Facial Dysmorphology and Odontogenic Tumor Development Associated With Inborn Errors of Metabolism: A Case Report

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Purpose: Inborn errors of metabolism (IEMs) are genetic disorders that alter normal physiologic functioning. Deficiency of 3-methylcrotonyl-coenzyme A carboxylase is one such IEM that can lead to major episodes of metabolic dysfunction. Certain IEMs are associated with characteristic congenital dysmorphic facial features. This can be problematic, because these dysmorphisms can mask underlying tumor growth. Literature is lacking on a causal relation between IEM and odontogenic tumor development.

Materials and Methods: This case was explained in detail and a review of the literature was undertaken. PubMed was used to search for articles involving surgical management of odontogenic myxoma (OM) and associations between odontogenic tumors and IEM.

Results: It was determined that the development of odontogenic tumors, specifically OM, is associated with IEMs. These tumors can easily be overlooked as a common dysmorphic feature of an IEM.

Conclusion: IEMs lead to major metabolic disturbances and, thus, can alter the cellular microenvironment. Hypothetically, these alterations can lead to the development of odontogenic tumors. With the diagnosis of IEM becoming more common owing to improved newborn screening, careful attention should be given to these patients because of the possibility that dysmorphologic facial features could be masking underlying tumor growth.

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The enzyme 3-methylcrotonyl-coenzyme A (CoA) carboxylase (3-MCC) is localized within the inner mitochondrial membrane that performs an integral function in the metabolism of leucine. Deficiency of 3-MCC is a relatively common autosomal recessive inborn error of metabolism (IEM).[1] A complete listing of all IEMs is vast and beyond the scope of this article. Relative to inborn errors of leucine metabolism, other similar disorders in this subcategory include maple syrup urine disease, isovaleric academia, 3-hydroxy-3-methylglutaryl-CoA lyase deficiency, and 3-methylglutaconic aciduria.

The 3-MCC deficiency affects roughly 1 in 36,000 people.[2] As part of normal metabolic function, leucine is involved in growth, energy production, and formation of sterols. It is stored in adipose, liver, and muscle tissues.[3] Leucine is an essential amino acid found in many protein-rich foods and, thus, must be ingested. Normal leucine metabolism progresses with the formation of 3-methylglutaconyl-CoA from 3-methylcrotonyl-CoA, a step catalyzed by 3-MCC. With 3-MCC deficiency, there is a buildup of metabolites that ultimately causes a metabolic acidosis (Fig 1). This acidosis is manifested in times of increased metabolic stress, such as during fasting and infection. Clinically, the phenotype of this deficiency can range from an asymptomatic patient to death.[4] Studies have elucidated the common clinical features at time of clinical diagnosis (not discovered

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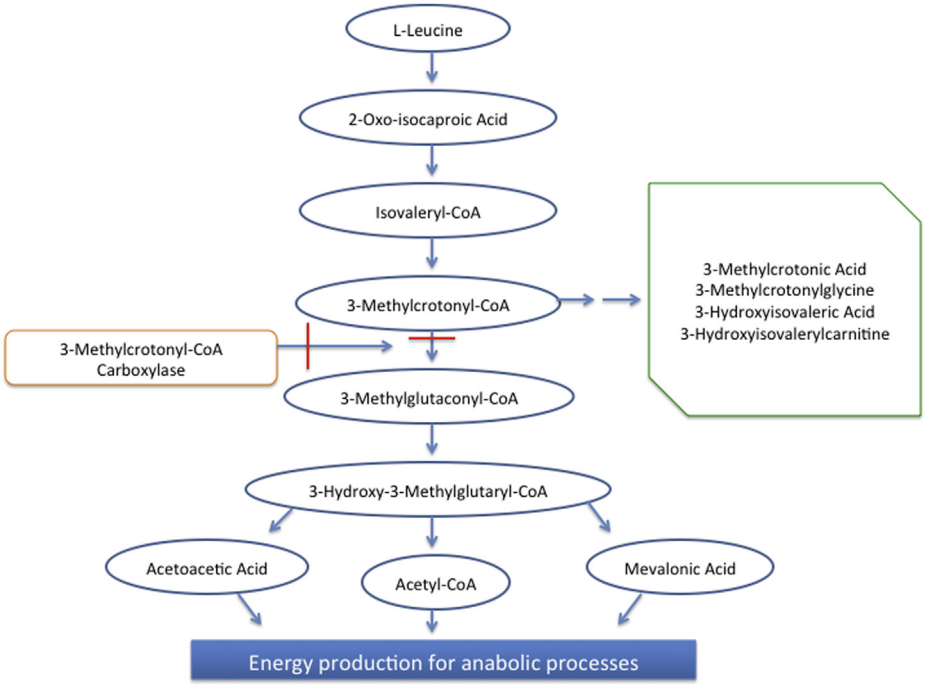

FIGURE 1. Metabolic pathway involving 3-methylcrotonyl-coenzyme A carboxylase and leucine breakdown (*blue oval,* molecular precursor in pathway; *orange rectangle,* enzyme; *green square,* metabolites). Adapted from Health2Media: 3-Methylcrotonylglycinuria. Published 2013. Available at: http://www.treatable-id.org/page79/3Methylcrotonylglycinuria.html. CoA, coenzyme A.

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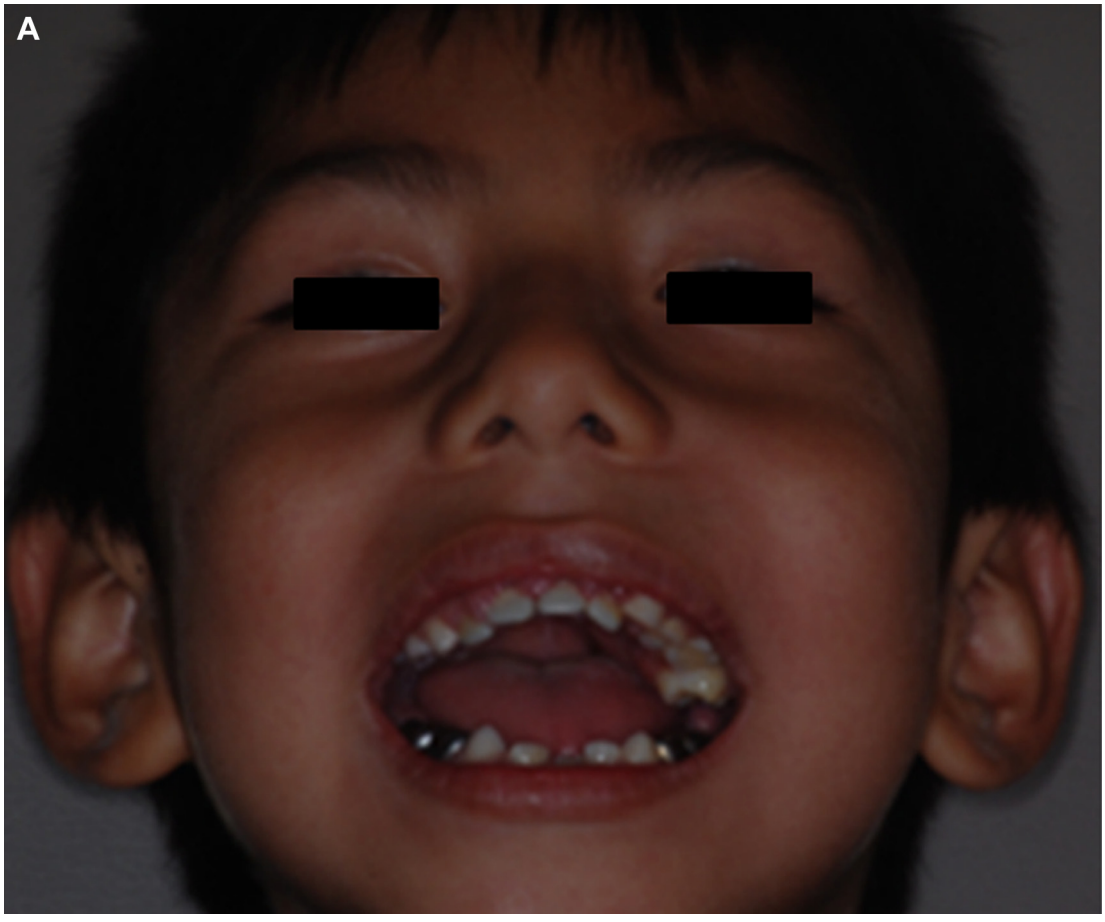

FIGURE 2. *A,* Extraoral photograph showing left midfacial swelling. **(Fig 2 continued on next page.)**

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