Oral manifestations of Smith-Lemli-Opitz Syndrome: a paediatric case report

G. PIZZO, M.R. PISCOPO, I. PIZZO, G. GIULIANA

ABSTRACT. Background The Smith-Lemli-Opitz Syndrome (SLOS) is an autosomal recessive genetic disorder, characterised by multiple congenital malformations, dysmorphic facial features and mental retardation. SLOS is caused by a genetically inherited deficiency of the enzyme 7-dehydrocholesterol Δ7-reductase (7-DHC reductase), the catalyst involved in the final step of cholesterol biosynthesis, with the consequence of an increased serum levels of 7-DHC and generalised cholesterol deficiency. Case Report A 5-year-old female child was referred to the Department of Paediatric Dentistry of the University of Palermo for caries, gingivitis and malocclusion. The medical history revealed the diagnosis of SLOS, confirmed by a biochemical analysis 5 weeks after birth. The child exhibited several dysmorphic craniofacial features, typical of SLOS. Dental treatment, including oral prophylaxis, was performed without sedation. Instructions on proper oral self-care and dental disease prevention were provided to the mother of the patient. Conclusion Suggestions regarding comprehensive dental care may be important to properly treat children with SLOS in the dental office.

KEYWORDS: Smith-Lemli-Opitz Syndrome, Cholesterol metabolism, 7-dehydrocholesterol reductase, Craniofacial manifestations.

Introduction
The Smith-Lemli-Opitz Syndrome (SLOS) is an autosomal recessive genetic disorder, characterised by multiple congenital malformations, dysmorphic facial features and mental retardation.

The disorder was first described in 1964 by Smith et al. in a report of three patients who had multiple congenital anomalies in common [Smith et al., 1964]. More complete delineation of SLOS was presented in 1969 as the “RHS syndrome”, named after the original patients’ surnames [Opitz et al., 1969]. The description of many new cases of SLOS over the subsequent years expanded the known characteristics of the syndrome [Kelley and Hennekam, 2000].

The estimated incidence of SLOS was initially between 1/40,000 births and 1/20,000 births, based exclusively on clinical diagnosis [Malgorzata et al., 1999; Kelley and Hennekam, 2000]. When knowledge of the biochemical defect was widespread, the incidence of SLOS diagnosed biochemically in similar populations appeared to be much lower: 1/60,000 births in the United Kingdom and even lower in Japan [Ryan et al., 1998; Tsukahara et al., 1998].

Initially, two types of SLOS, type I (classic) and type II (severe) [Curry et al., 1987; Opitz et al., 1969], were distinguished, but nowadays these types represent a spectrum of the same syndrome [Tint et al., 1995; Cunniff et al., 1997; Ginat et al., 2000].

SLOS is caused by a genetically inherited deficiency of the enzyme 7-dehydrocholesterol Δ7-reductase (7-DHC reductase), the catalyst mapped to chromosome 11q12-13 and involved in the final step of Kandutsch-Russell cholesterol biosynthesis [Kelley and Hennekam, 2000]. In individuals affected by SLOS, the normal conversion of 7-dehydrocholesterol (7-DHC) into cholesterol is blocked with the consequence of an increased plasma and tissue levels of 7-DHC and generalised cholesterol deficiency [Muzzin and Harper, 2003; Kelley and Hennekam, 2000].

Cholesterol, an important element in human metabolism, is essential for the synthesis of steroid
hormones and bile acids, and represents the major constituent of cell membranes and myelin. Since very little cholesterol is transported after the first trimester from the mother to foetus, systemic disorders and structural alterations occur. The discovery of the underlying defect that affects cholesterol synthesis led to the development of a biochemical diagnostic test for SLOS, based on the analysis of plasma or amniotic fluid levels of 7-DHC [Kelley and Hennekam, 2000].

**Physical and craniofacial manifestations of SLOS**

Characteristic physical manifestations of SLOS include microcephaly [Ryan et al., 1998; Curry et al., 1987], growth retardation, multiple internal anomalies and soft-tissue syndactyly of the second and third toes [Cunniff et al., 1997; Opitz, 1994; Irons et al., 1994; Ryan et al., 1998; Nowaczzyk et al., 1998].

Patients with SLOS have low-set and retro-versed ears [Ryan et al., 1998; Kelley and Hennekam, 2000], microtia, hypoplastic nose, which is a hallmark of the syndrome [Curry et al., 1987; Kelley and Hennekam, 2000]. Ocular defects include mainly congenital and occasionally postnatal cataracts, ptosis of the eyelids and strabismus [Curry et al., 1987; Ryan et al., 1998], while less frequently individuals affected by SLOS have external eye anomalies, such as hypertelorism, absence of lacrimal puncta, epicanticth folds and unusually long cilia [Curry et al., 1987; Malgorzata et al., 1999; Kelley and Hennekam, 2000].

Skeletal defects include club foot, dislocated hips and short stature [Ginat et al., 2000]. The multiple internal malformations include cardiac anomalies such as atrial septal defects, atioventricular canal defects [Lin et al., 1997], defects in pulmonary venous return [Curry et al., 1987; Cunniff et al., 1997], urogenital malformations [Curry et al., 1987; Ryan et al., 1998], gastrointestinal and haepatic problems [Ryan et al., 1998; Kelley and Hennekam, 2000], and genital malformations [Ryan et al., 1998; Curry et al., 1987]. Moreover, patients with SLOS present mental deficiency [Nowaczzyk et al., 1998; Malgorzata et al., 1999], learning disabilities, hyperactivity [Kelley and Hennekam, 2000; de Die Smulders and Fryns, 1990] and a characteristic facial appearance [Muzzin and Harper, 2003]. Craniofacial and oral manifestations are diagnostically important and include micrognathia, broad alveolar ridges, dental malocclusion, enamel hypoplasia, oligodontia or polydontia, defects of the hard and/or soft palate (cleft palate) which compromise the feeding of infants with SLOS [de Die Smulders and Fryns, 1990; Malgorzata et al., 1999; Antoniades et al., 1994; Kelley and Hennekam, 2000; Muzzin and Harper, 2003].

Currently, the most widely recommended treatment for SLOS consists in a dietary cholesterol supplementation, which has been shown to effectively reduce plasma levels of 7-DHC significantly increase the plasma cholesterol levels [Kelley and Hennekam, 2000; Sikora et al., 2004].

The present article describes the dentofacial features of a 5-year old child affected by SLOS and discusses oral care provided during a period of three years (February 2004-February 2007).

**Case Report**

A 5-year-old female child was referred at the Department of Paediatric Dentistry of University of Palermo in February 2004 for caries, gingivitis and malocclusion.

She was born after a caesarean delivery at 39.5-week gestation with a weight of 2,700 g. After nine days she was admitted to hospital with signs of regurgitation and serious difficulty in sucking, which resulted in feeding problems for the child. These problems were probably due to the cleft palate and the micrognathia, frequent clinical features in patients with SLOS.

The diagnosis of SLOS was confirmed four weeks after birth by a biochemical test, demonstrating a 7-DHC plasma level of 12.5 µg/dl.

An evaluation of the patient appearance revealed several dysmorphic craniofacial features: microcephaly, narrow high forehead, thin eyebrow, broad upturned nose, wide nasal bridge, ante-version of nostrils, hypertelorism, ptosis of the eyelids, unequal palpebral fissures, strabismus, low-set and retroverted ears (Fig. 1).

She also exhibited some skeletal defects, previously described in the literature, as ulna deviation, long fingers, valgus deformities of the feet, dislocated hips, scoliosis, short stature, and syndactyly of the second

![FIG. 1 - A female child with Smith-Lemli-Opitz syndrome.](image-url)
and third toes of the right foot, which has been reported in up to 99% of biochemical proven cases [Cunniff et al., 1997; Ryan et al., 1998]. Furthermore, the patient revealed other anomalies and clinical problems typical of SLOS, such as brief systolic murmur, genitals anomalies, and mental deficiency with moderate cognitive impairment.

An intraoral examination revealed thin lips, bifid uvula, low mobility of soft palate, cleft palate (Fig. 2), lip incompetence which is largely due to protrusion of the maxillary frontal teeth, severe micrognathia, anterior open-bite, and polyodontia of the primary dentition (Fig. 3). The right maxillary lateral incisor was linguoverted, while the left maxillary lateral incisor was mesially rotated. The mother of the patient reported a premature tooth eruption of the primary dentition. The patient initially exhibited a moderate mental impairment and poor cooperation, but the mother requested no sedation for her daughter during dental treatment. Therefore, the 13 caries lesions found on 13 deciduous teeth were treated without sedation in several appointments during the first year of follow-up. Routine oral prophylaxis and dental examinations were conducted every six months in the following two years.

Gingival inflammation and plaque accumulation were severe during the first year whereas it decreased up to mild during the second year. The increasing compliance of the child, in fact, allowed the dentist to complete oral prophylaxis in few sessions and the mother to perform proper oral hygiene measures. The mother was also instructed to use a pea-size amount of low-fluoride (<500 ppm F) toothpaste until the child was 6 years old.

**Discussion**

Due to the severity of the systemic condition of SLOS patients and the implications on oral health, members of dental team should provide appropriate oral health care.

Because various complications can occur in patients affected by SLOS, a detailed medical and dental history should be obtained to identify those factors that may affect dental treatment. Professional plaque removal and dental restorative treatment should be a primary aim to achieve an effective reduction of the risk of dental caries and periodontal disease, which can be partly attributed, in this case, to an incomplete lip closure, a severe micrognathia, a protrusion of the maxilla and the anterior open-bite.

Since almost half of SLOS patients have a congenital cardiovascular defect [Kelley and Hennekam, 2000], the American Heart Association’s Subacute Bacterial Endocarditis (SBE) Prophylactic Guidelines were followed before dental treatment and the patient’s cardiologist recommended 1.5 g of amoxicillin as prophylactic antibiotic coverage to prevent SBE.

During dental treatments, and especially during ultrasonic scaling, constant suctioning with high-speed evacuation was used to remove oral fluids. Furthermore the patient was kept in a semi-upright position to enhance breathing and prevent airway obstruction. The presence of the cleft palate and the micrognathia, in fact, results in abnormal sucking and swallowing difficulties for individuals affected by SLOS [Kelley and Hennekam, 2000; Malgorzata et al., 1999].

Due to the mental impairment of the patient, instructions on proper oral self-care and dental disease prevention, including dietary counselling, were provided to the mother.

The use of topical fluoride-containing products, especially the toothpaste (fluoride rinses are not indicated in SLOS patients for swallowing difficulties), may offer an optimal opportunity to prevent caries and, therefore, it should be part of the oral care for patients affected by SLOS.
Conclusion

Some systemic conditions, like SLOS, present several oral manifestations that oral health care providers should be able to diagnose and treat, especially in children who need to be in good health for ideal development.

The importance of effective oral hygiene should be particularly emphasized to the patient’s parents, because it is the most effective way to maintain good oral health. Moreover, topical fluorides should be a part of a specific oral care programme for patients affected by SLOS.

Early and proper diagnosis of the behavioural and oral manifestations could make a difference to the prognosis of many conditions and, to a greater extent, to the child’s life. Suggestions regarding proper dental care of these patients, described in this paper, could be important to provide safe and comprehensive dental care for children with SLOS.

References