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Oral health in two heterozygote female twins with congenital lactic acidosis

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Abstract

Introduction: *Congenital lactic acidosis (CLA) is a rare disease caused by mutations in Mithocondrial DNA (mtDNA), which affects the ability of cells to use energy that causes accumulation of lactic acid in the body. No oral manifestations have been documented in these patients.*
Methods: *We report the oral health status of two young adolescent heterozygote female twins, one of them being diagnosed at 8 weeks of life by muscle biopsy with a severe neonatal form of CLA. In order to avoid biopsy-related complications, the second twin did not undergo a diagnostic procedure and both girls were treated for CLA. They underwent clinical oral health examination at the age of 12, for caries evaluation (diagnostic threshold D1 - early enamel demineralization) by ICDAS II clinical assessment, photographic documentation and fluorescence intra-oral camera.*
Results: *Among the two twins, the CLA-diagnosed one presented with severe enamel carious hypomineralizations on upper and lower vestibular smooth surfaces. Moreover, deep occlusal enamel carious lesions were detected by intra-oral fluorescence camera. The second twin had no obvious decay lesions, neither on pit and fissures nor on vestibular smooth surfaces.*
Conclusions: *Congenital lactic acidosis might be associated with hypomineralized defects and caries susceptibility in young adolescents. Preventive measures and personalized caries risk assessment should be encouraged and implemented in these patients following current caries management systems protocols, as ICCMS (International Caries Classification and Management System).*

Keywords: *congenital lactic acidosis, twins, hypomineralization, fluorescence camera, caries.*

Introduction

Congenital lactic acidosis (CLA) is a rare disease caused by mutations in mitochondrial DNA (mtDNA), which affects the ability of cells to use energy that causes accumulation of lactic acid in the body. This condition leads to functional defects in mitochondrial enzymes crucial to aerobic metabolism and oxidative phosphorylation.

Deficiency of the nuclear-encoded pyruvate dehydrogenase complex (PDC), located in the mitochondrial matrix, is the most common cause of CLA. PDC decarboxylates pyruvate to acetyl CoA [1]. The mitochondrial pyruvate oxidation process is essential for aerobic cellular energy production. Disruption of this pathway may cause neurometabolic disorders with onset in early childhood [2].

Clinical manifestations that leads to diagnostic investigations usually begin from the 2nd week to the 4th year of age and the interval between birth and clinical symptoms may range from hours to weeks. CLA may present with non-specific symptoms such as respiratory distress, severe generalized hypotonia, poor sucking

reflex, vomiting, diarrhea, dehydration, lethargy, seizures: all signs that can be easily related to sepsis or some other common cause. In all of them a frequent finding is lactic acidemia, which is caused by increased conversion of pyruvate via the enzyme lactate dehydrogenase [2].

Elevation of blood (>27 mg/100 ml) and/or cerebrospinal fluid lactate is a non-diagnostic, but prevalent, biomarker of mitochondrial disorders [1]. Elevated lactic acid levels without infections or tissue hypoxia are an important finding. Diagnostic investigations are plasma redox states ratio (lactate: pyruvate ratio, 3hydroxybutyrate: acetoacetate), polarographic studies, Enzyme assays (muscle, lymphocytes, fibroblasts) [3].

To our knowledge, no oral manifestations have been described in these patients. We report here the clinical health status of two female heterozygote twins affected by CLA.

Case report

The two patients presented to our observation when they were 12 years old. One of them was diagnosed with a severe neonatal form of CLA by muscle biopsy at 8 weeks of life. The other one did not undergo such invasive diagnostic procedure to avoid the operational risks, but was anyway treated as she had CLA. They underwent therapy with idebenone and carnitine since the time of the diagnosis. Moreover, they underwent periodical antibiotics treatment for recurrent infections. In addition, the first one, was treated with proton-pump inhibitor for gastroesophageal reflux disease, since the 4th month of life.

Clinical oral health examination at baseline was performed by clinical assessment of the presence of caries (diagnostic threshold for early enamel demineralization – D1) by ICDAS II system (International Caries Detection and Assessment System) [4] and by fluorescence intra-oral camera (VistaCam iX Proof, Durr Dental, Germany) for occlusal surfaces evaluation [5]. Photographic documentation was performed.

Among the two twins, the one who underwent the diagnostic procedure for CLA presented with severe enamel hypomineralizations on upper and lower vestibular smooth surfaces. The lesions were previously treated by resin restorations with poor results **(Figure 1, 2, 3).** Visible supragingival plaque [6] and bleeding on probing (BOP) [7] were observed. Moreover, deep pit and fissures enamel carious lesions were detected on occlusal surface by intra-oral fluorescence camera. **(Figure 4-7**) The reported DMFT scored 10.

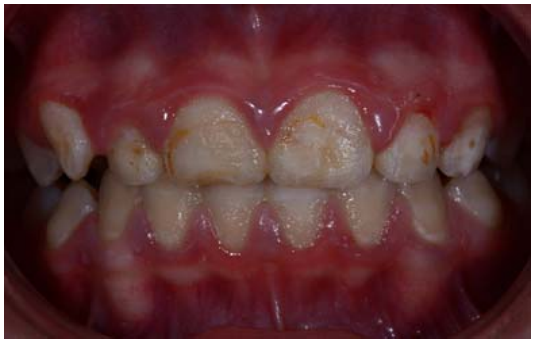

Figure 1. Frontal intraoral view. Hypomineralized enamel lesion on upper and lower arch, previously treated in the upper arch with direct resin restorations with poor results. Visible plaque and gingivitis.

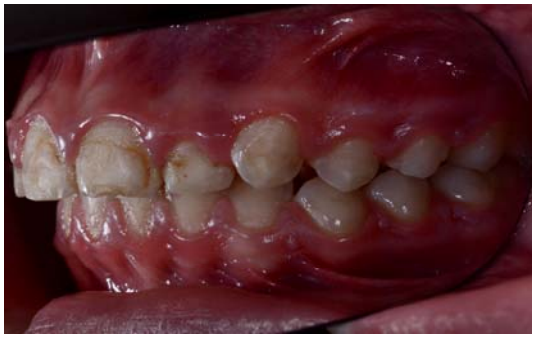

Figure 2. Right intraoral view. Visible hypomineralization on upper and lower central and lateral incisors, upper canine and two premolars. Signs of poor oral hygiene, gingivitis and plaque.

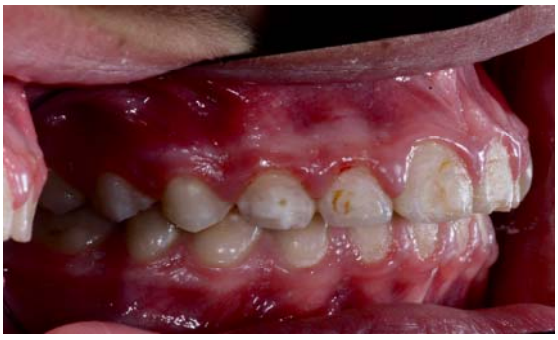

Figure 3. Left intraoral view. Hypomineralization of enamel on upper and lower arch. On the upper arch hypomineralized enamel on incisors central and lateral, canine and premolars. Presence of white demarcated areas with brown coloured spots on the affected teeth.

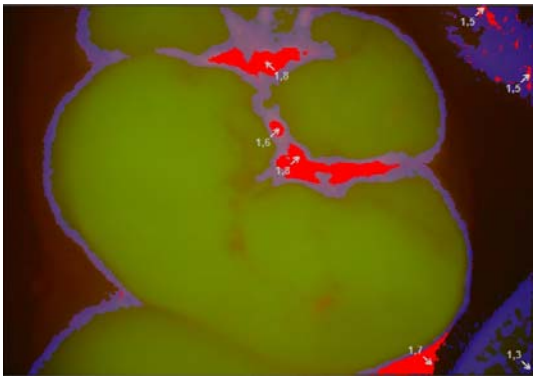

Figure 4. VistaCam Ix Proof assessment on upper right second molar. 1.8 score indicating a deep enamel decay.

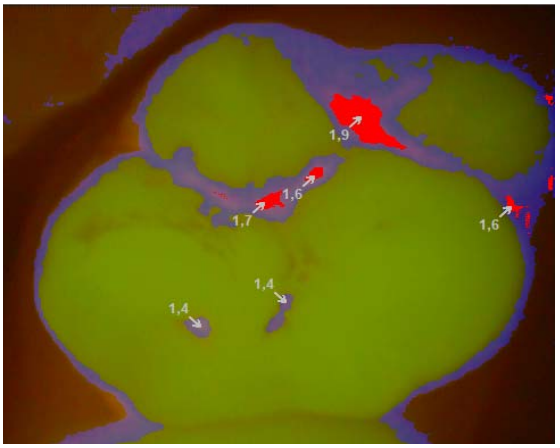

Figure 6. VistaCam Ix Proof assessment on upper left second molar. 1.9 score indicating a deep enamel decay.

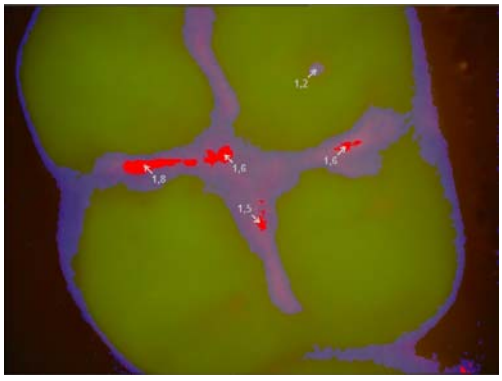

Figure 5. VistaCam Ix Proof assessment on lower right second molar. 1.8 score indicating a deep enamel decay.

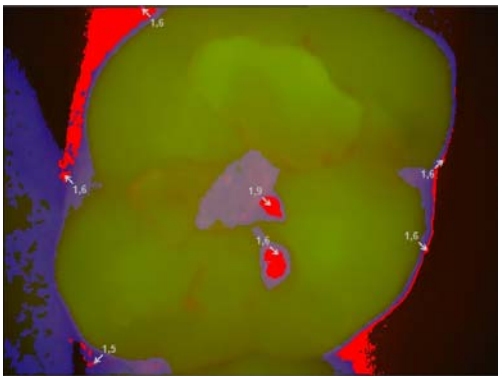

Figure 7. VistaCam Ix Proof assessment on upper left first molar. 1.6 score indicating a deep enamel decay under a pre-existing restoration.

The second twin had no obvious decay lesions, neither on pit and fissures nor on vestibular smooth surfaces **(Figure 8 -10)**, presenting with a good oral hygiene and with a DMFT of 1.

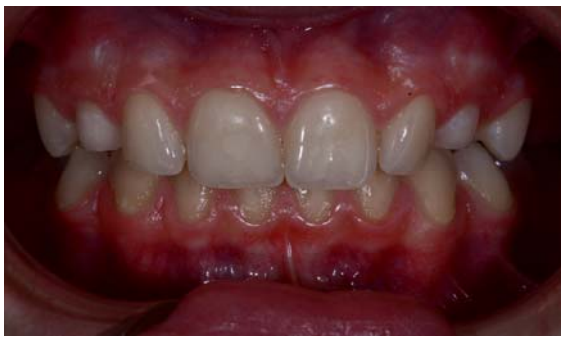

Figure 8. Intraoral frontal view of the second twin presenting with good oral hygiene and absence of enamel demineralization on vestibular surfaces of upper and lower arch.

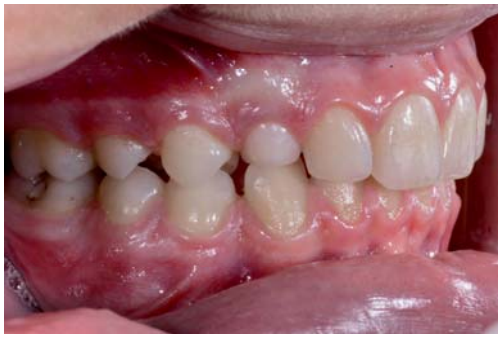

Figure 9. Intraoral left view.

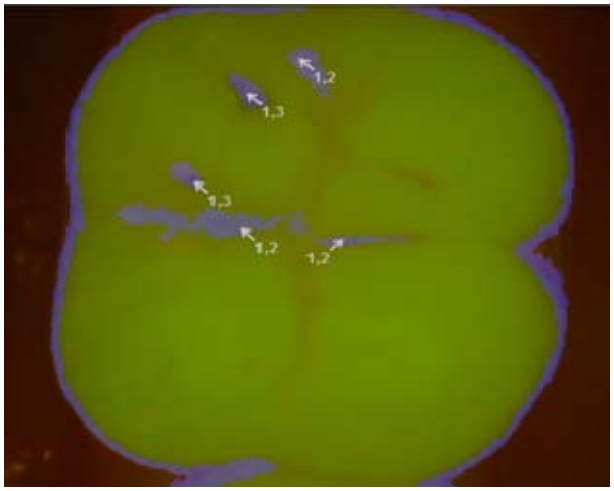

Figure 10. VistaCam Ix Proof assessment on upper left first molar. 1.3 score indicating an early enamel demineralization.

Discussion

We report herein two siblings who were treated for CLA since the 8th week of life and underwent therapy with idebenone and carnitine. They presented to us at the age of 12 years of age and a clinical oral examination was performed. The one with histologically proven CLA was found to have hypomineralizations on upper and lower vestibular surfaces of the clinical crowns and deep enamel demineralizations on the four first molars and one premolar, diagnosed by the use of an intra-oral fluorescence camera. Moreover, plaque index and BOP were found to be positive.

The other sibling did not show any of the above described findings, presenting with a good oral hygiene and with a DMFT of 1.

No previous reports are found in literature describing the possible association between CLA and Oral Health Status.

Interestingly both grew up in the same environment.

Therefore, it is not possible to ascribe all the conditions found in the first sibling to CLA only. On the other hand, some of the factors involved in the etiopathogenesis of CLA may contribute to the clinical picture we described.

Conclusion

In conclusion, CLA might be associated with hypomineralized defects and caries susceptibility in young adolescents. Preventive measures and personalized caries risk assessment should be encouraged and implemented in these patients following ICCMS protocol [6].

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