favorable prognosis without oral retinoid treatment, suggesting that long-term survival cannot be solely attributed to oral retinoids. Whether the favorable prognosis in HI is linked to specific ABCA12 mutations in patients remains uncertain.

ABCA12 encodes a group of highly conserved proteins involved in the adenosine triphosphate-binding cassette (ABC) transporter system, presumed to play a role in lipid transport.[2] Severe ABCA12 mutations disrupt lipid transport through lamellar granules in keratinocytes, resulting in abnormal assembly or formation of the epidermal keratinocyte surface lipid barrier and the manifestation of HI.[8] Most ABCA12 mutations in HI are truncation mutations, present as either homozygous or compound heterozygous truncations.[3] Reported ABCA12 mutations in HI include truncation mutations, missense mutations, exon deletions, and single amino acid deletions.[9] To induce the HI phenotype, at least one mutation on each allele must be a truncation or deletion mutation in a conserved region, leading to a significant loss of ABCA12 protein function.[9] The c.5932C>T variant in exon 40 found in our patient is predicted to result in a nonsense mutation at position 1978 (p.Gln1978*), leading to a truncated protein. The c.56T>A variant in exon 1 is predicted to cause an alternative amino acid substitution at position 19 (p.Val19Glu). To the best of our knowledge, both ABCA12 mutations identified in our patients are novel.

In conclusion, there is limited understanding of the course and prognosis of HI because of the high neonatal mortality rate. Our report highlights two siblings with HI who have achieved long-term survival, exhibiting improved dermatological symptoms and irreversible digital autoamputation caused by cutaneous constriction bands. Additionally, we identified novel ABCA12 mutations in our patients. Despite advances in medical care, HI still presents a risk of fatality, emphasizing the importance of early prenatal diagnosis facilitated by the discovery of new mutations.

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References

1 Tanahashi K, Sugiura K, Sato T, Akiyama M. Noteworthy clinical findings of harlequin ichthyosis: digital autoamputation caused by cutaneous constriction bands in a case with novel ABCA12 mutations. *Br J Dermatol*. 2016;**174**(3):689–91.
2 Rajpar SF, Cullup T, Kelsell DP, Moss C. A novel ABCA12 mutation underlying a case of Harlequin ichthyosis. *Br J Dermatol*. 2006;**155**(1):204–6.
3 Akiyama M. ABCA12 mutations and autosomal recessive congenital ichthyosis: a review of genotype/phenotype correlations and of pathogenetic concepts. *Hum Mutat*. 2010;**31**(10):1090–6.
4 Salehin S, Azizimoghadam A, Abdollahimohammad A, Babaeipour-Divshali M. Harlequin ichthyosis: case report. *J Res Med Sci*. 2013;**18**(11):1004–5.
5 Chu Y-Y, Lai M-Y, Liao H-T. Early escharotomy-like procedure for the prevention o f extremity autoamputation in harlequin ichthyosis. *Biomed J*. 2021;**44**(2):223–6.
6 Sharma A, Rozzelle A, Jahnke MN, Desai J, Shwayder TA, Kisseih E, et al. ABCA12 homozygous mutation in harlequin ichthyosis: survival without systemic retinoids. *Pediatr Dermatol*. 2019;**36**(3):339–41.
7 Pet MA, Gupta D, Tse RW. Harlequin ichthyosis: a surgical perspective. *Pediatr Dermatol*. 2016;**33**(5):e327–32.
8 Akiyama M, Sakai K, Wolff G, Hausser I, McMillan JR, Sawamura D, et al. A novel ABCA 12 mutation 3270delT causes harlequin ichthyosis. *Br J Dermatol*. 2006;**155**(5):1064–6.
9 Akiyama M, Sakai K, Sugiyama-Nakagiri Y, Yamanaka Y, McMillan JR, Sawamura D, et al. Compound heterozygous mutations with novel missense ABCA12 mutation in harlequin ichthyosis. *J Invest Dermatol*. 2006;**126**(7):1518–23.

Isolated primary syphilitic chancre in the lower lip of a teenager

Dear Editor,

In recent years, the increase of infectious diseases such as syphilis has reemerged worldwide.[1,2] Oral mucosa remains the most frequent extragenital location involved in syphilis, mainly lip, tongue, and palate,[1,2] and its early diagnosis can be a challenge because the lesions resemble other infectious, neoplastic, and traumatic oral diseases.[1,2] Here, we reported an isolated syphilitic chancre in the lower lip of a male teenager highlighting the clinical diagnosis challenge.

An 18-year-old male smoker was referred to the dentist for evaluation of an isolated and ulcerated lesion in the vermillion of the lower lip with hemorrhagic and crusted areas, indurated margin, measuring approximately 3 cm, accompanied by cervical lymphadenopathy, and with approximately 3 months of evolution (Figure 1a). The differential diagnoses were traumatic ulcer, oral squamous cell carcinoma, and oral syphilis. The patient's active sexual history was vaguely mentioned. An incisional oral biopsy was performed and sent for histopathological analysis. A complete blood count and serologic tests, including the Venereal Disease Research Laboratory (VDRL), fluorescent treponemal antibody absorption (FTA-Abs) – IgM antibody, and human

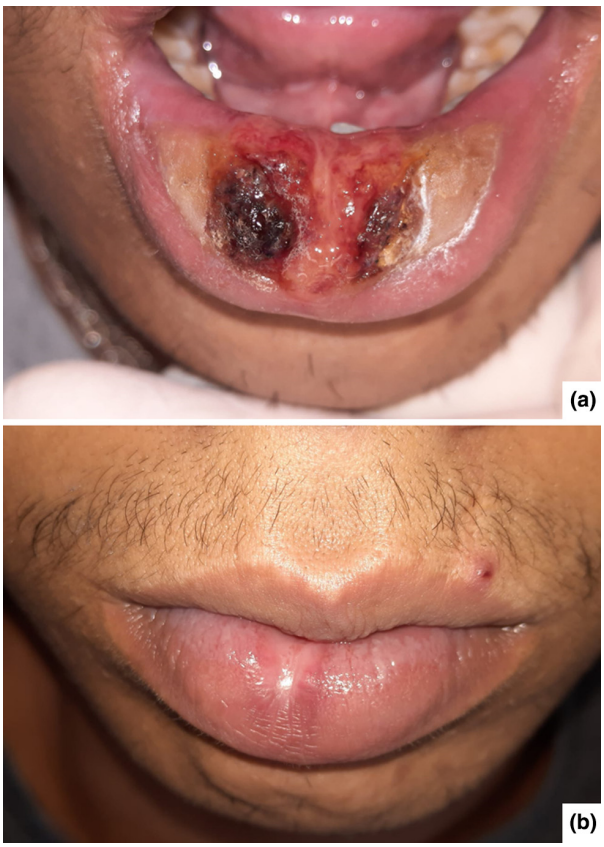

Figure 1 (a) Primary syphilitic chancre in the lower lip of a male teenager showing hemorrhagic and crusted areas and an indurated margin. (b) Complete involution of the primary syphilis in the lower lip after one month of treatment

immunodeficiency virus (HIV) antibodies, were requested. The microscopic sections showed an ulcerated lesion with a prominent perivascular and perineural arrangement of the dense inflammatory infiltrate composed of plasma cells, lymphocytes, and some multinucleated giant cells (Figure 2). The blood tests revealed moderate leukocytosis with a value of 17,300/mm^3 (reference: 4.5–11,000/mm^3). The serologic test was positive for VDRL with a titer of 1:256 and confirmed using treponemal assays as FTA-Abs IgM. The result of the HIV test was negative (value 0.06 – positive value >1.0). The diagnosis was primary syphilitic chancre. Because of the patient's inability to provide an accurate account of the duration of the lesion, he was treated with three doses of 2.4 million units of penicillin G benzathine intramuscularly at weekly intervals.[3] After one month of follow-up, a complete involution of the lip lesion was observed (Figure 1b), and the serologic test (VDRL) showed a titer of less than 1:2 after 6 and 12 months.

Primary syphilis arising in the oral mucosa is even rarer, affecting <10% of infected individuals.[4,5] Its occurrence on a lip has been typically associated with adult males who practice oral sex, and its diagnosis is challenging due to its nonspecific clinical features that mimic other benign or malignant oral lesions.[1,2] The extragenital chancre occurs as an ulcerative, indurated, and asymptomatic nodule, accompanied by lymphadenopathy while oral manifestations may present a diversity of clinical characteristics with variation in size, number, and location of lesions. In teenagers, as illustrated in this case, oral primary syphilis might not be the first hypothesis to be considered by a health professional because most patients are not comfortable mentioning their previous sexual history or the use of condoms as part of their sexual activities.[1,2]

The syphilis diagnosis is based on the patient's sexual history and clinicopathological features of the lesion supported by specific serologic tests.[1,2,4] In our patient, the histopathological analysis, characterized by nonspecific chronic inflammation, was important to rule out malignancy. Penicillin benzathine remains an effective therapy for primary syphilis in the oral cavity with regression of the lesions over a few weeks without complications, as occurred in this case report. Additionally, it is crucial to confirm the cure of infection by serologic test after 6 and 12 months, as presented here.

In view of the increase in the incidence of syphilis, it is essential that health professionals be prepared to recognize and manage primary oral syphilitic chancre minimizing the risks of disease transmission. Therefore, this case report reinforces that syphilis should be considered in the differential diagnosis of a solitary ulcerated oral lesion arising in the lip of teenagers.

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The patient provided informed written consent.

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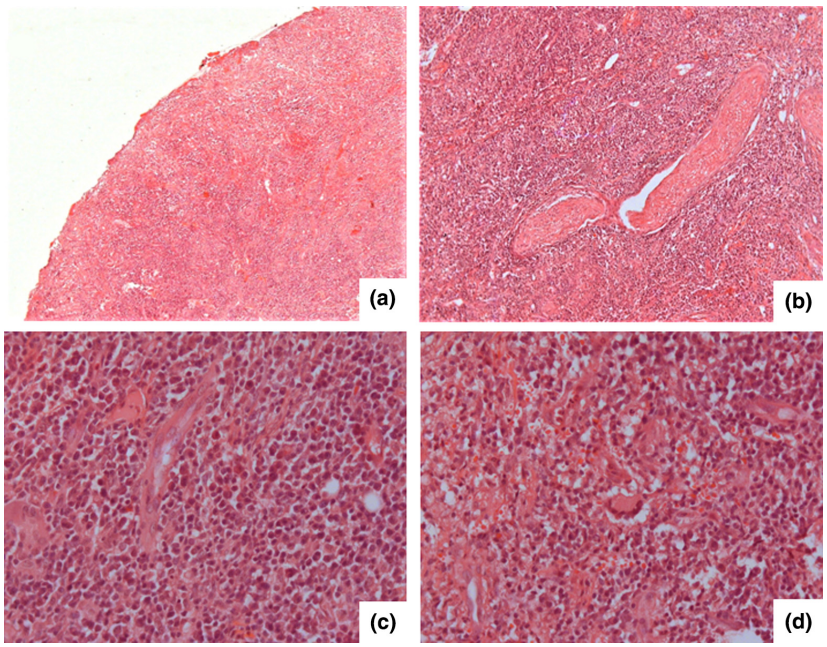

Figure 2 The photomicrography sections show an ulcerated lesion (a) with prominent perineural and perivascular arrangement of the dense lymphohistiocytic inflammatory infiltrate (b, c), mainly plasma cells, lymphocytes, and multinucleated giant cells (d) (Hematoxylin and Eosin, a = ×5, b = ×20, c = ×40, d = ×40)

References

1 Smith MH, Vargo RJ, Bilodeau EA, Anderson KM, Trzcinska A, Canterbury CR, et al. Oral manifestations of syphilis: a review of the clinical and histopathologic characteristics of a reemerging entity with report of 19 new cases. *Head Neck Pathol*. 2021;**15**:787–95.

2 Zhou X, Wu MZ, Jiang TT, Chen XS. Oral manifestations of early syphilis in adults: a systematic review of case reports and series. *Sex Transm Dis*. 2021;**48**:e209–14.

3 Dalby J, Stoner BP. Sexually Transmitted infections: updates from the 2021 CDC guidelines. *Am Fam Physician*. 2022;**105**:514–20.

4 Gibson EJ, Bell DL, Powerful SA. Common sexually transmitted infections in adolescents. *Prim Care*. 2014;**41**:631–50.

5 Taxy JB, Cibull T. Syphilis: a contemporary clinicopathologic assessment. *Am J Surg Pathol*. 2020;**44**:1274–81.

Race and ethnicity may not be associated with differences in hidradenitis suppurativa disease severity: a retrospective cohort analysis

Dear Editor,

Hidradenitis suppurativa (HS), a chronic disorder of follicular biology manifesting as painful nodules, abscesses, and sinus tracts, has been found more prevalent among patients with skin of color (SOC).[1] However, there is limited knowledge regarding the influence of race/ethnicity on HS severity. Two studies have demonstrated greater HS severity in patients of color by likelihood of hospitalization or highest recorded Hurley stage.[2,3] Nonetheless, in both studies, patients were missing objective measures of severity, and responses to treatment were not considered. From another perspective, HS has been associated with low socioeconomic status (SES), but prior studies of racial differences in HS severity have not controlled for SES.[4] We sought to investigate if race or ethnicity in a diverse cohort was associated with HS severity, controlling for relevant objective and subjective factors at initial presentation.

We performed an Institutional Review Board-approved (Einstein IRB #2015-5906) retrospective chart review of 500 patients who received care at our HS Center between 2018 and 2022. Initial visit notes were reviewed for information regarding HS severity (HS-Physician Global Assessment [HS-PGA]), patient-reported pain severity (Numerical Rating Scale [NRS-pain]), serologic inflammatory markers (c-reactive protein [CRP], erythrocyte sedimentation rate [ESR], interleukin-6 [IL-6]), body mass index [BMI], hemoglobin A1c levels [Hgb A1c], and current smoker status. The HS-PGA is a validated instrument categorizing HS severity by number of active lesions: 0-clear, 1-minimal, 2-mild, 3-moderate, 4-severe, 5-very severe.[5] Race/ethnicity were obtained from patient-reported demographics. Having Medicaid as the primary insurance provider was used as a proxy for low SES.

Participants were categorized by baseline disease severity into mild (HS-PGA of 0–2) or severe (HS-PGA of 3–5) disease. Age, gender, race/ethnicity, NRS-pain, inflammatory markers, Hgb A1c, current smoker status, and Medicaid status were compared with univariate *t*-tests and Chi-square tests where appropriate. The associations between disease severity and race/ethnicity were then estimated by multivariate logistic regression models adjusting for variables that were found to be