SKIN

BRIEF ARTICLE

Late Onset Junctional Epidermolysis Bullosa in Adulthood

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ABSTRACT

Epidermolysis bullosa (EB) is a heterogenous group of blistering diseases of the skin and mucous membranes and is classified into four main types based on the location of the epidermal-dermal separation.[1-3] Junctional EB, an autosomal recessive variant, is characterized by its cleavage within the lamina lucida. The typical age of onset is at birth, and it can present with either generalized or localized mucocutaneous findings.[3] A rare subtype of JEB is JEB of late onset (JEB-lo), which occurs in young adulthood or later with blisters primarily located on the hands and feet.[2] Other clinical features of this rare subtype include nail dystrophy, hyperhidrosis, loss of dermatoglyphs, and skin atrophy.[2,4,5] We report a case of JEB-lo diagnosed in late adulthood.

INTRODUCTION

Epidermolysis bullosa (EB) is a heterogenous group of blistering diseases of the skin and mucous membranes and is classified into four main types based on the location of the epidermal-dermal separation.[1-3] Junctional EB, an autosomal recessive variant, is characterized by its cleavage within the lamina lucida. The typical age of onset is at birth, and it can present with either generalized or localized mucocutaneous findings.[3] A rare subtype of JEB is JEB of late onset (JEB-lo), which occurs in young adulthood or later with blisters primarily located on the hands and feet.[2] Other clinical features of this rare subtype include nail dystrophy, hyperhidrosis, loss of dermatoglyphs, and skin atrophy.[2,4,5] We report a case of JEB-lo diagnosed in late adulthood.

CASE REPORT

A 58-year-old man initially presented to our clinic in January 2021 with a 34-year history of a persistent rash on his bilateral lower extremities which he referred to as “eczema”. On examination, he was noted to have multiple erythematous papules coalescing into plaques with several superficial erosions on his bilateral anterior legs, with a few intact, tense bullae. He was also noted to have dystrophic changes of his toenails, including medial curvature of the nails and ingrown nails (Figure 1). Based on these features, our clinical differential diagnosis included epidermolysis bullosa, bullous pemphigoid or other autoimmune subepidermal blistering diseases, and two 4-mm punch biopsies were performed, one for H&E and one for DIF. Punch biopsy for H&E showed a subepidermal blister with occasional eosinophils. However, the DIF studies were negative to all reactants used, making an autoimmune subepidermal blistering disease less likely (Figure 2).

After further discussion, immunomapping was pursued and two additional punch

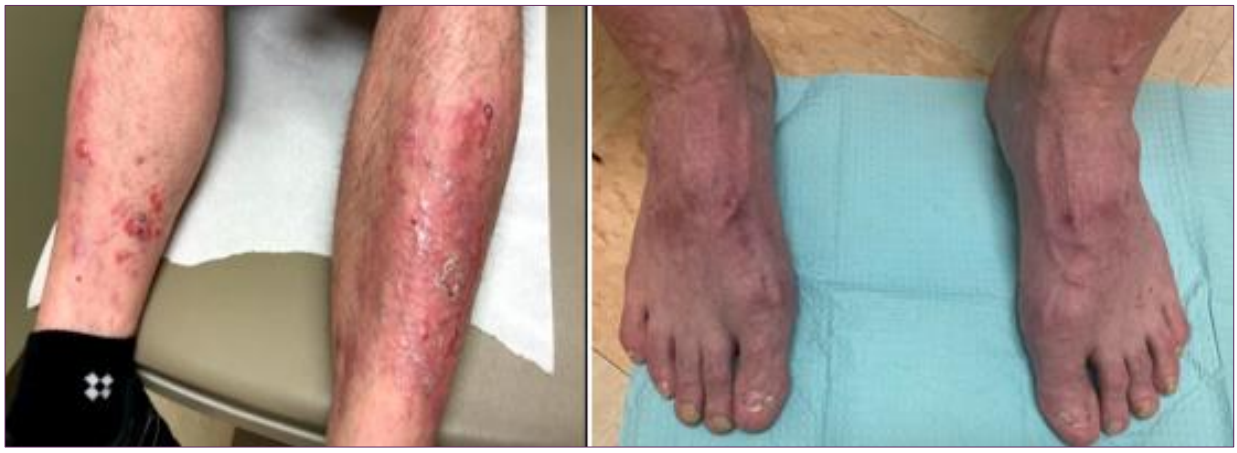

Figure 1.

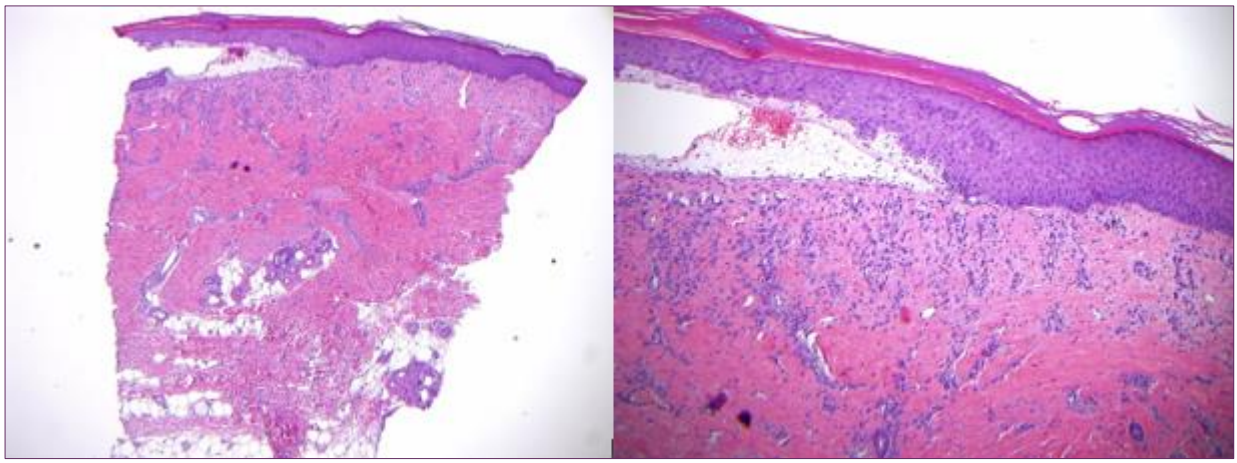

Figure 2.

biopsies, including one of an induced blister, were sent to Stanford University Medical Center. Immunofluorescence was stained with antibodies to basement membrane antigens, including LAD-1 (123, collagen XVII), D4B5 (laminin 332 gamma II chain), collagen IV, and collagen VII, which showed normal intensity staining with D4B5, collagen IV, and collagen VII with localization of these antigens to the blister floor. LAD-1 showed relatively normal intensity staining but was absent in areas of the split with possible weak staining on the floor of the blister. Overall, the findings were suggestive of junctional epidermolysis bullosa with mutation in COL17A1, consistent with a late-onset variant of JEB.

DISCUSSION

Based on the patient's history of recurrent tense blisters on his lower extremities, recent skin exams, histologic findings in his biopsy and negative DIF studies as well as immunomapping, the most likely diagnosis is a late-onset variant of JEB due to a mutation in COL17A1.

Upon further review of the patient's history, his likely initial cutaneous manifestations were the development of his dystrophic toenails in his teenage years, which later required nail avulsion. Around the age of 24 years old, he began developing tense blisters

on his shins. He also has a history of dystrophic changes of his teeth necessitating dental crowns and root canals. He denies any oral lesions, hair abnormalities, or ocular lesions. Family history is non-contributory. Further examination did not reveal any involvement of his hands, including milia or changes in dermatoglyphs. The recommendations given to the patient included trauma avoidance and topical steroids for any symptoms of pruritus.

JEB-lo is a rare subtype of JEB with varying clinical presentations. Two JEB-lo patients described by Yuen *et al,* a brother and sister, presented with blistering on the feet and around the toenails and fingernails starting at the age of 6 years old.[2] Both patients presented with loss of dermatoglyphs and waxy hyperkeratosis. Two other siblings with JEB-lo were also reported by Stouthamer *et al*.[5] Their onset of symptoms occurred at the age of 4 and 10 years old, with mechanobullous lesions, nail dystrophy, loss of dermatoglyphs, tooth enamel abnormalities, and hyperhidrosis.[5] A 17-year-old boy diagnosed by Vanotti *et al* has a homozygous missense mutation in COL17A1 and blisters starting at the age of 8 years old with atrophic skin, abnormal dermatoglyphs, dystrophic nails, and speckled pigmentation on the elbows.[6] The patient did not have hyperkeratosis or mucosal lesions.

CONCLUSION

Previous cases of JEB-lo reported within the literature had younger ages of onset and varying associated features compared to our patient. Our case of JEB-lo is diagnosed in the oldest patient with the latest age of onset. This may be attributed to limited testing availability for the mutations involved, such as COL17A1, leading to the underdiagnosis of JEB-lo. The patient also declined genetic testing. We report this case to highlight the existence of an exceedingly rare subtype of JEB that can be late onset and hope to increase clinician awareness.

Conflict of Interest Disclosures: None

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