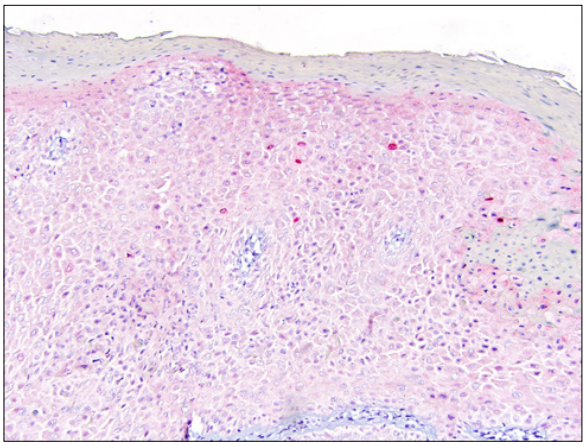

Figure 4. Human papillomavirus in situ hybridization showing positive staining for the high-risk subtypes, 16/18 (red nuclear staining). [Copyright: ©2015 Kupetsky et al.]

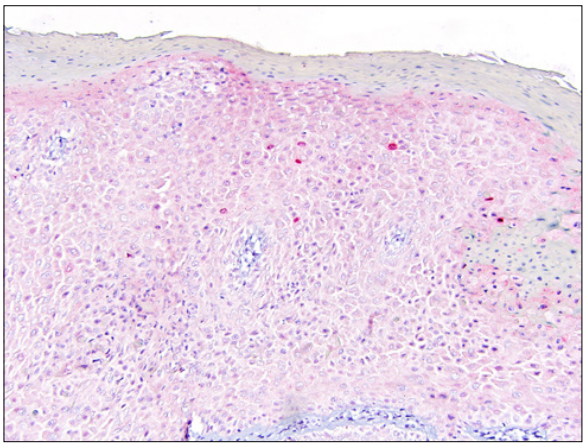

Figure 5. p16 immunoperoxidase stain shows strong diffuse positive staining of the lower portion of the lesion with individually positive cells extending into the upper reaches of the epithelium (brown staining). [Copyright: ©2015 Kupetsky et al.]

In 2012, a Consensus Panel of the College of American Pathologists and the American Society for Colposcopy and Cervical Pathology recommended a change in terminology for BP from "bowenoid papulosis" to "high-grade squamous intraepithelial lesion." They noted that bowenoid papulosis could be added to the diagnosis in parentheses if it could be verified that the lesion was small and had been excised. If verification could not be accomplished but the clinical setting was one of small papules, they wrote that, "a note stating that the differential diagnosis includes Bowenoid papulosis may be warranted." They also stated that, "Bowenoid papulosis may have a lower risk of progression to cancer than cutaneous HSIL [high- grade squamous intraepithelial lesion] found in larger plaques (Bowen disease)." [21]

Treatment for oral BP is similar as that for genital BP and includes intralesional, topical or oral medication as well as surgical excision. Fluoropyrimidine TS-1 (prodrug of 5-FU, gimestat (CDHP), and oteracil potassium (Oxo)), 100 mg daily for three weeks was administered in one elderly woman with HPV-16 positive oral BP and resulted in regression of the lesion [16]. Intralesional interferon alpha followed by topical imiquimod has also been reported as successful [17]. Other treatments that have been used for genital BP and may be appropriate in oral lesions include 5-FU, podophylin, retinoic acid, and cidofovir. Surgical modalities include simple excision, cryosurgery, laser vaporization, and electrodessication of small lesions. Podophyllin is toxic in large amounts but has been used successfully for the treatment of oral hairy leukoplakia and could potentially be used to treat refractory BP [22,23]. Our patient was treated successfully with 5-fluorouracil cream followed by imiquimod cream each applied five times per week for five weeks with two weeks between each medication. He remains lesion-free five months post treatment.

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