

# Orofacial manifestations of the Levy–Hollister syndrome

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## ABSTRACT:

The Levy–Hollister syndrome, also known as the lacrimo-auriculo-dento-digital (LADD) syndrome, shows different phenotypes, resulting in a variety of local and systemic signs and symptoms. It is a rare hereditary disorder that mainly causes lacrimal, auricular, and auditory apparatus disturbances and dental and digital anomalies. Here, we describe a case of the Levy–Hollister syndrome in a 24-year-old woman and focus on its orofacial manifestations. The patient had chronic lacrimation, low-set ears, thumb agenesis, elbows with limited pronation and supination movements, pronounced hallux on the left foot, concave facial profile, and tooth roots with atypical morphology. The case emphasizes the importance of a multidisciplinary approach for early diagnosis of the Levy–Hollister syndrome.

**Keywords:** dental anomalies, diagnosis, digital anomalies, hereditary disorder.

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## INTRODUCTION

The Levy–Hollister syndrome, also known as the lacrimo-auriculo-dento-digital (LADD) syndrome, was first described by Levy, in 1967, and Hollister et al., in 1973<sup>1,2</sup>. It is an autosomal dominant disorder characterized by a variety of local and systemic signs and symptoms because of different phenotypes<sup>3,4</sup>. It is a rare syndrome, as only about 30 cases have been described in the pediatric and genetic literature<sup>5</sup>; until now, less than 60 cases have been observed worldwide<sup>6</sup>.

Some of the main clinical characteristics of the LADD syndrome are as follows: lacrimal anomalies including nasolacrimal duct obstruction with chronic disease of the lacrimal apparatus and hypoplasia or aplasia of the lacrimal glands<sup>5,7,8</sup>; auricular anomalies such as low-set and cup-shaped ears and unilateral or bilateral hearing loss<sup>1,2,9-11</sup>; digital anomalies including aplasia, hypoplasia, partial syndactyly and abnormal localization of the thumbs, clinodactyly, partial syndactyly and absence of the terminal phalanx of the other fingers<sup>5,11-13</sup>; and limb anomalies including radial aplasia, radioulnar synostosis, limited elbow pronation and supination, and radio-deviation of the hands. Deformities of the lower limbs are less common and comprise syndactylism, large hallux, supernumerary metatarsal bone, and talus-shaped abnormality<sup>7,14,15</sup>.

Among the main orofacial manifestations of the LADD syndrome, dental anomalies are observed in most patients. The global nondental literature includes references to “misshapen teeth”<sup>16-18</sup>. These anomalies include hypodontia, microdontia, cone-shaped teeth, and enamel hypoplasia<sup>5-7,12,19</sup>. Hollister et al. suggest that the enamel dysplasia observed in both dentitions is a form of amelogenesis imperfecta, which is a hereditary disorder<sup>2,20</sup>. The dentofacial deformity most described in the literature is midfacial hypoplasia with Angle class III malocclusion, a combination that results in a concave facial profile<sup>18</sup>. Another orofacial manifestation is hypoplasia or aplasia of the major salivary glands, resulting in xerostomia; the decreased salivary flux also affects the antimicrobial and self-cleaning properties of saliva<sup>1,2,6,12</sup>. Consequently, the prevalence of oral candidiasis, dental caries, especially cervical and root decay, and chewing and swallowing difficulties and discomfort increases<sup>5,12,18,20</sup>.

Here, we describe a case of the LADD syndrome in a young woman and focus on its orofacial manifestations.

## CASE REPORT

A 24-year-old female AJS patient was attended by the health team of the Professor Edgard Santos University Hospital at the Federal University of Bahia. She had a natural birth without complications. At birth, she presented microphthalmia with opaque cornea and chronic lacrimation of the right eye; at

2 years of age, she had vision loss due to glaucoma and currently uses an ocular prosthesis (Figure 1). Both hands showed thumb agenesis (Figure 2), and her elbows showed limited pronation and supination movements (Figure 3). She had low-set ears (Figure 4), muscular hypotonicity, coordination problems, difficulties in locomotion, and a large hallux on the left foot (Figure 5). She had been diagnosed with the LADD syndrome at the age of 8 years.



**Figure 1.** Frontal view showing chronic lacrimation of the right eye and mandibular deviation to the left side.

The patient was referred to the Stomatology Service of the Faculty of Dentistry at the Federal University of Bahia. The extraoral examination showed mandibular deviation to the left side and a concave facial profile (Figures 1 and 4). The intraoral examination revealed the absence of the maxillary anterior teeth, mandibular incisors, and right mandibular canine (Figure 6). Panoramic radiography showed other dental anomalies (Figure 7).

## DISCUSSION

The LADD syndrome is rare, and this might be the first case described in Brazil. An autosomal dominant trait has been ratified in some families; nevertheless, most cases occur spontaneously<sup>18</sup>. Our patient had no family history of the LADD syndrome.



**Figure 2.** Thumb agenesis.



**Figure 3.** Elbows showing limited pronation and supination movements.

It is a scientific consensus that this syndrome manifests different levels of phenotypic expression resulting in a variety of local and systemic signs and symptoms<sup>3,4,8,12</sup>. A patient with the LADD syndrome mainly shows lacrimal, auricular, and auditory apparatus disorders and dental and digital anomalies. Our patient has all these features. Chronic lacrimation of the right eye was verified at birth and is still present, which suggests nasolacrimal duct obstruction, a sign also observed in another case<sup>5</sup>. Although 70% of the affected patients present cup-shaped ears, the condition was not observed in this patient. However, she has low-set ears, a relevant sign in other cases<sup>2,5,9-11</sup>.

Abnormalities of the thumbs are the most common and consistent findings of the LADD syndrome<sup>5</sup>. These abnormalities are pathognomonic signs of the disease<sup>6</sup>. The manifestations range from little variances and syndactyly to digital deformities, such as lobster-claw deformity and digital agenesis or aplasia<sup>6,11-13</sup>. Our patient has bilateral thumb agenesis.



**Figure 4.** Concave facial profile and low set ears.



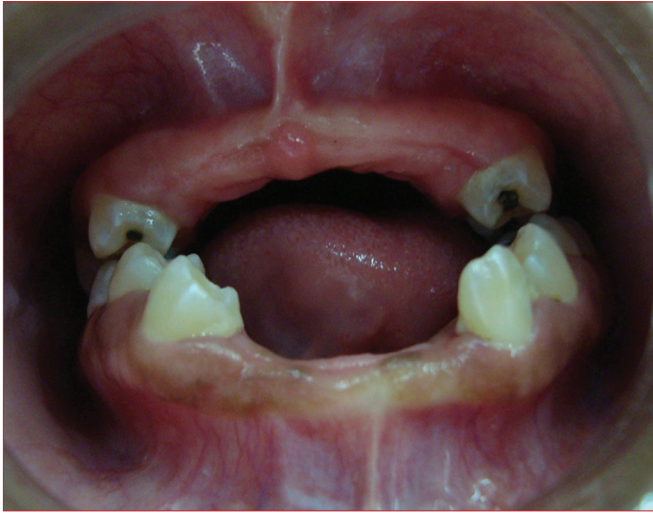
**Figure 5.** Hallux on the left foot.

The upper limbs are affected with greater intensity in this syndrome; nevertheless, lower limb defects are more tender and less recurrent<sup>14,15</sup>. In the present case, the upper limbs were more affected, with limited elbow pronation and supination movements, muscular hypotonicity, and coordination problems; in the lower limbs, a pronounced hallux was noted on the left foot.

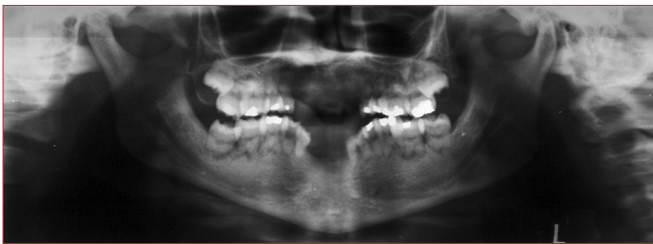
In addition to the main signs and symptoms, clinical findings such as renal abnormalities, facial asymmetries, ophthalmological malformations, and epiglottis hypoplasia have been reported<sup>6,12,14,16,17</sup>.

The orofacial deformity described predominantly in the literature is midfacial hypoplasia with Angle class III malocclusion, causing anterior cross bite<sup>18</sup>. Our patient shows this typical





**Figure 6.** Intraoral view.



**Figure 7.** Panoramic radiograph.

growth pattern; the concave facial profile is further accentuated by the lack of anterior teeth. The literature also describes the occurrence of mandibular deviation<sup>18</sup>, as found in this patient.

The type and level of dental abnormalities are highly variable<sup>8,12</sup>. Hypodontia, microdontia, cone-shaped teeth, enamel hypoplasia, and amelogenesis imperfecta are some dental abnormalities described in the literature. Although none of these features were noted in the present case, panoramic radiography verified that the tooth roots have atypical morphology, compatible with the radiographic appearance of dentin dysplasia type I. A similar morphology has been reported by others<sup>18,19</sup>. The radiographic examination also suggested enlargement of the dental follicle or a dentigerous cyst involving the maxillary third molars; this finding should be analyzed in the future to determine its relationship with the syndrome.

Salivary gland malformation is discussed intensely in the literature as an orofacial characteristic of this syndrome; it was first described by Shiang and Holmes<sup>18</sup>. Hypoplasia and aplasia of the major salivary glands, resulting in xerostomia, play an important role in oral candidiasis predisposition and tooth decay<sup>1,2,6,12,20</sup>. Most reports describe an increased incidence of caries with consequent premature tooth loss due to xerostomia<sup>6,12,18,20</sup>. The present case is in agreement with these reports:

the patient lost 11 teeth due to caries and the remaining teeth have been restored to control the disease. However, in this case, xerostomia does not seem to be the causative factor for caries, because it was imperceptible and salivary gland malformation was not confirmed. The elevated caries rate could be due to the coordination problems caused by the syndrome, which limits oral hygiene maintenance.

Ramirez and Lammer<sup>6</sup>, on the basis of their case report, recommend the inclusion of cleft lip and palate as an orofacial manifestation of the LADD syndrome, but this condition was not observed in the present case.

## CONCLUSION

In conclusion, the case emphasizes the importance of a multidisciplinary approach for early diagnosis of the LADD syndrome, which is difficult to establish because of the different phenotypes. In future cases, the possible correlation between the presence of an enlarged dental follicle or dentigerous cyst and the radiographic appearance of dentin dysplasia type I with the orofacial manifestations of the LADD syndrome should be analyzed. Deficits in motor coordination affect oral hygiene maintenance and consequently increase the caries rate. The treatment of this syndrome is symptomatic and includes reduction of all reversible symptoms to improve the patient's life quality.

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