Saudi Dental Journal (2018) **30**, 260–264

King Saud University

Saudi Dental Journal

www.ksu.edu.sa
www.sciencedirect.com

CASE REPORT

Dentofacial characteristics in a child with Meier–Gorlin syndrome: A rare case report

Rahul G. Morankar *, **Ashima Goyal, Krishan Gauba, Aditi Kapur**

Unit of Pedodontics and Preventive Dentistry, Oral Health Sciences Centre, PGIMER, Chandigarh, India

Received 18 June 2017; revised 26 April 2018; accepted 29 April 2018
Available online 16 May 2018

KEYWORDS

Meier-Gorlin syndrome;
Dentofacial characteristics;
Management

Abstract Meier–Gorlin syndrome (MGS) is a rare autosomal recessive disorder characterized by the triad of microtia, absent or small patellae and short stature. The other associated clinical features may include developmental delay, congenital pulmonary emphysema, gastro-esophageal reflux, urogenital anomalies, such as cryptorchidism and feeding problems. The facial characteristics during childhood are typical, comprising of a small mouth with full lips and micrognathia/retrognathia. The condition is rare affecting about one to nine individuals per million. Mutation in the genes of pre-replication complex involved in DNA-replication is detected in the majority of patients. This impedes the cellular proliferation resulting in a reduction of total cell number and thereby retardation of overall growth. This case report describe the typical dentofacial characteristics in a 5 years old child affected with Meier-Gorlin syndrome along with other associated anomalies and a multidisciplinary approach for their management.

1. Introduction

Meier–Gorlin syndrome (MGS) is a rare autosomal recessive disorder. It is characterized by the triad of short stature, absent or small patellae and microtia. In most of the patients with MGS at-least two of these three clinical features are present. The combination of patellar hypoplasia and microtia are most prevalent (De Munnik et al., 2012a). The patients can exhibit short stature, without microtia or patellar anomalies, indicating that the clinical phenotype can be variable (Bicknell et al., 2011).

The first case of MGS was reported by Meier in 1959 and Gorlin in 1975 and only 67 patients with MGS have been reported in the literature till date. There is no reported data on the prevalence of MGS, but it is estimated to be less than one to nine individuals per million. It is based on number of cases reported in the literature. Though, this might be an underestimated figure due to missed diagnosis and underreporting (De Munnik et al., 2015).

The underlying mechanism responsible for clinical features of MGS remains unknown. Mutations in five genes of the pre-replication complex have been detected in patients with MGS (De Munnik et al., 2012a). The impaired function of pre-replication complex is presumed to reduce the G1 phase of

* Corresponding author at: Room No. 202, Unit of Pedodontics and Preventive Dentistry, Oral Health Sciences Centre, PGIMER, Chandigarh 160012, India.
E-mail address: captainrahul88@gmail.com (R.G. Morankar).
Peer review under responsibility of King Saud University.

Production and hosting by Elsevier

https://doi.org/10.1016/j.sdentj.2018.04.004

DNA replication. This limit the available time for origin licensing and retard the cellular proliferation resulting in a reduction of total cell number. This results in diminished overall growth (Klingseisen and Jackson, 2011; Kuo et al., 2012).

The diagnosis of MGS should be considered in a patient with short stature and microtia. The presence of these features necessitates a comprehensive examination of patellae. Ultrasound investigations are advised in children in the first five to six years of life since patellae are radiolucent and would not be visible in conventional radiography (De Munnik et al., 2015). Furthermore; the dentofacial characteristics are the specific findings for MGS and can assist in diagnosing the condition.

This paper describes a case of Meier-Gorlin syndrome with its dentofacial characteristics and suggests a multidisciplinary approach for its management.

2. Case report

A 5 year old child reported to the Department of Oral Health Sciences Center, PGIMER, Chandigarh with multiple carious teeth. Intraoral examination was suggestive of severe early childhood caries involving all primary teeth. The child had a small oral cavity with limited mouth opening. The family history was non-contributory with non-consanguineous marriage. No other family member was affected. The child had an overall short stature and the anthropometric variables like height, weight and occipitofrontal head circumference were deficient for age according to the WHO Child Growth Standards 2006 (Table 1). The prenatal history revealed intra-uterine growth retardation (IUGR) and microcephaly. The child was evaluated for endocrinal abnormalities and the results were within normal limit. Medical history was significant with a child suffering from recurrent seizures and was under oral phenobarbitone therapy for the same. The karyotyping results revealed 23 pairs of chromosomes (46, XY) without any abnormality or structural defects. The general examination was suggestive of developmental delay with delayed attainment of developmental milestones. There was overall growth retardation with delayed speech, short stature, and microcephaly. External ears were deformed indicative of mild microtia. A moderate hearing loss was present in both the ears. A reduced mouth opening with bilateral fibrous ankylosis of Temporomandibular joint was present. Other features included preaxial polydactyly at right hand, gastro-esophageal reflux and penile deviation. The renal ultrasound was suggestive of an ectopic kidney with normal functions. MRI brain revealed poor grey-white matter differentiation and partially deficient falx cerebri. It also showed absence of septum pellucidum with a few gyri interdigitating in the anterior hemispheric fissure (Table 2). The ultrasound examination of patellae was carried out as it is radiolucent in first 5–6 years of life and may not be visible by conventional radiography. The ultrasound revealed poorly developed patellar bone (De Munnik et al., 2015). The blood profile of was suggestive of anemic state with a normal coagulation profile.

The facial examination was suggestive of a dysmorphic face with microstomia. Mandible was retrognathic with a prominent upper and middle third of face (Fig. 1a). The child had a reduced mouth opening since the birth. Intraoral examination revealed severe early childhood caries involving all maxillary and mandibular primary teeth (Fig. 1b).

Cleft involving the junction of hard and soft palate was present with an occasional nasal regurgitation. Cleft remained untreated due to reduced mouth opening. Radiographic examination with orthopantomogram (Fig. 2a) revealed a normal tooth development and the presence of developing permanent teeth expected for dental age. The cephalometric radiograph (Fig. 2b) confirmed the clinical observation of prominent upper and middle third of face with a retrognathic mandible. There was a deficiency in overall length of maxilla and mandible with an increase in the gonial and mandibular plane angle (Table 3).

The parents were explained about the complications that can occur after the birth. However, this disorder has a variable expression and relatively low chances of life-threatening complications or intellectual disability. As there were no structural congenital anomalies, the ethical issue of possible termination of a pregnancy was difficult to justify. MGS being an autosomal recessive disorder with a recurrence risk for a couple with an affected child is about 25% (De Munnik et al., 2015). Therefore, the genetic counselling was provided to the parents to explain the risk of recurrence in having another child.

3. Discussion

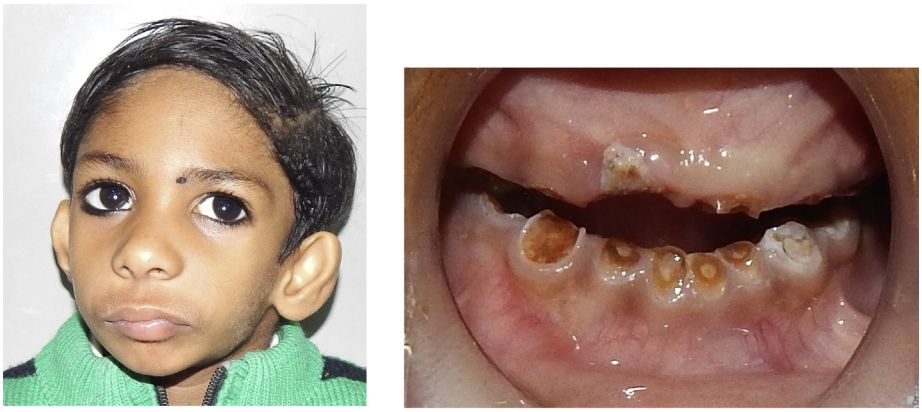
There are number of recognized genetic traits and diseases which can involve the orofacial structures. Thus, it is becoming increasingly important for a dentist to be capable of recognizing and dealing with genetic diseases. Ideally, the management of Meier-Gorlin syndrome should begin at birth. This involves a proper diagnosis, identification of needs and proper facilities to provide the required treatment.

Table 1 Anthropometric variables.

Anthropometric variables	Patient parameter (Deficiency)
Weight	7.4 kg (−7.49)
Height	79.6 cm (−5.86)
Occipitofrontal head circumference	39.6 cm (−9.24)

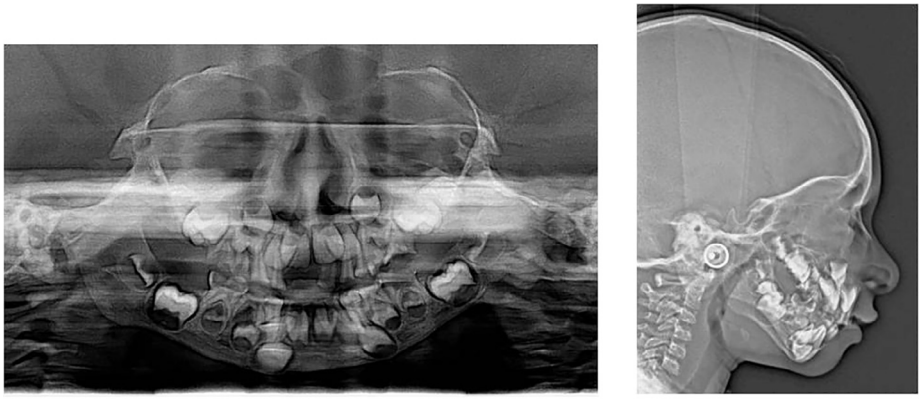
Table 2 Clinical features suggestive of Meier-Gorlin syndrome in the present case.

Primary diagnostic features	Other associated anomalies
• Overall short stature • Microtia with ear deformation • Patellar hypoplasia	• Developmental delay • Partial hearing loss • Fibrous ankylosis of TMJ • Retrognathic mandible • Reduced mouth opening • Preaxial polydactyly at right hand • Penile deviation • Ectopic kidney • Gastro-esophageal reflux • Cleft palate • Ankyloglossia • Structural brain defect



a b

Fig. 1 (a) Dysmorphic face, microstomia with a retrognathic lower jaw. (b) Reduced mouth opening and severe early childhood dental caries with multiple carious root stumps.



a b

Fig. 2 (a) An orthopantomogram revealed a full complement of primary and permanent dentitions. (b) A cephalometric radiograph revealed a prominent upper face with mandibular retrognathism.

Table 3 Dental and skeletal parameters on Lateral cephalogram.

Parameters (normal value)	Patient values
SNA (81° ± 1.8°)	84
SNB (79° ± 1.8°)	73
ANB (3.12° ± 1.8°)	11
Gonial angle(Ar-Go-M) (123° ± 7)	138
Y-axis(S-Gn/FH) (59° ± 3)	58
Saddle Angle (N-S-Ar) (123 ± 5)	132
FMA (23.8° ± 2°)	32
Maxillary length (44 mm)	36 mm
Mandibular length (62 mm)	45 mm
Inter-incisor Angle (123°)	135

Table 4 Clinical characteristics of cases reported with Meier-Gorlin syndrome (De Munnik et al., 2012a).

Clinical features	Percentage of cases exhibing features
Microtia	34/36 (94%)
Patellar anomalies (missing/absent)	31/33 (94%)
Intra uterine growth retardation (IUGR)	35/36 (97%)
Microcephaly (head circumference)	13/30 (43%)
Normal Intellect	30/31 (97%)
Feeding problems including gastro esophageal reflux	26/32 (80%)
Cryptorchidism in males	9/14 (64%)
Post-pubertal mammary hypoplasia in females	10/10 (100%)
Joint contractures, including club feet	7/30 (23%)
Congenital pulmonary emphysema	12/28 (43%)
Bronchomalacia, laryngomalacia or tracheomalacia	10/24 (42%)

Table 5 Proposed guidelines for diagnostic evaluation and management of patients with Meier-Gorlin syndrome (Munnik et al., 2015).

Age	Involved system	Signs and symptoms	Investigation	Period of evaluation	Treatment options
From birth till late childhood (Birth to 12 years)	*Ears*	Small external auditory meatus Conductive hearing loss	Otoscopy Hearing tests	At diagnosis and annually when indicated	Hearing aids
	Skeleton	Patellar hypoplasia Knee complaints, hypermobile joints	Knee imaging: Ultrasonography ≤ 5–6 yrs, X-rays > 5–6 yrs Orthopedic assessment	At diagnosis and in case of signs and symptoms	Rehabilitation advice Arch support Surgical intervention
	Growth	Impaired growth velocity after 1 year of age, Low Insulin-like growth factor 1	1. Evaluation of growth 2. Complete endocrine work-up	1. At diagnosis and annually 2. At diagnosis and in case of signs and symptoms	Growth hormone treatment
	Central nervous system	Delayed motor development, muscle weakness, Speech delay	Developmental assessment	Annually	Speech therapy Extra assistance at school
	Gastrointestinal tract	Poor weight gain, poor intake, Gastro-esophageal reflux	1. Monitor feeding and growth 2. Esophageal pH monitoring	1. Annually 2. In case of signs and symptoms	Nasal tube feeding Gastroesophageal reflux disease treatment
	Respiratory tract	Respiratory tract infection, Laryngo-/tracheomalacia, Congenital pulmonary emphysema	1. Physical examination 2. Evaluation by pulmonary specialist	1. At diagnosis 2. In case of signs and symptoms	Antibiotics when indicated Surgery when life-threatening/ disabilitating
	Genitourinary tract	Cryptorchidism in males Hypoplastic labiae in females	1. Physical examination 2. Ultrasound investigations of the inguinal region in males	1. At diagnosis 2. In case of symptoms and signs	Orchidopexy
	Heart	Congenital cardiac defect	1. Physical investigation 2. Cardiac ECG and ultrasound	1. At diagnosis 2. At diagnosis	Cardiac surgery
From childhood onwards (12 year onwards)	*Skeleton*	Knee complaints, arthrosis	Orthopedic assessment	In case of signs and symptoms	Surgical intervention
	Secondary sexual development	Mammary hypoplasia in females, Sparse/absent axillary hair in both males and females	Physical examination	Annually during puberty In case of signs and symptoms	Estrogen treatment Breast augmentation surgery
	Genitourinary tract	Irregular menses, polycystic ovaries, small uterus	Gynecologic assessment	In case of signs and symptoms	Hormonal treatment when diagnosed with polycystic ovaries
	Pregnancy	Possible risk of premature delivery	Antenatal care in a secondary care centre	During pregnancy	

3.1. Antenatal diagnosis

The prenatal ultrasound investigations at 18–20 weeks of gestation may contribute to the recognition of MGS. However, there is no evidence that the overall growth is delayed at this period. In presence of a known underlying molecular defect, the prenatal diagnosis by chorionic villi sampling is possible (De munnik et al., 2012b).

An association of short stature, microtia and patellar anomalies as such has not been described in other syndromes. Microtia and congenital pulmonary emphysema can be seen along with certain facial features, such as micrognathia. However, the ultrasound abnormalities may be absent or mild and are difficult to interpret due to lack of structural congenital anomalies (De munnik et al., 2012b). However, the phenotypic expression of disorder may be variable (Table 4) (De Munnik et al., 2012a). The child in the present case was also diagnosed

with intra-uterine growth retardation (IUGR) and microcephaly.

3.2. Management

Meier-Gorlin syndrome is characterized by multisystem involvement and is usually accompanied by developmental variations. A multidisciplinary approach is necessary due to variable phenotype and its complex nature. A multidisciplinary team may consist of a craniofacial surgeon, neurologist, ENT specialist, speech pathologist, audiologist, oral surgeon, orthodontist and a pediatric dentist. De Munnik et al. (2015) (De Munnik et al., 2015) has proposed the guidelines for diagnostic evaluation and management of patients with Meier-Gorlin syndrome based on their clinical experience (Table 5). A team approach is essential to determine the best collaborative corrective plan for deficiencies in the child.

The child in the present case represents the characteristic triad of clinical features consists of short stature, microtia and patellar hypoplasia which are diagnostic of Meier-Gorlin syndrome. The parents were explained about the molecular testing of the condition but they were not ready as the molecular diagnosis would not have added to their child's care as well as it was costly too. The multisystem involvements in the present case include the hearing impairment, structural renal defects, gastro-esophageal reflux disease and abnormalities related to maxillofacial structures.

There is no data in the literature regarding the prevalence of dental caries and other dentofacial anomalies in individuals with Meier-Gorlin syndrome. The present case represents significant dental findings which include a dysmorphic face, fibrous ankylosis, reduced mouth opening, mandibular retrognathism, cleft palate, ankyloglossia and dental caries with multiple carious root stumps. Dental management of these children depends on the level of their mental development and cooperation in the dental setting. Those with normal mental development can be treated as normal children, while the more uncooperative patients would require sedation or general anesthesia. In general, however, the mainstay of dental management of these patients should be the prevention of dental diseases. Early institution of good dietary and oral hygiene practices and the adjunctive use of fluoride supplements, when appropriate, can help to prevent the deleterious dental consequences experienced by the patient. Dental services for such a patient should include the education of the parents on the possible dental consequences of the syndrome and their prevention. The child in the present case had undergone extraction of symptomatic and non-restorable teeth under local anesthesia and other carious teeth were managed conservatively. The cleft closure is difficult to perform at present due to reduced mouth opening. The surgery to release fibrous union of TMJ and tongue tie was planned under general anesthesia but couldn't performed, as anesthetic clearance was not obtained due to difficulty in airway anticipated owing to retruded mandible, palatal cleft and reduced mouth opening. Also, the parents were not willing to give a high risk consent which was required in this case. Therefore the patient has been kept under observation since then and would be treated for retrognathia and ankyloglossia once the conditions become favorable.

4. Conclusion

The multisystem clinical consequences in the individuals with Meier-Gorlin syndrome can be managed and their quality of life can be improved by a multidisciplinary approach involving dental and medical specialists.

Financial support

Nil.

Conflict of interest

None.

Acknowledgement

None.

References

De Munnik, S.A., Bicknell, L.S., Aftimos, S., Al-Aama, J.Y., Van, B. Y., Bober, M.B., et al, 2012a. Meier-Gorlin syndrome genotype-phenotype studies: 35 individuals with pre-replication complex gene mutations and 10 without molecular diagnosis. Eur. J. Hum. Genet. 20 (6), 598–606.

Bicknell, L.S., Walker, S., Klingseisen, A., Stiff, T., Leitch, A., et al, 2011. Mutations in ORC1, encoding the largest subunit of the origin recognition complex, cause microcephalic primordial dwarfism resembling Meier-Gorlin syndrome. Nat. Genet. 43, 350–355.

De Munnik, Hoefsloot, Roukema, Jolt, Schoots, Jeroen, Brunner, et al, 2015. Meier-Gorlin syndrome – review. Orphanet J. Rare Diseases 10, 114.

Klingseisen, A., Jackson, A.P., 2011. Mechanisms and pathways of growth failure in primordial dwarfism. Genes Dev. 25 (19), 2011–2024.

Kuo, A.J., Song, J., Cheung, P., Ishibe-Murakami, S., Yamazoe, S., et al, 2012. The BAH domain of ORC1 links H4K20me2 to DNA replication licensing and Meier-Gorlin syndrome. Nature 484, 115–119.

De munnik SA et al, 2012b. Meier-Gorlin syndrome: growth and secondary sexual development of a microcephalic primordial dwarfism disorder. Am. J. Med. Genet. A 158A (11), 2733–2742.