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Case Report

Management of Smith-Lemli-Opitz Syndrome Type II associated with Cleft Palate

Sabrin Ali Azim[1], Lovely M Annamma[2,3], Shayan Iqbal Khan[4], Tippu MSR[5], Sudhir Varma[6], Biji Thomas George[7]

[1]Associate Professor in Oral and Maxillofacial Surgery, Department of Diagnostic and Surgical Dental Sciences, Gulf Medical University, United Arab Emirates.

[2]Adjunct Clinical Faculty, Department of Clinical Sciences, College of Dentistry, Ajman University, Ajman, United Arab Emirates.

[3]Center of Medical and Bio-Allied Health Sciences Research, Ajman University, Ajman, United Arab Emirates.

[4]Dental Surgeon, United Arab Emirates.

[5]Specialist and lecturer, Oral and Maxillofacial Surgery, Gulf Medical University Ajman, United Arab Emirates.

[6]Assistant Professor, Department of Clinical Sciences, Center of Medical and Bio-Allied Health Sciences Research, College of Dentistry, Ajman University, Ajman, United Arab Emirates.

[7]Professor, Department of Surgery, RAK College of Medical Sciences, RAK Medical and Health Sciences University, Ras al Khaimah United Arab Emirates.

Correspondence

Sabrin Ali Azim,

Associate Professor in Oral and Maxillofacial Surgery, Department of Diagnostic and Surgical Dental Sciences, Gulf Medical University, United Arab Emirates.

E-mail: dr.sabrin@gmu.ac.ae

ORCID id: orcid.org/0000-0002-8933-2196

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Abstract

Rationale: *This case report presents the management of a patient with the rare occurrence of Smith-Lemli-Opitz Syndrome (SLOS) and complete cleft palate*

Patient Concerns: *The patient's cleft palate repair was not done in infancy, and she reported to the dental institution complaining of difficulty with proper food intake and speech. A clinical examination revealed muscle deformity, limited neck mobility, scoliosis, malocclusion, and inadequate oral health. The patient exhibited facial and limb anomalies characteristic of SLOS, in tandem with substantial challenges in speech and nutrition due to the cleft palate.*

Diagnosis: *The patient was referred to the dental wing to manage the cleft palate defect. On dental examination a complete cleft of the hard and soft palate, which had not been surgically corrected during infancy, was confirmed through clinical and radiological investigation. Additional musculoskeletal complications, including scoliosis and muscle deformity, were also identified.*

Interventions: *The treatment plan addressed both SLOS and cleft palate. A prosthodontic appliance was prepared to assist with palatal function and speech therapy. Comprehensive care for SLOS included genetic counselling, nutrition management, and targeted physical therapy. The patient was also referred to an orthodontist, oral surgeon and a speech-language therapist further intervention.*

Conclusion: *This case emphasizes the importance of early diagnosis and intervention in congenital disorders. It advocates for proactive, multidisciplinary care from infancy to enhance the quality of life for individuals with complex syndromes, underscoring the need for ongoing support and resources.*

Introduction

Smith-Lemli-Opitz Syndrome (SLOS) is attributed to mutations in the DHCR7 gene, which is crucial for cholesterol synthesis. The deficiency in the 7-dehydrocholesterol reductase enzyme catalysed by these mutations precipitates a range of clinical manifestations, from mild to severe. The diagnosis of SLOS hinges on the biochemical detection of decreased cholesterol levels alongside elevated 7-dehydrocholesterol (7-DHC) and 8-dehydrocholesterol (8-DHC), further corroborated by molecular genetic testing revealing mutations in the DHCR7 gene. This genetic and biochemical profile is essential for accurately diagnosing and understanding SLOS, setting the stage for targeted therapeutic interventions[1]. The central role of cholesterol in foetal development, particularly in forming cell membranes, hormones, and vitamin D, is the reason for multifaceted congenital defects. Dietary cholesterol supplementation is a form of treatment alongside supportive therapies tailored to the individual's needs. Pursuing further research into specific and effective therapies for SLOS is paramount, aiming to improve the quality of life and outcomes for affected individuals [1].

SLOS is an autosomal recessive syndrome with microcephaly, growth, mental retardation, facial, genital abnormalities and syndactyly, as reported by Smith in 1964 [2]. A more complex case series of SLOS was reported with multiple abnormalities as SLOS type II [3]. In Type 1 SLOS, the cholesterol levels were low, and cholesterol precursor 7 dehydrocholesterol and isomer 8 dehydrocholesterol were extremely high. In Type II, plasma cholesterol levels were low, and total dehydrocholesterol levels were higher than in Type 1. A study observed that

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children with less than 7mg/dl did not survive above 13 weeks. In both type 1 and Type II, the enzyme responsible for converting 7 dehydrocholesterol to cholesterol was dysfunctional [4]. In type II cases, abnormalities such as pseudohermaphrotism, Hexadactyly, congenital heart diseases, cleft palate, cataracts, unilobulated lungs, pancreatic islet cell hyperplasia and large adrenals were observed [3]. Other forms of mutational variants are also reported, and SLOS is common amongst the European population[5,6].

Amongst the types, the type II is associated with dentofacial anomalies. The frequently observed dental anomalies were a spectrum of dental and facial irregularities. These include, but are not limited to, crowded teeth, widely spaced incisors, oligodontia, polydontia, premature tooth eruption, enamel hypoplasia, and a bifid uvula. Furthermore, broad alveolar ridges, a bifid tongue, and features of the Pierre-Robin sequence, such as glossoptosis, retrognathia, and cleft palate, are frequently observed. Identifying these anomalies, especially in the presence of other clinical signs of SLOS, necessitates a careful and considered approach to diagnosis. Early recognition and diagnosis of these dentofacial features can significantly influence the management and treatment outcomes, emphasizing the importance of a multidisciplinary approach in treating patients with SLOS [7,8] For SLOS existing conditions in the family, a prenatal evaluation is recommended [9] or maternal urinary profiles for steroids can be done [10]. A biochemical analysis of 7-DHC and 8-DHC is also recommended. This case report elaborates on managing delayed closure of cleft palate defect associated with SLOS. The management also included a follow-up on the quality of life after and before the surgical procedure, which was conducted via a survey to evaluate the outcome of delayed cleft palate closure.

Case Presentation

The patient presented to our multidisciplinary tertiary care centre with a cleft palate defect that was not closed at an early age. She was twenty-eight, and her chief complaint was that she could not eat and speak properly. Patient consent was obtained for evaluation and further treatment. On history taking, it was observed that she was diagnosed with Smith Lemli Opitz syndrome. Laboratory tests and further radiographs were taken to confirm the diagnosis. Upon clinical examination, musculoskeletal anomalies were observed, and the patient had difficulty in neck movements, which included reduced forward and backward cervical movements. (Figure 1a, b) and reduced side-to-side neck movements (Figure 2).

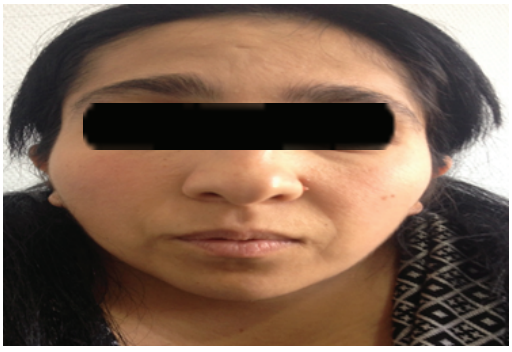

***Figure 1a**. Reduced forward neck movement*

***Figure 1b**. Reduced backwards neck movement*

***Figure 2**. Reduced side-to-side neck movement*

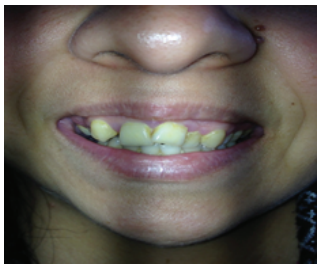

***Figure 2**. Reduced side-to-side neck movement*

The personal history indicates that an adult with a cleft palate can have psychosocial issues along with health problems due to proper lack of nutrition. The family history offered no insights into the aetiology of SLOS or the reason for the non-interventional approach taken during the patient's infancy. SLOS diagnosis, along with scoliosis and cleft palate, were mentioned in the patient's previous medical records. A blood test indicated decreased cholesterol levels with an increase of 7 and 8- Dehydrocholesterol confirmed SLOS. On intraoral examination, class I malocclusion with anterior crowding was observed. (Figure 3)

A Veau Class II classification of cleft palate was observed on palatal examination. (Figure 4) The patient was unable to speak or eat properly; hence, an obturator was recommended for a better quality of life, along with a surgical consultation for the probable possibility of cleft closure. A consultation with a dietitian, as the patient was anaemic, along with physical therapy for limited neck movements, was recommended.

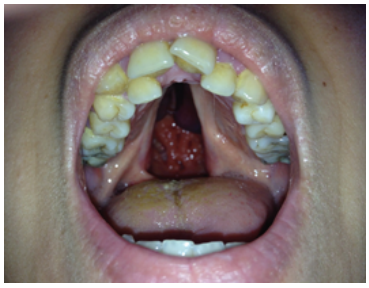

***Figure 4**. Palatal examination*

Prosthodontic intervention

SAs the defect involved the soft palate and hard palate, a pharyngeal obturator prosthesis was considered for treatment planning to improve the patient's function and speech. The primary impression was made using a pink modelling plastic impression compound (Kerr Corporation, California, USA). The impression was finalised by adding the yellow modelling plastic (Kerr Corp, Orange, California, USA) in increments while asking the patient to move the head in a circular motion and saying "ah" repeatedly. The wash impression was made with zinc-oxide eugenol impression paste (SS White impression paste, England). After beading and boxing, a model was created on which a heat-cured acrylic plate was fabricated. (Heraeus Kulzer GmbH, Hanau Germany). A wax-up was done for the pharyngeal bulb, and a hollow obturator was made with a cold-cured acrylic covering. Heraeus Kulzer GmbH, Hanau Germany. The appliance was adjusted to fit the crowded anterior tooth as a temporary prosthesis. (Figure 5) The patient was referred for orthodontic consultation. After the prosthodontic rehabilitation, a six-month recall interview was conducted to assess the outcome of the speech and function. Further lab tests revealed that the patient regained proper nutrition as the patient was no longer anaemic, and the speech was coherent. The patient was more confident in her social interactions and had a better quality of life.

Discussion

This case presents the need for interventional treatments for Smith-Lemli-Opitz Syndrome (SLOS). If the intervention of cleft palate closure was done in infancy, the patient could have had proper nourishment and a good quality of life from an early age. This case was reported to advocate early intervention and to prevent deterioration of the existing case. The presented case is a mild form of SLOS, with the patient able to manage her life.

***Figure 5**. Temporary prosthesis*

Current literature illustrates a spectrum of clinical presentations and interventions, ranging from dietary cholesterol supplementation to more invasive surgical corrections. In concordance with recent clinical guidelines, early surgical intervention remains the cornerstone for managing cleft palate to circumvent the myriad complications that ensue from postponed treatment[11]. According to the literature, 40-50% have cleft palate associated with SLOS [7,12]. The commonest genetic syndromes associated with cleft palate are in order of frequency Pierre Robins, Smith Lemli Opitz, Dandy-Walker, DiGeorge, Ectrodactyly ectodermal dysplasia, Treacher Collins, Turners and Weissenbacher-Zweymuller syndromes [13]. The authors also highlighted differences between the surgical procedures of syndromic cleft palate patients and non-syndromic cleft palates. The chief difference between the two was those syndromic cases related to clefts had a delay in primary cleft repair surgeries, due to airway and feeding issues. In case other urgent surgical procedures such as cardiorespiratory or urogenital abnormalities were present, they were given priority over cleft palate procedure [13]. In syndromic patients, secondary surgeries for speech and tympanostomy were common[14]. Hence, each SLOS patient should be diagnosed prenatally and treated appropriately.

Conclusion

Early intervention is crucial, particularly within Smith-Lemli-Opitz Syndrome, as it can impact speech, nutrition, and psychosocial development. This case reinforces the criticality of timely intervention. Besides early intervention, comprehensive care for SLOS is required with supplements, surgical interventions, and dietary regulation. The management of SLOS extends beyond the repair of structural anomalies, necessitating genetic counselling, nutritional support, and physical therapy, emphasizing a multidisciplinary approach for these patients.

Each patient with SLOS presents with unique challenges. Personalised treatment plans, which consider physical and psychological aspects, are essential for improving outcomes and quality of life.

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