

# Acrodermatitis dysmetabolica secondary to isoleucine deficiency in infant with maple syrup urine disease

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## Abstract

Acrodermatitis dysmetabolica (AD) describes eruptions characterized by the clinical triad of acral dermatitis, diarrhea, and alopecia. AD can be caused by various metabolic disorders, one of which is maple syrup urine disease (MSUD). We present a 2-month-old boy diagnosed with MSUD by the age of 5 days and treated with branched-chain amino acid (BCAA) restricted diet, BCAAs formula, and thiamine supplementation. He was referred to dermatology with a 3-week history of diarrhea, progressive acrodermatitis enteropathica like cutaneous eruption and hair loss over the scalp treated with topical mometasone ointment, isoleucine supplementation and leucine restriction. Complete resolution of skin eruption was achieved by 4 weeks, which correlates with normalization of BCAA levels based on close monitoring of biochemical lab values and growth. This case emphasizes

the dangers of limiting BCAA intake when treating MSUD, as well as the importance of close monitoring during the amino acid depleting period of growth.

## Introduction

Acrodermatitis dysmetabolica (AD) describes eruptions characterized by the clinical triad of acral dermatitis, diarrhea, and alopecia in association with metabolic disorders. AD is clinically identical to acrodermatitis enteropathica (AE). However, it results from deficiency of essential amino acids and fatty acids rather than zinc.<sup>1,2</sup> Maple syrup urine disease (MSUD) is an autosomal recessive inborn error of metabolism caused by a defect in the branched-chain alpha-ketoacid dehydrogenase (BCKDH) which breaks down the branched-chain amino acids (BCAA) leucine, isoleucine, and valine, and branched chain keto-acids (BCKA).<sup>3</sup> Failure to break down BCAA and BCKA lead to their accumulation, subsequently resulting in ketoacidosis, neurological disorders, developmental disturbances, and cutaneous manifestation.<sup>4</sup> MSUD is treated by restricting BCAA intake and thiamine supplementation, with liver transplantation as last resort.

## Case Report

A 2-month-old boy, referred with a 3-week history of diarrhea, progressive cutaneous eruption and hair loss. The child was diagnosed with MSUD by the age of 5 days, confirmed by BCKD mutation at gene sequencing, and treated with BCAA restricted diet, BCAAs formula, and thiamine supplementation. He was admitted to the hospital due to metabolic decompensation and multifocal neonatal seizures as manifestation of MSUD. Physical examination revealed scaly erythematous plaques over perioral area, napkin area, bilateral proximal upper and lower extremities, acral hands, with scalp hair loss (Figure 1). Laboratory investigation showed normal zinc level (15.7 micro-mol/L, range 11.5-18.5), and valine (200 omul; 200-400 umol/mL), low isoleucine (27 umol/mL; 100-200 umol/mL), and elevated leucine (864 umol/mL; 100-200 umol/mL). Histological examination of thigh skin punch biopsy showed parakeratosis with underlying pale keratinocytes in the upper epidermis, spongiosis and psoriasiform hyperplasia, which is consistent with nutritional dermatosis (Figure 2). Diagnosis was AD secondary to MSUD. Treatment was as follows: isoleucine supplementation and leucine restriction, and topical Mometasone 0.1% ointment twice daily for 14 days.

The eruptions improved after treatment initiation in relation with the correction of isoleucine and valine level. Complete resolution of cutaneous eruption was achieved by 4 weeks, with normalization of BCAA levels based on close monitoring of biochemical lab values and growth.

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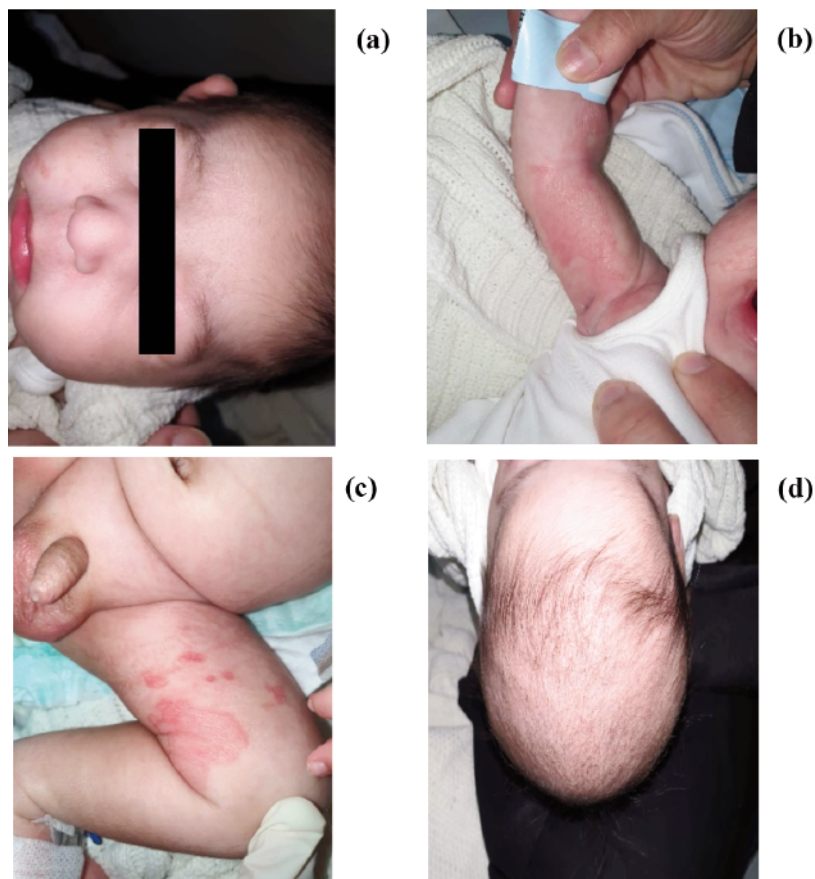
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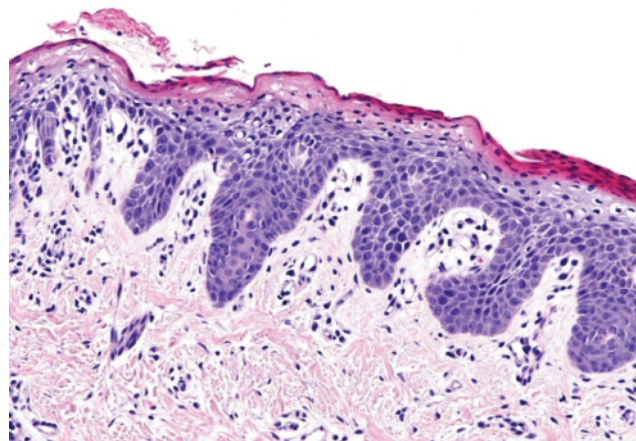
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**Figure 1.** a) Infant known case of maple syrup urine disease presenting with scaly erythematous plaques over perioral area and face; b) lesions of similar morphology were noted on the upper limbs; c) lower limbs and scrotal area; d) hair loss (alopecia) was noted as well.

## Discussion

The term acrodermatitis dysmetabolica describes acrodermatitis enteropathica like eruption in association with many metabolic disorders including MSUD. In maple syrup urine disease, the appearance of cutaneous lesions is likely related to isoleucine deficiency, which can interfere with protein synthesis essential for keratinocyte metabolism.<sup>5,6</sup> There have been previous reports of cases with MSUD who developed AD in the setting of BCAA restriction. Two MSUD cases were described with eruptive dermatitis that improved after supplementation with isoleucine.<sup>6</sup> Another study reported peri-oral dermatitis in eight cases with MSUD that were treated with BCAA restricted diet. The presence of dermatitis correlate with a low plasma isoleucine level and the severity related to the duration of low-level plasma isoleucine.<sup>7</sup> In addition, a study reported complete resolution of cutaneous eruption of AD in child with MSUD after normalization of isoleucine value and optimization of amino acid levels.<sup>1</sup> This highlights the role of isoleucine deficiency in the pathogenesis of AD, and the importance of carefully balancing BCAA levels while treating MSUD, as deficiency can precipitate AD.



**Figure 2.** High power view showing confluent parakeratosis, cytoplasmic pallor of upper epidermis, and spongiosis. Granular cell layer is absent. These histologic features are seen in cases of nutritional deficiency dermatitis. Hematoxylin and eosin stain used, 20x magnification.

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## Conclusions

We report the case of infant with MSUD who developed AD secondary to isoleucine deficiency with complete resolution of cutaneous eruption with isoleucine supplementation, which emphasizes the risk of BCAA diet restriction when treating MSUD and highlights the importance of close monitoring during the amino acid depleting period of growth.

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## References

1. Flores K, Chikowski R, Morrell DS. Acrodermatitis dysmetabolica in an infant with maple syrup urine disease. *Clin Exp Dermatol* 2016;41:651-4.
2. Rosa J, Fraga AB, de Carvalho R, et al. Acrodermatitis dysmetabolica as a sign of methylmalonic aciduria decompensation. *Clin Case Rep* 2018;6:1048-50.
3. Blackburn PR, Gass JM, Pinto e Vairo F, et al. Maple syrup urine disease: mechanisms and management. Vol. 10. *Application of clinical genetics*. Dove Medical Press Ltd.; 2017. p. 57–66.
4. Burrage LC, Nagamani SC, Campeau PM, Lee BH. Branched-chain amino acid metabolism: from rare mendelian diseases to more common disorders. 2014. Available from: <http://hmg.oxfordjournals.org/>
5. Tabanlıoğlu D, Ersoy-Evans S, Karaduman A. Acrodermatitis enteropathica-like eruption in metabolic disorders: Acrodermatitis dysmetabolica is proposed as a better term. *Pediatr Dermatol* 2009;26:150-4.
6. Gupta N, Jain P, Kabra M, et al. Acrodermatitis dysmetabolica - report of two cases. Vol. 82. *Indian J Pediatr* 2015:869-70.
7. Abad RMR, Pauline J, Lazo-Dizon H. A 1-year-old female with maple syrup urine disease presenting with acrodermatitis-enteropathica-like lesions. *Acta Med Philipp* 2023;52.