Two Filipino Children with Oromandibular Limb Hypogenesis Spectrum

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ABSTRACT

Oromandibular Limb Hypogenesis Spectrum (OMLHS) [OMIM 103300] is a rare disease characterized by congenital defects of the face, mandible, tongue and hypoplastic limbs. The exact etiology remains unknown. We present two Filipino children diagnosed with OLMHS. Patient 1 is a 2-year-old female noted to have micrognathia, sygnathia and hypoplasia of distal extremities. Patient 2 is a 6-year-old male with hypoplastic mandible, micrognathia, micromelia of both lower extremities and syndactyly of hands. The early recognition of this disease is important so that early surgical correction of deformities particularly the hypoplastic mandible be addressed to avoid complications such as respiratory distress and feeding difficulties.

Key Words: OMLHS, oromandibular limb hypogenesis syndrome, ankyloglossia, Hanhart syndrome

Introduction

Oromandibular Limb Hypogenesis Spectrum (OMLHS) [OMIM 103300] was first described as aglossia-adactylia in 1932 by Rosenthal[1] in a 3-year-old child with micrognathia, a cleft of the lower lip, absence of lower incisors, and a tongue with a small median rudiment, anomalies of both hands and of the right foot. It is also known as hypoglossia-hypodactylia, glossopalatine ankylosis syndrome and facial-limb disruptive spectrum.[2]

In 1971, Hall[3] made a classification using "hypoglossia" as the only necessary inclusion criteria which could explain this condition's overlapping features with Charlie M syndrome, Mobeius syndrome and Hanhart syndrome.[4] Previous authors have suggested that overlapping clinical features support a continuum of malformation, rather than discrete syndrome.[5] OMLHS is characterized by congenital defects of the face, jaw and tongue with asymmetric hypoplastic abnormalities of distal extremities.[6]

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The reported incidence of this syndrome is 1 in 175,000.[7] In 1990, Weckx[8] noted that there have been 47 cases of hypoglossia-hypodactyly reported. The etiology remains unknown, but both environmental and genetic factors have been postulated.[9] However, there has been disagreement regarding the genetics of this disease because majority of the reported cases are sporadic and genetic factors do not appear to be operative in this disorder.[6]

We report two cases of Filipino children with oromandibular limb hypogenesis spectrum diagnosed and managed at our institution. Informed consent was obtained from the parents to publish the medical information and photographs.

Case Reports

Patient 1

Patient 1 is a girl from Olongapo City first seen at the Philippine General Hospital when she was 2 years old. She was born to a then 34-year-old mother who took Cefalexin and Mefenamic acid for 1 week during the 6th month age of gestation for a toothache. There is no reported teratogen exposure or intake. Patient 1 is the youngest in a sibship of 9 born to a non-consanguineous couple of Filipino descent. At birth, she had good activity but her mouth was small and did not have an opening. She also had associated limb defects. Nasogastric tube was inserted for feeding. Surgical management was suggested but not done due to financial constraints. At 2 years of age, there was note of marked motor and speech delay but she was able to follow simple commands.

Physical Examination during the first consult showed a child who was proportionately small for age, with a weight of 10 kg (p5-10), height of 80cm (<p5) and head circumference of 47cm (p2-p50). She had epicanthal folds, syngnathia, micrognathia, thin lips. She also had multiple limb reduction defects which include: absent right hand with adactylia, absent left hand, absent right foot, absent left foot with adactylia (Figures 1 and 2).

A facial CT Scan showed fusion of mentum of mandible to alveolar process, shortening of the head and condylar process of mandible, and flattening of the temporomandibular joint. Results of the chromosomal

analysis, echocardiography, whole abdominal ultrasound were normal. Radiographs for this patient are not available on file.

The immediate surgical treatment objectives were: (1) Establishment of a secure airway, (2) Osteotomy of the maxilla-mandibular fusion, and (3) Release of the temporomandibular joint ankylosis. A tracheostomy was done under local-IV sedation (Figure 3), after which the patient was put under general anesthesia (Figure 4). Exposure of the maxilla-mandibular fusion was done after infiltration of the overlying mucosa with 1:100,000 epinephrine with 1% lidocaine (Figure 5). An osteotomy of the bony fusion from the right 1st molar up to the left 1st molar was done (Figure 6). Upon release, the oral cavity was inspected with note fusion of the tongue anterior to the palatal mucosa (Figure 7). The tongue was released from the

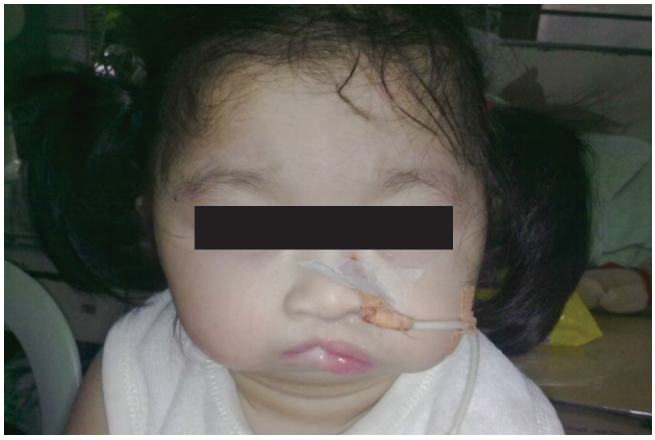


Figure 1. Patient 1.

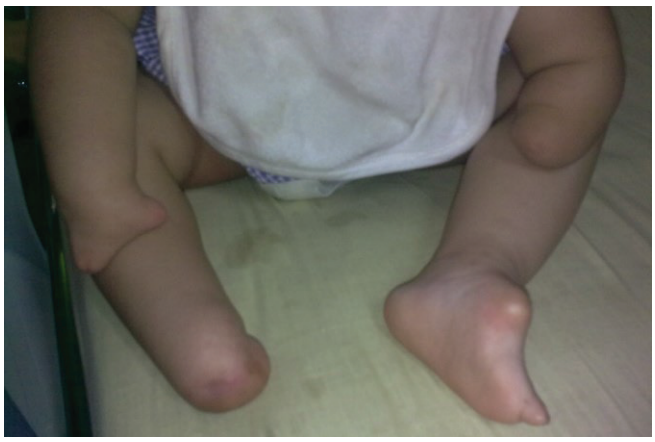


Figure 2. Limbs of Patient 1.

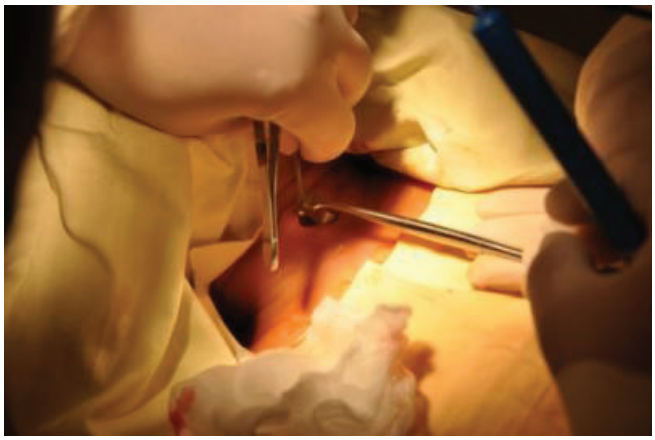


Figure 3. Placement of the Tracheostomy.

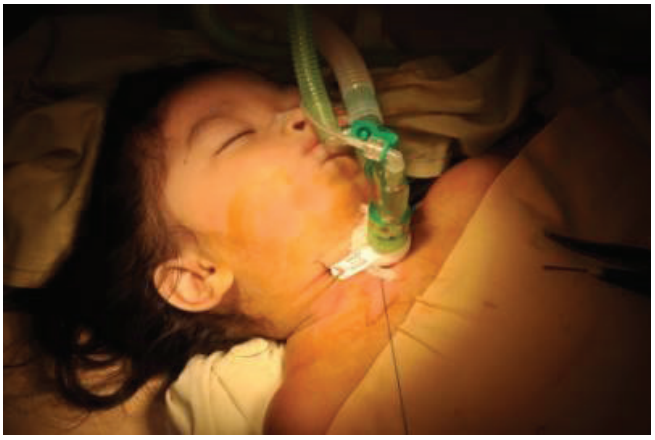


Figure 4. Induction with general anesthesia.

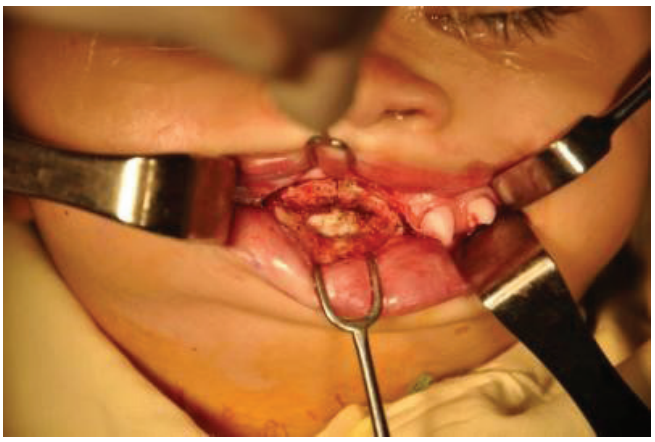


Figure 5. Exposure of the maxillo-mandibular fusion.

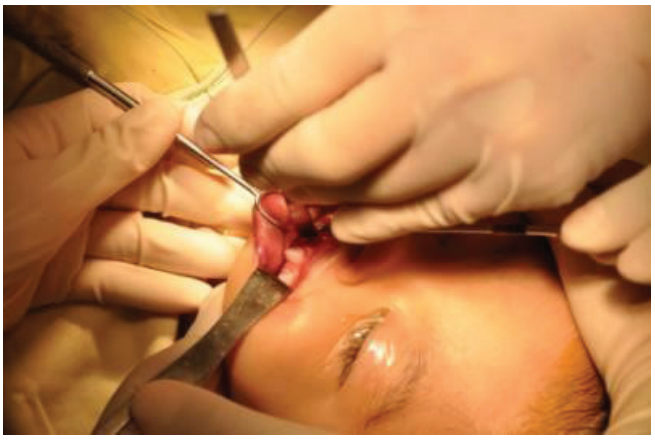


Figure 6. Osteotomy of the maxillo-mandibular fusion.

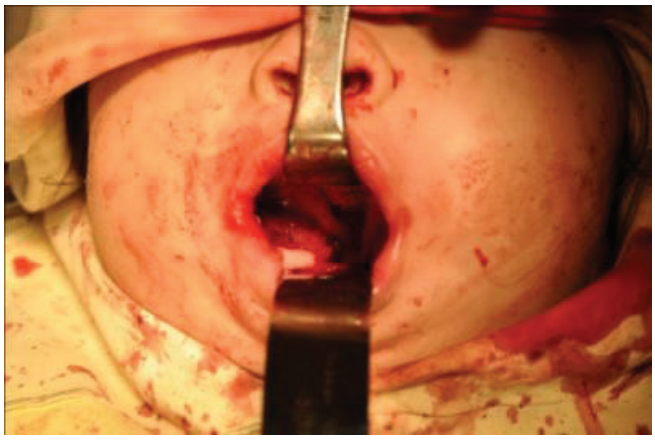


Figure 7. Fusion of tongue to anterior palatal fistula.

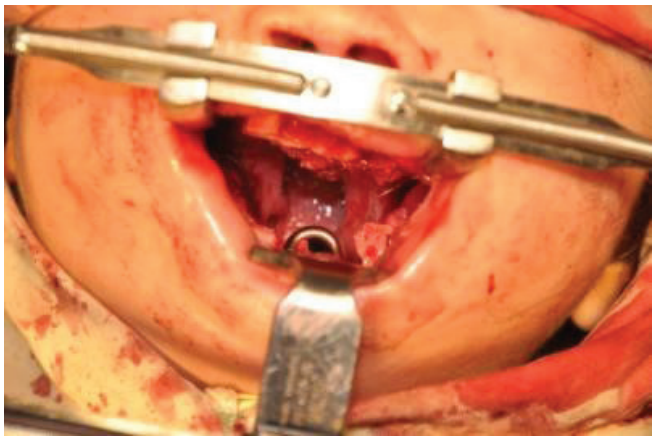


Figure 8. Note of incomplete cleft palate upon release of tongue form anterior palate.

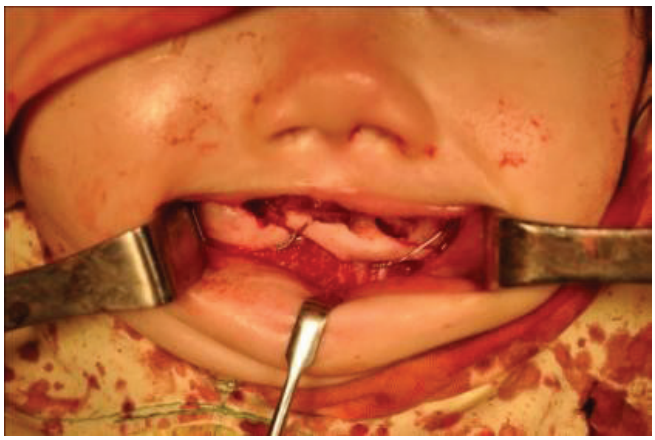


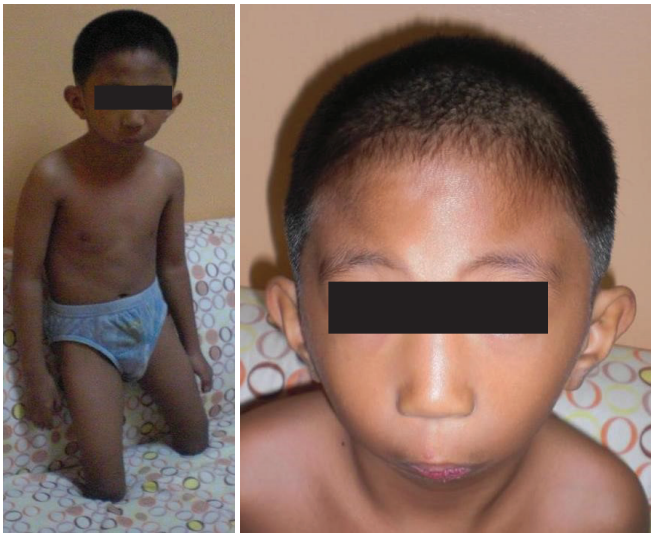
Figure 9. Wire fixation of mandibular fracture.

mucosal attachments which revealed the presence of an incomplete cleft palate (Figure 8). Coronoidectomy was done on both mandibles and released from the temporalis attachments which released the TMJs. While the osteotomy was being done, there was an inadvertent fracture of the mandibular segments and wire fixation of the mandibular fractures was applied (Figure 9). Mucosal closure was achieved and a nasogastric tube was inserted for feeding. The immediate post-operative course was unremarkable. Ventilatory support was discontinued on the 2nd post-operative day and general liquids were started orally on the 4th post-operative day. The patient was discharged on the 6th post-operative day. The tracheostomy tube was removed on follow-up. There was adequate mouth opening and healing of wounds observed during subsequent follow-ups.

Patient 2

Patient 2, a boy from Cagayan, was 6 years old when first seen at our institution He was born term to a then 42-year-old mother, the youngest in a sibship of 6 born to a healthy non-consanguineous couple of Filipino descent. Mother denied any teratogen exposure or intake. At birth, he was noted to have hypoplastic mandible, micrognathia, micromelia of both lower extremities, and syndactyly of hands.

He is proportionately small for age with a weight of 13.75kg (<p5), height of 78cm (<p5) and a head circumference of 49cm (<p5). There is note of down slanted palpebral fissures, hypoplastic supraorbital ridge, hypoplastic mandible, micrognathia, cleft palate, ankyloglossia, hypoglossia, brachydactyly, syndactyly of the bilateral hands, micromelia of the bilateral lower extremities with absence of the tibia and fibula (Figures 10 and 11).



Figures 10 and 11. Patient 2.

A skeletal survey (Figures 12 and 13) showed brachycephalic skull, underdeveloped mandible, bilateral absence of carpal bones, save for a single ossification center on the right; bilateral absence of proximal phalanges except for the right third; absence of the left third metacarpal, proximal and middle phalanges; hypoplasia of the right third metacarpal and left fourth middle metacarpal; fusion of both 4th and 5th metacarpal bones, 4th and 5th middle

phalanges, 2nd and 3rd distal phalanges of the left hand. There is absence of tibia, fibula, tarsal and metatarsal bones and phalanges bilaterally with note of a soft tissue stump below both femoral epiphyses (Figures 14 and 15).

A chromosomal analysis showed normal results. Patient 2 is a kindergarten student and has been assessed to have global developmental delay. Due to financial constraints, further work-up of the developmental delay such as whole exome sequencing or array CGH was not done. No surgical intervention has been advised and patient is continuously undergoing rehabilitation.

Discussion

Oromandibular limb hypogenesis spectrum is characterised by recessed or hypoplastic mandible, reduction in tongue size, absence of mandibular incisors, hypertrophy of sublingual and submandibular glands, and anomalies of digits and limbs.[10] Due to the variability in the appearance of the mandibular hypoplasia and the limb defects, this disease is thought to be part of a spectrum that

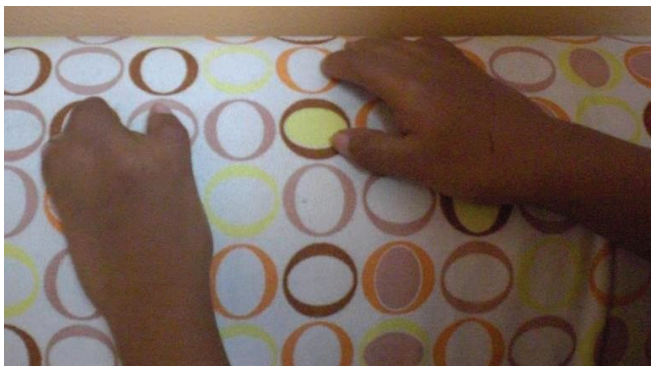


Figure 12. Patient 2's hands which showed brachydactyly and syndactyly.

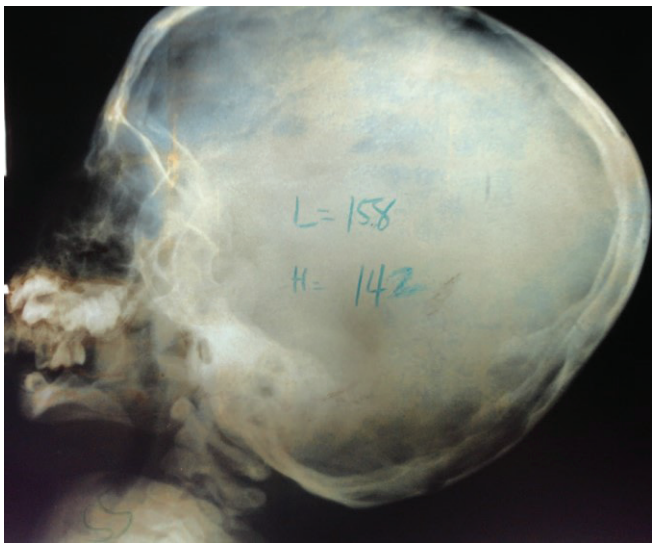


Figure 13. Skull x-ray of Patent 2 showing hypoplastic mandible.

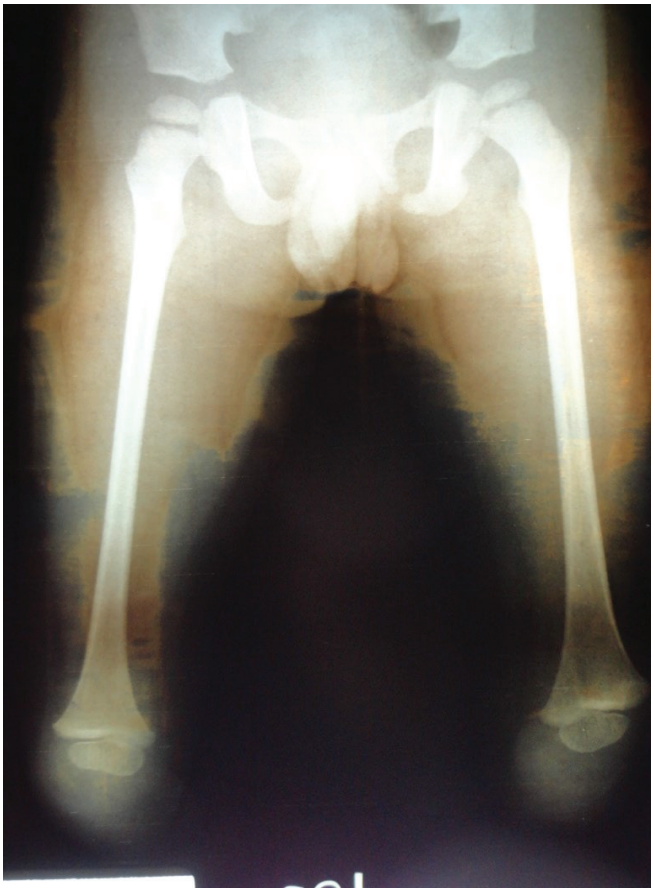


Figure 14. Lower extremity x-ray of Patient 2 showing absence of tibia and fibula.

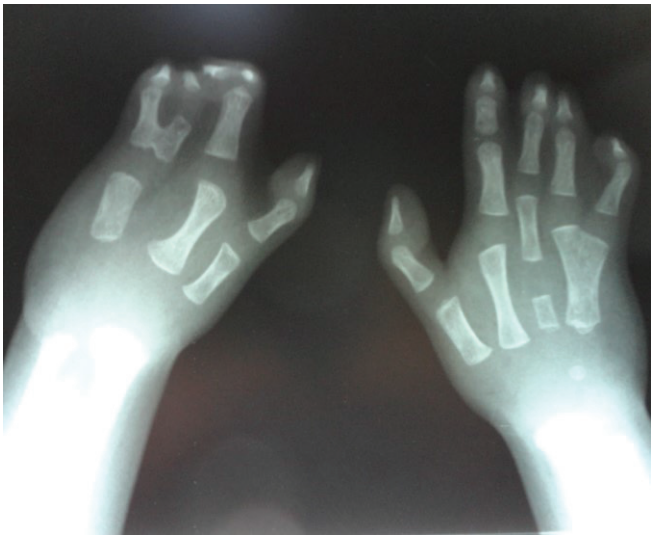


Figure 15. Hand x-rays of Patient 2 which showed bilateral absence of proximal phalanges except for the right third; absence of the left third metacarpal, proximal and middle phalanges; hypoplasia of the right 3rd metacarpal and left 4th middle metacarpal; fusion of both 4th and 5th metacarpal bones, 4th and 5th middle phalanges, 2nd and 3rd distal phalanges of the left hand.

includes aglossia-adactylia, hypoglossia-hypodactylia, glossopalatine ankylosis syndrome, and facial-limb disruptive spectrum. The three features essential for the diagnosis of this syndrome are: (1) variable reduction in the tongue size or microglossia, (2) micrognathia of the mandible (or maxilla) and (3) limb anomalies of varying severity.[11]

There has been much speculation as to the etiology of the disease. Both environmental and genetic factors have been postulated.[9] Tuncbilek[12] has suggested an autosomal recessive inheritance pattern after presenting three cases of aglossia-adactylia born to consanguineous families. This is similar to a case reported by Al Kaissi[13] of a 5- year-old male diagnosed with oromandibular limb hypogenesis with associated craniocervical defect who was born to a consanguineous couple. Temtamy and McKusick[14] has suggested an autosomal dominant mode of inheritance with reduced penetrance and variable expression. Most cases have occurred sporadically.[15] Despite the disagreement with the inheritance patterns, there remains a probability that other factors could contribute to the etiology of the spectrum. Environmental factors, drug intake during pregnancy, amniotic bands, thromboembolic events, maternal infection, and maternal diabetes have been implicated.[11,14]

Shear[16] and Gorlin[17] postulated that ruptured amniotic bands during the first trimester of pregnancy could be the cause of the deformities seen in the spectrum. Johnson and Robinow[18] theorized that due to the close chronologic relationship between the development of tongue and limbs at the 4th-5th week of gestation, impairments or insults of the fetus during this period of development may be responsible for the abnormalities. Scott[19] and Gruber[7] states that the distal deformities could be due to ischemic or embolic events in the fetus following thrombosis in placental vessels while David[20] believes that the vascular accident could be related to maternal diabetes mellitus.

The use of maternal drugs during pregnancy have also been implicated particularly trimethobenzamide hydrochloride, meclizine hydrochloride and marijuana.[4] Maternal infection has likewise been cited as a possible etiology. Hyperthermia, beginning at 1.5°C above the normal core body temperature, has been proven to cause limb reduction defects due to heat induced vascular disruption.[21] Superneau and Wertelecki[22] have reported two children with oromandibular limb hypogenesis spectrum where mothers have febrile illnesses at either 8 weeks or 10-11 weeks age of gestation.

Patient 1's mother had a history of toothache treated with an antibiotic and a pain reliever. Both these medications have not been associated with any congenital anomalies. Furthermore, intake of these medications was relatively late in the pregnancy (24th week of gestation), after the critical period for the development of the face and limbs. Patient 2's mother had an advanced maternal age but literature has not given a clear correlation between maternal age and the incidence of OMLHS. On the basis of absence of similar condition in the family, the etiology is not clear in these two patients. This is in line with Kitamura's[6] observation that all reported cases are sporadic. Genetic counselling was done and the focus is now on the patient's rehabilitation in order to maintain their functionality and achieve independence in caring for oneself.

The early diagnosis of this disease is of utmost importance so that early surgical intervention can be done to address severe anomalies that are life threatening particularly those that impair swallowing and breathing.[10] Further, we must recognize that this condition is indeed a spectrum, the degree of affectation of limb development and mandibular hypoplasia varies from patient to patient as it was illustrated in this case report.

Statement of Authorship

All authors have approved the final version submitted.

Author Disclosure

All the authors declared no conflict of interest.

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