

# Meier-Gorlin syndrome with ventriculomegaly and hypoplastic corpus callosum: a rarely reported congenital malformation

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## Abstract

Meier-Gorlin syndrome (MGS) or ear-patella-short stature syndrome (MIM 224690) is a rarely reported autosomal recessive disorder having characteristic triad of microtia, short stature and aplastic or hypoplastic patella. Only 67 cases are reported.

We are reporting a newborn female baby with typical features of MGS along with some other features never described before, ventriculomegaly and hypoplastic corpus callosum.

We did x-rays of whole body (infantogram) and MRI of brain for microcephaly.

Ultrasonography of both knees showed absence of patellae and brain MRI showed ventriculomegaly and hypoplastic corpus callosum.

To our best knowledge this is the second case report of MGS in India; the first reported a MGS associated with papilledema. In previously reported cases, there was no statement regarding agenesis of corpus callosum.

## Keywords

Meier-Gorlin syndrome, ear-patella-short stature syndrome, microtia, ventriculomegaly, hypoplastic corpus callosum.

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## Introduction

Meier-Gorlin syndrome (MGS) or ear-patella-short stature syndrome (MIM 224690) is a rarely reported autosomal recessive disorder [1, 2]. Named after the authors who first reported this syndrome, J. Meier et al. [3] and R.J. Gorlin et al. [4], MGS still remains a very rare syndrome. 82% of the reported cases had the classical triad of MGS i.e. microtia, short stature and aplastic or hypoplastic patella, explaining the reason to think of a wider variety of phenotypes than expected previously. MGS is included in the disorders of primordial dwarfism [2, 5]. This group of disorders includes five disorders: ear-patella-short stature (Meier-Gorlin) syndrome, Seckel syndrome, Russell-Silver syndrome, and Majewski osteodysplastic bird-head dwarfism type I/II/III. Overlapping features may be present in all these subtypes especially Majewski osteodysplastic primordial dwarfism I and II with some distinguishing points and different genetic mutations.

## Case report

A newborn girl was admitted in our newborn care unit at 3 hours of life for having multiple congenital defects. The baby was born to a primigravida mother of non-consanguineous marriage. Antenatal period of mother was uneventful except for poor weight gain. There was no history of any infection or intake of any drug. The mother's age was 20 years with normal mental status and no other family member had similar features like that of the baby. Due to severe intrauterine growth retardation revealed by ultrasonography, the baby was delivered prematurely (35 weeks of gestation) by caesarean section with a birth weight of 1,000 grams. The APGAR score at 1 and 5 minutes were 8 and 9, respectively. On examination her head circumference was 22 cm (< 3 SD), chest circumference was 20 cm (< 3 SD), length was 37 cm (< 3 SD) with upper segment and lower segment ratio 1.4:1 (**Fig. 1**). She had dysmorphic facies with beaked nose, high nasal bridge, full lips and underdeveloped low set ears (**Fig. 2**). Genu recurvatum of right leg with absent of patella on both sides were noted. Genital abnormality was also present in the form of underdeveloped (hypoplasia) labia majora. Respiratory and cardiovascular examination was within normal limits and there was no organomegaly. Ultrasonography of abdomen was done, which revealed no abnormality of internal organs.



**Figure 1.** On examination her head circumference was 22 cm (< 3 SD), chest circumference was 20 cm (< 3 SD), length was 37 cm (< 3 SD) with upper segment and lower segment ratio 1.4:1.



**Figure 2.** She had dysmorphic facies with beaked nose, high nasal bridge, full lips and underdeveloped low set ears.

Absent patella was noted by palpation and confirmed by ultrasonography and x-ray of both knee joints (**Fig. 3**). Chest radiography showed slender ribs (**Fig. 4**). Brain MRI showed ventriculomegaly with hypoplastic posterior aspect of body and splenium of corpus callosum (**Fig. 5**). The diagnosis of MGS should be considered in

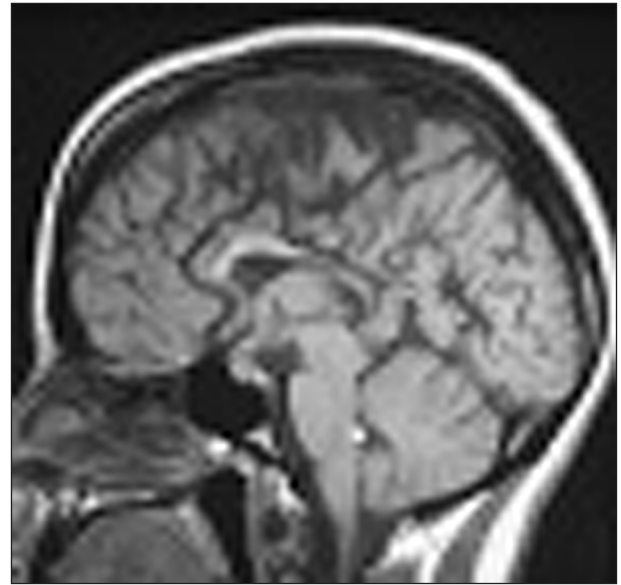


**Figure 3.** Absent patella was noted by palpation and confirmed by ultrasonography and x-ray of both knee joints.



**Figure 4.** Chest radiography showed slender ribs.

patients with at least two of the three features of the clinical triad of microtia, patellar anomalies, and pre- and postnatal growth retardation [6]. Therefore, in the presence of features like microcephaly, microtia, short length, genu recurvatum with absent patella of both knees, the girl baby was diagnosed as MGS. The parents could not afford genetic testing and knowing the fact that the confirmation of the disease will not help in treatment, we could not perform the genetic testing.



**Figure 5.** Brain MRI showed ventriculomegaly with hypoplastic posterior aspect of body and splenium of corpus callosum.

The baby did not develop any respiratory distress, feeding was started soon and she was discharged at day 31, when would feed well and her weight was 1.9 kg. She was asked to follow-up, but unfortunately she did not come for follow-up.

### Discussion

MGS is rare syndrome. Till date only 67 cases are reported. Recently, mutations in five genes from the pre-replication complex (*ORC1*, *ORC4*, *ORC6*, *CDT1*, and *CDC6*) were identified in individuals with MGS [7, 8]. The syndrome is autosomal recessive, characterized by microcephaly, severe pre-natal and postnatal growth retardation, microtia, absent or hypoplastic patella [2, 9]. Other skeletal abnormalities, such as genu recurvatum, and delayed mineralization of bones can be present. Most babies with MGS have specific facial features, in addition to microtia, which ranges from slightly small, normal shaped and normally positioned ears to abnormally shaped and abnormally positioned ear. There is presence of narrow nose with high nasal bridge, full lips, small mouth and occasionally micrognathia [4]. Abnormalities in sexual development may also occur in MGS. Affected males can have small testes, undescended testis (cryptorchidism), micropenis or hypospadias. Females may have unusually small external genital folds (hypoplasia of the labia majora) [10]. Even case presenting

papilledema [11] and unilateral renal aplasia and renal stone have been reported [10]. These babies have frequently feeding and respiratory difficulties due to presence of laryngomalacia, bronchomalacia or trachea-esophageal fistula [10]. Despite microcephaly, the intelligence can be normal [7]. Some of the features of MGS can be present in microcephalic osteodysplastic primordial dwarfism type I (MOPDI) and type II (MOPD II), but microtia is typically present in MGS [5]. Patients with MOPD II due to mutation in *PCNT* gene have additionally abnormally pigmented skin, subglottic stenosis, mesomelic shortening of forearms and vascular abnormalities like intracranial aneurysm. Characteristic skeletal abnormalities include small iliac wings with flat acetabular angles, coxa vara, V-shaped distal femoral metaphyses and triangular distal femoral epiphyses as well as metacarpal pseudoepiphyses, short first metacarpals and brachymesophalangy V [12]. Mothers of affected patients of MOPD II have mental retardation [12]. MOPD I caused by mutations in *RNU4ATAC* gene can have agenesis of corpus callosum and microcephaly, but they present with seizures and apnea and have sparse scalp hair, short vertebrae, elongated clavicle, bent femora and hip displacement [13]. Another new syndrome comes in very close relation to MGS i.e. genitopatellar syndrome. Genitopatellar syndrome is characterized by the association of absent patellae, genital anomalies, dysmorphic features (coarse face, large nose, microcephaly), renal anomalies (multicystic kidneys or hydronephrosis), and intellectual deficit [14]. The coarse facies in genitopatellar syndrome comprises of prominent cheeks and eyes, a nose with a rounded tip or a broad bridge, an unusually small chin (micrognathia) or a chin that protrudes (prognathism), and a narrowing of the head at the temples [15].

The life span of patients with MGS depends on the severity of the disease. There is no definitive treatment available for MGS, only complications arising from skeletal anomalies and other associated problems should be regularly checked and managed accordingly.

### Key message

In previously reported cases, there was no statement regarding agenesis of corpus callosum. Brain MRI should be done in suspected cases and agenesis of corpus callosum can be included in the

associated conditions for MGS, which may or may not alter the disease course that is to be followed.

### Declaration of interest

Funding and competing interests: nil.

### References

- Cohen B, Temple IK, Symons JC, Hall MC, Shaw DG, Bhamra M, Jackson AM, Pembrey ME. Microtia and short stature: a new syndrome. *J Med Genet.* 1991;28:786-90.
- Shalev SA, Hall JG. Another adult with Meier-Gorlin syndrome – insights into the natural history. *Clin Dysmorph.* 2003;12:167-9.
- Meier Z, Rothschild M. Ein Fall von Arthrogryposis multiplex congenita kombiniert mit dysostosis mandibulofacialis (Franceschetti-Syndrom). *Helv Paediatr Acta.* 1959;14:213-6.
- Gorlin RJ, Cervenka J, Moller K, Horrobin M, Witkop CJ. Malformation syndromes: a selected miscellany. *Birth Defects Orig Artic Ser.* 1975;11:39-50.
- National Organization of Rare Disorders. Ear-patella-short stature syndrome. Available at: <http://www.rarediseases.org/rare-disease-information/rare-diseases/byID/1064/viewFull%20Report>, last access: January 2016.
- de Munnik SA, Hoefsloot EH, Roukema J, Schoots J, Knoers NV, Brunner HG, Jackson AP, Bongers EM. Meier-Gorlin syndrome. *Orphanet J Rare Dis.* 2015;10:114.
- Bicknell LS, Walker S, Klingseisen A, Stiff T, Leitch A, Kerzendorfer C, Martin CA, Yeyati P, Al Sanna N, Bober M, Johnson D, Wise C, Jackson AP, O'Driscoll M, Jeggo PA. Mutations in *ORC1*, encoding the largest subunit of the origin recognition complex, cause microcephalic primordial dwarfism resembling Meier-Gorlin syndrome. *Nature Genet.* 2011;43:350-5.
- Guernsey DL, Matsuoka M, Jiang H, Evans S, Macgillivray C, Nightingale M, Perry S, Ferguson M, LeBlanc M, Paquette J, Patry L, Rideout AL, Thomas A, Orr A, McMaster CR, Michaud JL, Deal C, Langlois S, Superneau DW, Parkash S, Ludman M, Skidmore DL, Samuels ME. Mutations in origin recognition complex gene *ORC4* cause Meier-Gorlin syndrome. *Nat Genet.* 2011;43:360-4.
- Terhal PA, Ausems MGEM, Van Bever Y, Ten Kate LP, Dijkstra PF, Kuijpers GMC. Breast hypoplasia and disproportionate short stature in the ear, patella, short stature syndrome: expansion of the phenotype? *J Med Genet.* 2000;37:719-21.
- de Munnik SA, Bicknell LS, Aftimos S, Al-Aama JY, van Bever Y, Bober MB, Clayton-Smith J, Edrees AY, Feingold M, Fryer A, van Hagen JM, Hennekam RC, Jansweijer MC, Johnson D, Kant SG, Opitz JM, Ramadevi AR, Reardon W, Ross A, Sarda P, Schrandt-Stumpel CT, Schoots J, Temple IK, Terhal PA, Toutain A, Wise CA, Wright M, Skidmore DL, Samuels ME, Hoefsloot LH, Knoers NV, Brunner HG, Jackson AP, Bongers EM. Meier-Gorlin syndrome genotype-phenotype studies: 35 individuals with pre-replication complex gene mutations and 10 without molecular diagnosis. *Eur J Hum Genet.* 2012;20(6):598-606.

11. Kalappanavar NK, Gouli C, Syed Nasiruddin I. Meier-Gorlin syndrome with papilloedema. *J Pub Health Med Res.* 2013;1(1):53-4.
12. Majewski F, Goecke TO. Microcephalic osteodysplastic primordial dwarfism type II: report of three cases and review. *Am J Med Genet.* 1998;80:25-31.
13. He H, Liyanarachchi S, Akagi K, Nagy R, Li J, Dietrich RC Li W, Sebastian N, Wen B, Xin B, Singh J, Yan P, Alder H, Haan E, Wiczorek D, Albrecht B, Puffenberger E, Wang H, Westman JA, Padgett RA, Symer DE, de la Chapelle A. Mutations in U4atac snRNA, a component of the minor spliceosome, in the developmental disorder MOPD I. *Science.* 2011;332:238-40.
14. WHO. Genitopatellar syndrome. Available at: <http://id.who.int/icd/entity/376039493>, last access: January 2016.
15. Genetics Home Reference. Genitopatellar syndrome. Available at: <http://ghr.nlm.nih.gov/condition/genitopatellar-syndrome>, last access: January 2016.