Case Report

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Larsen Syndrome: A Rare Case Report

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Abstract

Larsen syndrome is a rare form of osteochondrodysplasia presenting with features like frequent joint dislocation and craniofacial anomalies. Here, we report a case of five-year-old female diagnosed previously as Larsen syndrome by genetic analysis, who presented with multiple missing and malformed teeth and flexible large joints.

Keywords: Craniofacial anomalies; Dental anomalies; Hypodontia; Joint dislocation; Larsen syndrome.

Declarations

Ethics approval and consent to participate: Not applicable.

Consent for publication: Informed consent was obtained from the patient's parents for the publication of photographs of the patient.

Availability of data and materials: Data will be made available upon request.

Competing interest: None.

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BACKGROUND

Larsen syndrome is a rare form of osteochondrodysplaia with genetic or sporadic origin [1, 2]. Danish pediatrician Dr. Oluf Daniel Larsen in 1950, first described the case of multiple orthopedic anomalies along with the craniofacial abnormalities as a common entity and termed it as Larsen syndrome [3]. It has heterogenous genetic origin, and can present with either autosomal dominant or autosomal recessive inheritance. The autosomal dominant type has shown to have a favorable prognosis [4].

The orthopedic anomalies reported are multiple congenital dislocations of the hip, knee and elbow joints, equinovarus or equinovalgus foot deformities, cylindrical shaped fingers, spinal anomalies, malformed ear ossicles, supernumerary carpal and tarsal bones, short and broad distal phalanges, particularly of thumb [1]. Larsen and Latta along with their associates stated that hypertelorism and depressed nasal bridge also are the traits of Larsen syndrome [5]. Craniofacial abnormalities include dish shaped facies with a saddle nose, prominent frontal bossing, depressed nasal bridge, hypertelorism and midface hypoplasia [2]. Dental anomalies commonly linked are hypodontia, microdontia, cleft palate and bifid uvula [2]. Along with the symptoms of orthopedic and craniofacial origin, patients with Larsen syndrome frequently present with respiratory and cardiovascular abnormalities [6, 7].

Here, we report a rare case of Larsen syndrome in a five-year-old female patient who presented with multiple skeletal, craniofacial and dental anomalies.

CASE

A five-year-old female who was diagnosed as Larsen syndrome visited the pediatric dental outpatient department of People's Dental College and Hospital, Nayabazar, Kathmandu, Nepal with the chief complaint of decayed teeth. She was a single child born from healthy parents of a non-consanguineous marriage. There was no history of any similar or other genetic disorder in the family. Diagnosis of Larsen syndrome was made by genetic analysis done previously suggested by the family pediatrician based on the clinical findings like flexible joints and multiple missing teeth. Biochemical type of genetic analysis was done where missense mutation of Filamin-B (FLNB) gene of 3-58084597-C-A variant where threonine to asparagine amino acid change was noted. This variant was not reported in dbSNP or gnomAD databases, indicating it to be a novel variant.

On general examination, the height, weight and built of the patient were within the normal range. There was a presence of hyperflexible shoulder joints with bony protuberance on extension, **(Figure 1)** cylindrical shaped fingers with spatulate thumb and webbed digits **(Figure 2).** On extraoral examination, the patient had moon facies, prominent frontal bossing, depressed nasal bridge, widely set eyes (hypertelorism) and partial median cleft on the lower lip **(Figure 3).** On Temporomandibular joint (TMJ) examination there was a presence of bilateral synchronous movement, no any deviation, deflection and abnormal joint sounds were noted and patient had adequate mouth opening. Since, there were no any abnormal clinical presentation on TMJ examination, TMJ radiographs were not made. In the present case hearing loss and respiratory problems were not detected.

Figure1: Flexible shoulder joint with bony protuberance on extension

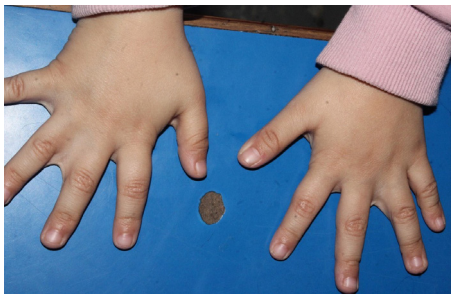

Figure 2: Spatulate thumb and webbed digits

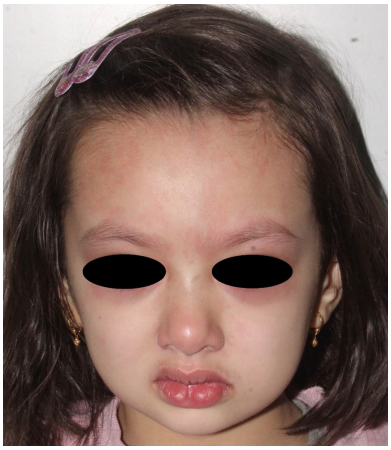

Figure 3: Moon-facies, prominent frontal bossing, depressed nasal bridge, hypertelorism and partial median cleft of lower lip

On intraoral examination, multiple primary teeth were missing. In the maxillary arch, all primary teeth were missing except for the second molar. The missing teeth were the first molars, canines and incisors. In mandibular arch, the missing teeth were first molars, canines and incisors except left lateral incisor. There was no previous history of tooth extraction. The teeth present showed abnormal morphology. The anterior teeth were conical in shape and the crowns of molars were mulberry shaped. Multiple carious lesions were present on the occlusal aspect of dysmorphic primary teeth **(Figure 4).** Orthopantomograph (OPG) was done **(Figure 5)** which revealed the presence of follicles of 16 14 13 25 26 27 37 36 35 45 46 and 47; decreased alveolar bone height and abnormal root morphology of 55. Also, a faint radiopaque tooth-like structure in the right maxillary sinus region was noted. To locate the radiopaque structure Cone-beam computed tomographic (CBCT) was done. It was in the favor of OPG findings except for the presence of radiopaque structure in the maxillary sinus area. After obtaining the informed consent from the parents, restoration of 55 and 65 were done with Glass Ionomer Cement. Various treatment options like fabrication of Removable Partial Denture (RPD), Groper's appliance, pediatric dental implants were discussed for the rehabilitation of missing areas. The patient had difficulty due to frequent food lodgment in the carious portion of the tooth and after restoration she felt better. The patient was kept in regular follow-up for the same. An interim prosthesis was suggested, for which the patient party refused at that time.

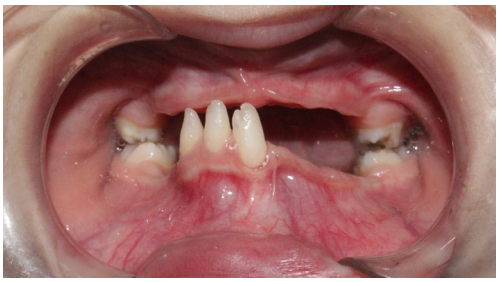

Figure 4: Multiple missing teeth and anomalous primary teeth

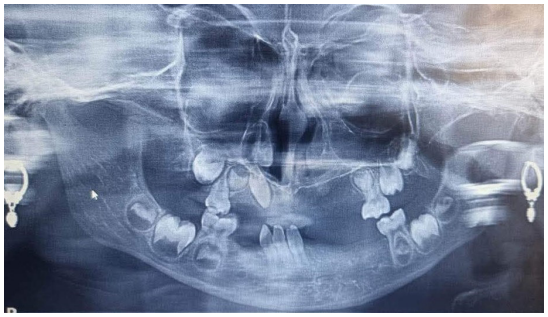

Figure 5: Orthopantomographic images showing multiple missing teeth, decreased alveolar bone height, and abnormal tooth morphology

DISCUSSION

Larsen syndrome is a rare condition with a generalized defect of collagen protein [5]. The reported incidence is 1 in 100,000 to 200,000 live births. There is no gender-predilection [3]. To the best of authors' knowledge, there has been no report of Larsen syndrome among Nepalese population till date. The underlying cause of this syndrome is attributed to the clusters of missense or small in frame mutation in FLNB, carbohydrate sulphonyl transferase-3 (CHST3), B4GALT7, GZF1 genes [5]. FLNB gene is responsible for the classic form of Larsen syndrome which has an autosomal dominant inheritance pattern [5, 7].

Filamin-B gene is responsible for the formation of FLNB protein, which is required for the formation of inner framework of cell (cytoskeleton) that gives structure to cells and allows them to change shape and move. The exome sequencing in the present case reported that 3-58084597-C-A variant of missense mutation which occurred due to the exchange of threonine to asparagine amino acid in the FLNB protein.

A detailed history, comprehensive clinical evaluation, and the identification of distinctive clinical and radiological findings are the foundations for the diagnosis of Larsen syndrome. Molecular genetic testing confirms the presence of mutations in the above-mentioned genes. Although the dental findings are not so common as compared to the skeletal and craniofacial findings, few cases are reported. Mitra N et al have reported abnormal facial dysmorphism as well as hypodontia in the patient with Larsen syndrome [8]. Tsang et al. have reported delayed tooth eruption, hypodontia, generalized gingival hyperplasia, cleft lip and palate and malocclusion in the patient with Larsen syndrome [5]. Similarly, Chien et al. have reported macroglossia, advanced periodontitis, generalized gingival hyperplasia [9]. Sajnani et al. described the patient of same syndrome with advanced periodontitis, hypodontia and malocclusion [10]. Most of the cases reported hypodontia however, Percin et al. have reported supernumerary teeth along with cleft lip and palate, microdontia and macroglossia [11]. In the present case, the typical clinical features of Larsen syndrome like hyper-flexibility of shoulder joints, frontal bossing, hypertelorism, flat nasal bridge were present along with multiple missing teeth and anomalous teeth.

The management of Larsen syndrome is based on the presentation of symptoms. An interdisciplinary approach is required to address the symptoms. The multidisciplinary team often consists of pediatrician, geneticist, orthopedic surgeon, craniofacial specialist, pediatric dentist and audiologist. Joint manipulation, corrective cast or traction

and physical therapy are recommended for the correction of skeletal dislocations or deformities. Reconstructive surgery might be required for the correction of nasal growth deficiency and palatal defects [12]. Prosthetic rehabilitation should be considered in case of missing tooth/teeth which results in improved mastication, speech and esthetics [13]. In the present case, though functional impairment secondary to the orthopedic abnormalities was not seen but functional and esthetic impairment was present due to multiple missing teeth for which prosthetic rehabilitation was advised. Various treatment option includes the rehabilitation with RPD, semi-fixed appliance like Groper's appliance or Hollywood bridge and pediatric implants were discussed to the parents.

CONCLUSIONS

Larsen syndrome itself is a very rare condition. Very few literature has been reported the abnormal dental findings. The most common dental manifestations till date reported are hypodontia and periodontal diseases. In the present case there is oligodontia and abnormal tooth morphology. Thus, if patient presents with multiple missing teeth, Larsen syndrome should be considered as a differential diagnosis. A detailed history, comprehensive clinical and radiological evaluation, and genetic testing are recommended to rule out disorder.

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