International Journal of Pediatric Otorhinolaryngology Extra (2007) 2, 169—172

International Journal of Pediatric Otorhinolaryngology @Extra

www.elsevier.com/locate/ijporl

CASE REPORT

Sensorineural hearing-loss in the Smith—Lemli-Opitz syndrome

Federica Di Berardino [a,*], Dario Alpini [b], Umberto Ambrosetti [a], Chiara Amadeo [a], Antonio Cesarani [a]

[a] *Department of Audiology/Otolaryngology-Head & Neck Surgery, University of Milan, Via Pace 9, 20100 Milano, Italy*
[b] *Department of Otolaryngology, S. Maria Nascente Don Gnocchi, Milano, Italy*

Received 29 January 2007; received in revised form 3 May 2007; accepted 3 May 2007

KEYWORDS
Smith—Lemli-Opitz syndrome;
RSH;
SLO;
Newborn hearing screening;
Sensorineural hearing loss

Summary The Smith—Lemli-Opitz (SLO) syndrome is an autosomal recessive disorder caused by a mutation in the 7-dehydrocholesterol reductase gene, which in turn provokes a defect in cholesterol biosynthesis. SLO is characterised by a specific physical, behavioural and developmental pattern, and the main clinical features include minor facial anomalies, multiple congenital anomalies, failure to thrive and mental retardation.

This report describes a case in a newborn child with the typical clinical signs and symptoms of SLO syndrome, who was also affected by profound bilateral sensorineural deafness, and revises the literature suggesting that audiological examination of patients with SLO syndrome may be useful.

1. Introduction

Forty years ago, a new syndrome called Smith—Lemli-Opitz (SLO or RSH syndrome) was first reported. It was described as being characterised by mental retardation, short stature, craniofacial dysplasia, and genital anomalies [1—6]. Approximately 20 years later, a more severe form defined as SLO-type II [7] was reported. This was associated with defective cholesterol biosynthesis [8]. Since then, there has been widespread confirmation of these data [9—11] although only one study has been carried out regarding SLO incidence. The results of this study, carried out in Canada, showed a minimum incidence of 1 in 70,358 live births and a minimum prevalence of approximately 1 in 950,000. Eighteen percent of patients were mildly affected of whom the mean age was 5.3 years [12].

SLO is a congenital multiple anomaly syndrome caused by an abnormality in cholesterol metabolism resulting from a deficiency of the enzyme 7-dehydrocholesterol reductase (DHCR7). It is characterised by abnormally low plasma cholesterol levels and elevated concentrations of the 7-dehydrocholesterol cholesterol precursor which can

* Corresponding author. Tel.: +39 02 70126502; fax: +39 02 70126502.
E-mail address: federica.diberardino@unimi.it (F. Di Berardino).

1871-4048/$ — see front matter © 2007 Published by Elsevier Ireland Ltd.
doi:10.1016/j.pedex.2007.05.002

reach several thousand-fold above normal. The syndrome is characterised by prenatal and postnatal growth retardation, microcephaly, moderate to severe mental retardation, and multiple major and minor malformations. These malformations include distinctive facial features, cleft palate, cardiac defects, underdeveloped external genitalia in males, post-axial polydactyly, and 2—3 syndactyly of the toes. Since DHCR7 deficiency was identified, the possibility of an early diagnosis during the prenatal period has repeatedly been suggested. DHCR7 can be measured in the amniotic fluid, even during the first trimester of pregnancy [13—18], or in tissue obtained from chorionic villus samples at about 10—12 weeks' gestation. Moreover, it has been concluded that molecular prenatal diagnosis of SLO syndrome is reliable and efficient [19].

Molecular genetic tests (mutations in the DHCR7 gene, mapped to 11q13 chromosome) may also be used in place of biochemical testing or to clarify equivocal results [19]. However, no correlation has been observed between mutations and phenotype, thus suggesting that the degree of severity of SLO may also be affected by factors other than plasma cholesterol [20].

Although reports of SLO syndrome have also included neuropathological and ophthalmological observations, and cases of cardiovascular malformations [21,22], to our knowledge, otolaryngologic evaluation signalling congenital sensorineural or conductive hearing-loss has never been reported.

2. Case report

VM was the first born of healthy, unrelated parents. Her family history was unremarkable as regards genetic disease or deafness. The pregnancy was normal, but an ultrasound foetal examination (at 23 weeks) showed ambiguous genitalia and renal dysplasia. The infant was born post-term (40 + 3 weeks) by eutocic delivery. The Apgar score was 9/9. She showed polydactyly, renal dysplasia, atrial septal ostium secundum type defect and pseudohermaphroditism. The results of biochemical laboratory examinations carried out by the Neonatology Department and subsequently confirmed by genetic tests, led to the correct diagnosis of SLO and the decision to administer cholesterol implementation therapy.

The infant was also referred to our Department for audiological evaluation after newborn hearing screening with automated transiently evoked otoacoustic emissions (TEOAEs) and automatic auditory brainstem responses (a-ABR) at 15 days gave negative results.

Syndromologic evaluation: weight at birth was 2950 g, head circumference was 33 cm, 46 XY kariotype and no evidence of chromosomal abnormalities. The infant had distinctive facial features including set eyes, micrognatia, posterior cleft palate and low-set ears, as well as congenital clubfoot, esadactyly of the fingers and toes with a complete skin syndactyly between the second and third toes and a sixth toe on the left foot, female external genitalia and renal dysplasia.

Ophthalmological evaluation, flash visual evoked potential and electroretinogram recordings were normal. Ecocardiography showed an atrial septal ostium secundum type defect with a significative shunt.

Neurological examination showed a hypotonic infant with delayed neural and motor development. Cerebral magnetic resonance imaging revealed microcephaly, reduced anteroposterior diameter of the corpus callosum and slightly dilatated cortical sulci ventricles.

Audiological evaluation: TEOAEs and a-ABR tests repeated in our Department confirmed the previous negative result. With the exception of syndromic features, there were no other perinatal or postnatal risk factors according to the Joint Committee on Infant Hearing (JCIH) guidelines. Bilateral otomicroscopy was normal. Threshold and neurological click-evoked auditory brainstem response tests (ABR) and bone-conducted stimuli ABR, slow vertex response tests at 500 and 1000 Hz, impedence with reflex thresholds and behavioral observation audiometry were performed and confirmed a profound bilateral sensorineural hearing loss at 6 weeks after birth.

In accordance with the JCIH criteria [23], the patient was referred for adequate hearing aid amplification (digital behind-the-ear hearing aids fitted with a multi-step protocol at 4 months), a 3-month auditory rehabilitation protocol with a speech therapist and psychological support.

In an attempt to understand the natural history of this presentation of hearing loss more clearly, the patient was also tested for connexins 26 and 30, but these proved to be negative.

The patient discontinued the follow-up 4 months after the hearing aid had been fitted.

3. Discussion

In this particular case, the implementation of newborn hearing screening permitted early detection of hearing loss and prompt intervention.

Infant patients with a diagnosis of SLO syndrome should be referred for an audiological examination with TEOAEs and threshold and neurological