

A Child with Hoarseness and Recurrent Cheek Erosions: A Quiz

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A 5-year-old boy exhibited delayed healing of erosions on his cheeks without the presence of blisters since the age of 2 years. Previously diagnosed with eczema, he remained unresponsive to multiple topical therapies. In addition, he had a history of hoarseness since birth.

On physical examination, scattered granulation tissue, atrophic scars, and crusts were observed on the face (Fig. 1A), along with subungual granulation tissues (Fig. 1B). No erosions or blisters were evident elsewhere on his body or within his mouth.

Video laryngoscopy demonstrated bilateral vocal cord adhesion (Fig. 1C). Bacterial and fungal cultures from

the erosions demonstrated negative results. No anomalies were detected on abdominal and urinary ultrasonography, hearing test, and dental or ophthalmologic examination.

What is your diagnosis?

Differential diagnosis 1: Laryngo-onycho-cutaneous syndrome

Differential diagnosis 2: Hydroa vacciniforme

Differential diagnosis 3: Chronic mucocutaneous candidiasis

Differential diagnosis 4: Atopic dermatitis

See next page for answer.

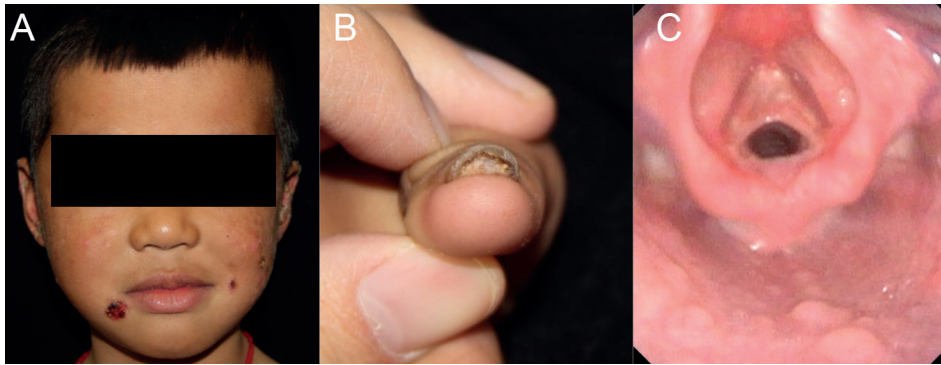


Fig. 1. Clinical features of the patient.

(A) Scattered granulation tissue, atrophic scars, and crusts on the face. (B) Subungual granulation of fingernails. (C) Laryngoscopy showing bilateral vocal cord adhesion.

ANSWERS TO QUIZ

A Child with Hoarseness and Recurrent Cheek Erosions: A Commentary

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Diagnosis: Laryngo-onycho-cutaneous syndrome

Histopathological analysis indicated an abundance of granulation tissue and mixed inflammatory cell infiltration (Fig. 2). Further genetic study revealed a pathogenic homozygous missense mutation (c.171+1G>A) in the *LAMA3* gene. Based on these findings, a diagnosis of laryngo-onycho-cutaneous (LOC) syndrome was made. After a 2-month treatment with 0.5% topical timolol, moderate improvement was observed in the facial lesions. Due to the absence of breathing obstruction symptoms and potential post-surgical granulation tissue formation, the patient's parents declined a surgical procedure for releasing vocal cord adhesions.

Laryngo-onycho-cutaneous syndrome (OMIM 245660) is a localized form of autosomal recessive junctional epidermolysis bullosa (EB) characterized by delayed wound-healing and mucosal granulation (1).

The prevalence of LOC is uncertain, but exceptionally rare, with less than 100 reported cases globally. However, potential underdiagnosis exists. Most typical cases of LOC are attributed to mutations in the *LAMA3* gene, specifically within the N-terminal domain of *LAMA3A*, which encodes the laminin- α 3a isoform (2). Loss of this N-terminal region

is believed to contribute to the pronounced granulation tissue response in patients with LOC (2).

Unlike other EB types marked by widespread blistering, patients with LOC present with minimal blistering and prominent granulation tissue, often leading to misdiagnosis (3). Notably, slow-healing facial erosions constitute one of the hallmark features of LOC. Healed lesions frequently result in atrophic, pigmented scars, which may be mistaken for conditions such as eczema or hydroa vacciniforme. Granulation tissue can develop in the larynx, nail beds, and ocular surface, inducing early-onset hoarseness, recurrent nail loss and formation of symblepharon (2, 3). Recognition of these distinctive features may facilitate earlier identification of LOC. Although these findings can also be seen in other types of EB occasionally, genetic testing serves to confirm the diagnosis by identifying mutations in the N-terminal region of *LAMA3A*.

The management of LOC requires a comprehensive, multidisciplinary approach and long-term follow-up (3). Chronic erosions could be treated with topical steroids or topical timolol (4). However, disease severity varies, with prognosis contingent on the extent of mucosal involvement. The growth of granulation tissue in the larynx and adjacent structures can lead to airway obstruction and, in severe cases, premature mortality (2, 3). Consequently, repeated endoscopic investigations are recommended. Patients with severe larynx symptoms may require surgical intervention, such as tracheostomy. Due to the high frequency of ocular involvement, consultation with an ophthalmologist is also advisable. Genetic counselling is crucial for affected families to comprehend the risk of recurrence and make informed decisions regarding future pregnancies.

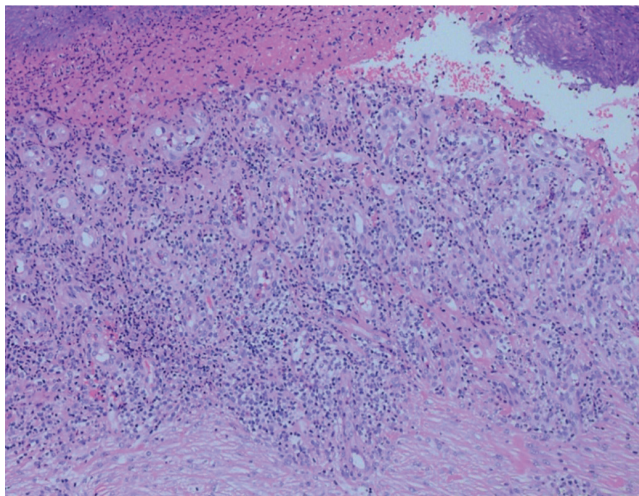


Fig. 2. Histological findings. Haematoxylin-eosin staining of the biopsy specimen taken from a skin lesion revealed epidermal necrosis, prominent vascular proliferation, and infiltration of abundant lymphocytes and neutrophils (original magnification $\times 100$).

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The authors have no conflicts of interest to declare.

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