Another adult with Meier-Gorlin syndrome – insights into the natural history

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The Meier-Gorlin syndrome (MGS) is a rare autosomal recessive disorder, characterized by bilateral microtia, aplasia or hypoplasia of the patellae, and severe intra-uterine and post-natal growth retardation. We describe the phenotype and report the medical history of a 25-year-old woman with MGS. Her phenotypic evolution was characterized by severe growth retardation with decelerated growth of the head and subsequently a relatively small head, normal intelligence, alteration of the facial features to a more proportionate appearance, improvement of joint function and incomplete breast development. Other characteristics of her phenotype in adulthood include a cheerful personality, a high forehead and accentuated naso-labial folds, relatively very small ears, hypoplastic breasts, and normal menstruation. *Clin Dysmorphol* **12:167–169 © 2003 Lippincott Williams & Wilkins.**

Clinical Dysmorphology 2003, **12**:167–169

Keywords: Meier-Gorlin syndrome, growth retardation, microtia, absent patellae, adulthood

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Received 14 May 2002 **Accepted** 7 February 2003

Introduction

The Meier-Gorlin syndrome (MGS) or ear, patella short stature syndrome (MIM 224690) is thought to be a rare disorder, associated with bilateral microtia, aplasia or hypoplasia of the patellae, and severe intra-uterine and post-natal growth retardation. MGS is an autosomal recessive condition, based on the occurrence in several pairs of sibs, almost equal numbers of affected males and females, and parental consanguinity reported in three cases (Bongers *et al.*, 2001). We report a 25-year-old woman with MGS, and describe the change of the phenotype over time.

Case report

The proposita is the second-born daughter of an unrelated couple. The pregnancy was uneventful. The parents are healthy and of normal height. She was born at term via vaginal delivery, presenting as a frank breech. Her weight at birth was 1900 g and the length was 31 cm. At birth both her hips and knees were dislocated. The patellae were absent. Infancy was characterized by feeding problems associated with poor weight gain, and frequent upper respiratory infections. Unusual features noted in infancy and childhood were a triangular face and a small jaw, small but normally formed ears, although the antihelix was noted to be incomplete, and the position thought to be somewhat low (Figure 1).

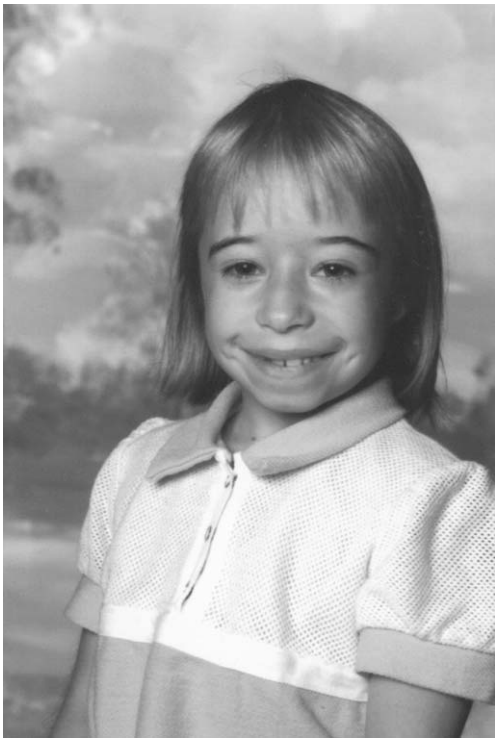
Through childhood and adolescence growth was always severely affected. The knees were unstable with moderate laxity. The patellae were never palpated. Her ankles were extremely loose, and hyper-extensibility of shoulders, wrists and fingers was also present during childhood. Her knees have become more stable over the years, and she walks independently, including climbing stairs. Her skin was soft with the appearance of increased translucency over the shoulders and upper limbs. Reduced muscle mass was said to be present over the lower part of the limbs. First menstruation occurred at the age of 12 years, and ever since then has continued monthly. No increase in the size of the breast tissue mass was noted prior to or following the menarche. Puberty was not associated with a growth spurt. She did well at school, graduated from high school, and spent 3 years in college. Currently she works as a front desk receptionist in a motel.

At the age of 25 years, her physical examination revealed proportionate severe short stature. Her height was 127 cm (consistent with a height age of 8 years). Considering the height age, the weight was at the 75th centile, and the head circumference was a little below the 2nd centile. Her face appeared triangular, with reduced facial fat and hypoplasia of her mid-face. The forehead appeared relatively high, and her eyes were mildly up-slanted. The nasal bridge was narrow but not elevated, the nose became mildly prominent with a bony angle approximately at the point of the cartilage border, and was relatively long. (Accentuated naso-labial folds were noted.) The mandible appeared regressed compared with the maxilla, but both were apparently anteriorly located. She had very small ears, 4 cm long, with normal morphology and relatively large adherent lobules. The

0962-8827 © 2003 Lippincott Williams & Wilkins DOI: 10.1097/01.mcd.0000065052.36236.32

neck was apparently long (Figure 2). No breast tissue was palpated, but the nipples appeared normal post-pubertal, and had moderate pigmentation. Sparse axillary and normal pubic hair were noted. Her hands and fingers appeared normal in proportion to the rest of her body. Very mild hyperextensibility of the small joints was present. The muscle mass and strength of her upper limbs appeared normal. The muscle mass of her lower limbs was diminished distally in both the upper and lower legs. Most of the muscle bulk appeared on the upper part of the thighs and the calves. The knees appeared stable, but the bony medial aspects were very prominent, and the patellae were not palpable. Her gait was normal. Very mild flexible bilateral talipes equinovarus was noted, with bilateral incurved 3rd–5th toes. Multiple nevi were present over the trunk, with slight prominence of blood vessels over the shoulders and upper limbs. A hoarse and somewhat croaky voice was noted. She attributes this to cigarette smoking (a habit that begun when she was 14 years old). The patient had normal hearing and vision.

Fig. 1



The patient at the age of 5 years. Note the long face, high forehead and long narrow nose.

Investigations included normal female karyotype (550 bands). Radiographs at the age of 10 months showed an overall skeletal age of 1 month. The cranial vault appeared asymmetric. The osseous mineralization of the limbs appeared normal. There was marked medial subluxation of the lower leg relative to the femur at the knee, and marked accentuation of the longitudinal arch of the left foot. At the age of 3.5 years, bone age was consistent with 2 years. Review of her X-rays at the age of 7 years suggested metaphyseal flaring of the long bones, absence of patellae bilaterally, and an irregular appearance of the epiphyses of most of the long bones. The long bones were thin with poorly mineralized cortices. The femoral necks were straight without the usual angulation. The spine appeared normal. At the age of 25 years, the

Fig. 2

The profile at the age of 25 years. The small ears with attached lobules, bony angle of the nose, more proportionate facial features.

lateral view of the skull showed relatively prominent convolution-like markings over the calvarium. The iliac wings appeared relatively small, but the hip joints were well developed. The lateral femoral condyles appeared underdeveloped relative to the medial, and the patellae were not seen.

Discussion

The Meier-Gorlin syndrome, which has also been called the ear-patella-short stature syndrome, is characterized by a distinct pattern of features. Clinical findings of eight new cases and 21 cases from the literature were reviewed by Bongers *et al.* (2001). All patients presented with short stature (almost always proportionate), microtia, delayed bone age and slender long bones. Almost all had early feeding problems, microcephaly, atretic or small auditory canals, mandibular hypoplasia and joint abnormalities. Most of the reported individuals affected with the MGS are children. There are few reports that include descriptions of the evolving phenotype or natural history of adult patients (Gorlin, 1992; Lacombe *et al.*, 1994; Fryns, 1998; Terhal *et al.*, 2000).

The patient we describe in this paper might represent the more severe end of the spectrum of growth retardation and joint involvement of MGS. Growth spurt did not occur in puberty. Unlike the patients described by others, who had mild to moderate short stature (Fryns, 1988; Gorlin, 1992; Terhal, 2000; Lacombe *et al.*, 1994) she has severe short stature of 127 cm in adulthood, far below the lower normal range. We postulate that, considering her profoundly delayed bone age, her menarche at the age of 12 years might actually have been a relatively early puberty and consequently led to early closure of epiphyseal growth plates, causing severe short stature in adulthood.

The patient's sexual development was similar to that described by Terhal *et al.* (2000) and Lacombe *et al.* (1994) in three unrelated females: menarche occurred at appropriate chronological age (12 years), but was not accompanied by normal development of post-pubertal breasts. The presence of definite breast hypoplasia in four unrelated affected females (including our patient) at pubertal and post-pubertal-age, seems to represent a consistent syndromic feature.

Our patient had congenital contractures of hips and knees as a result of dislocation of these joints. Surgical repairs were done at a young age, but nevertheless the knees appeared unstable throughout her childhood. General improvement of her joint structure and function, specifically the increase in the stability of her knees, was consistently noticed over the years, and has allowed our patient to walk independently. Absence of patellae was noted even in adulthood, unlike in the case of Fryns (1998). Interestingly, she also had an unusual appearance of the muscles on her lower limbs, which has been described as reduced distal muscle mass. It was a constant finding, and was not accompanied by any neurological deficits or apparent abnormal tendon attachment.

The facial appearance in MGS among adults appears more proportionate than in younger individuals, but is also characterized by reduced subcutaneous fat. The mouth of our patient appeared relatively wide (definitely not small), and the naso-labial folds have become accentuated. A relative microcephaly is present, with apparent decelerated growth of the skull during childhood and adolescence.

The personality of our patient was notably pleasant and sociable. A happy and friendly personality was specifically described in other individuals with MGS (Bongers *et al.*, 2001; patients 2, 5 and 6; Boles *et al.*, 1994, patient 1). More descriptions of the personality and behaviour of patients with MGS are required to delineate the typical features of this condition.

Our patient was noticed to have a hoarse and somewhat croaky voice, which she attributes to prolonged smoking. Bongers *et al.* (2001) noticed high-pitched voices in monozygotic female twins with MGS (patients 5 and 6) and a low-volume hoarse cry in another female (patient 8).

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