Dental issues in lacrimo-auriculo-dento-digital syndrome

An autosomal dominant condition with clinical and genetic variability

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ABSTRACT

Background and Overview. Lacrimo-auriculo-dento-digital (LADD) syndrome is an autosomal dominant disorder with variable lacrimal and salivary gland hypoplasia and aplasia, auricular anomalies and hearing loss, dental defects and caries, and digital anomalies.

Case Description. The authors present the cases of 2 unrelated children with enamel defects and history of dry mouth leading to recurrent dental caries. The referring diagnoses were Sjögren disease and hypohidrotic ectodermal dysplasia, respectively. The geneticist suspected LADD syndrome, which was confirmed by means of molecular studies showing mutations of 2 genes: fibroblast growth factor receptor 2 and fibroblast growth factor 10, respectively. Similarly affected relatives indicated an autosomal dominant inheritance. These relatives needed multiple dental rehabilitations during childhood and dentures in adulthood.

Conclusions and Practical Implications. Dry mouth, multiple caries, enamel defects, and abnormal tooth morphology were the reasons for seeking care from dentists. However, clinical evaluation and diagnostic imaging studies helped identify anomalies of the lacrimal and salivary glands, ears, and digits, indicating involvement of different areas of the body, compatible with LADD syndrome. Accordingly, dentists should consider genetic disorders in patients with multiple anomalies. For instance, oculodentodigital syndrome, oral-facial-digital syndrome, and LADD syndrome (among others) may have dental issues as the major clinical manifestation. Accurate identification of a particular syndrome is now commonplace with the use of genetic testing. When a patient has multiple anomalies suggestive of a syndromic condition, appropriate genetic testing can help verify the clinical diagnosis. Keeping genetics in mind helps earlier identification of other affected family members with diagnostic genetic testing and appropriate treatment; the economic advantage is to shorten the diagnostic odyssey and possibly preserve dentition.

Key Words. Dental enamel; caries; salivary glands; genetics; Sjögren disease.

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Severe early childhood caries is defined as any sign of smooth-surface caries in a child younger than 3 years.[1] Parents and siblings similarly may be affected because of shared dietary or oral hygiene habits or shared cariogenic microbes. However, in pediatric cases in which dietary habits and oral hygiene are noncontributory, the clinician should consider an underlying genetic condition.

Lacrimo-auriculo-dento-digital (LADD) syndrome, also known as Levy-Hollister syndrome (Online Mendelian Inheritance in Man no. 149730), is a rare congenital condition associated with lacrimal duct obstruction; auricular anomalies; conductive, sensorineural, or mixed hearing deficit; aplasia or hypoplasia of the salivary glands; dental anomalies (small, peg-shaped incisors, enamel dysplasia); and digital anomalies (syndactyly, clinodactyly, or duplicated or triphalangeal thumb).[2,3]

We describe 2 families with primary features of dental caries and enamel defects with variable expression of other related findings of LADD syndrome. Although features associated with LADD syndrome bridge multiple specialties, dental anomalies such as abnormal number of teeth, abnormal tooth size or morphology, enamel hypoplasia, or severe early childhood

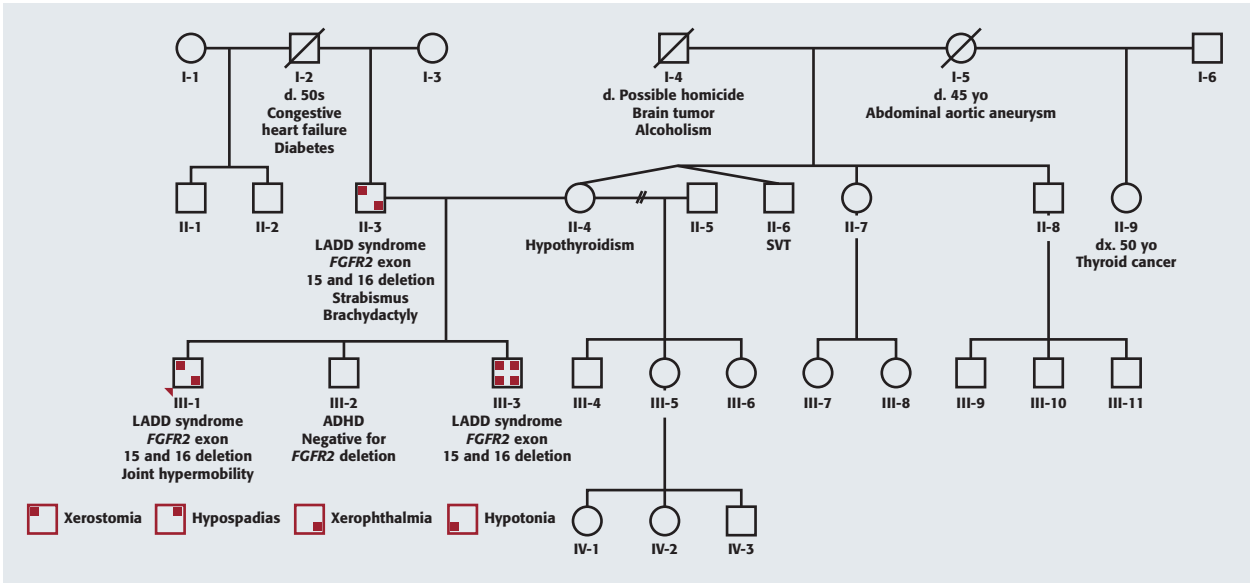

Figure 1. Family 1 pedigree. //: Separated or divorced. ADHD: Attention deficit hyperactivity disorder. d: Died. dx: Diagnosis. FGFR: Fibroblast growth factor receptor. LADD: Lacrimo-auriculo-dento-digital. SVT: Supraventricular tachycardia. yo: Years old.

caries could be the reason for seeking care. Therefore, pediatric dentists should be aware of these features because early diagnosis can assist in treatment and follow-up care. A positive family history for similar dental findings and other supportive clinical features will direct the dentist toward consideration of an inherited genetic condition and referral of the patient for genetic evaluation.

CASE REPORTS

Family 1. Proband 1 (III-1 on the family 1 pedigree) (Figure 1) is a 9-year-old boy referred for genetic and rheumatologic evaluation because of multiple dental carries, enamel defects, and a history of dry mouth (xerostomia) and dry eyes (xerophthalmia). There were specific concerns for Sjögren disease.

Clinical features included dry mouth, multiple dental caries, enamel hypoplasia, and normal basal tears but no extra tear production in response to stimuli and minimal salivary pooling. Craniofacial dysmorphic features included hypertelorism, epicanthic folds, broad nasal bridge, low-set ears, high-arched palate, flat facial profile, and nevus flammeus of the forehead (Figures 2 and 3). Digital findings included clinodactyly of the fifth finger and moderate syndactyly of the second and third toes (Figure 4). The primary teeth showed taurodontism of the molars and thin incisor roots, but there were no missing teeth. He required multiple dental procedures and restorations because of carious lesions in the primary dentition. The permanent teeth were slightly smaller than average, with enamel hypoplasia and taurodontism with long, thin roots of the first molars (teeth nos. 3, 14, 19, and 30) and some occlusal wear of the enamel because of bruxism. The third molars were not developed yet and might be congenitally missing (Figure 5).

He had also a history of failure to thrive due to gastrointestinal problems, which responded to treatment, and marked joint hypermobility. He had no history of parotitis, frequent fever, joint pain, rash, adenopathy, arthritis, or neurologic problems.

His family history and pedigree (Figure 1) is remarkable for xerophthalmia, xerostomia, and dental caries in the proband's father (II-3; not pictured), who eventually required full dentures. He had a history of dry skin, strabismus, and joint hypermobility. The proband has a 2-year-old full brother (III-3; not pictured) with reported xerostomia and xerophthalmia but normal tooth morphology without enamel hypoplasia, hypodontia, or carious lesions. He was not cooperative in obtaining radiographs. This brother also had a history of hypospadias, hypotonia, and gross motor delay. Another full brother (III-2), mother (II-4), and 3 maternal half siblings (III-4, III-5, and III-6) were unaffected. The mother had mild syndactyly of the second and third toes.

Laboratory test results were negative for Sjögren disease; these tests included serum amylase,

ABBREVIATION KEY. ADHD: Attention deficit hyperactivity disorder. **d:** Died. **dx:** Diagnosis. **FGF:** Fibroblast growth factor. **FGFR:** Fibroblast growth factor receptor. **LADD:** Lacrimo-auriculo-dento-digital. **SVT:** Supraventricular tachycardia. **VUS:** Variant of uncertain significance. **yo:** Years old.