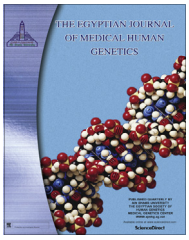
The Egyptian Journal of Medical Human Genetics (2014) 15, 199–202

Ain Shams University

The Egyptian Journal of Medical Human Genetics

www.ejmhg.eg.net
www.sciencedirect.com



CASE REPORT

Bilateral absence of fifth ray in feet, cleft palate, malformed ears, and corneal opacity in a patient with Miller syndrome

Rabah M. Shawky [a,*], Nermine Amr [b], Heba Salah [a], Shaimaa Gad [a]

[a] *Pediatric Department, Genetics Unit, Ain Shams University, Egypt*
[b] *Pediatric Department, Endocrinology Unit, Ain Shams University, Egypt*

Received 6 December 2013; accepted 15 December 2013
Available online 4 January 2014

KEYWORDS

Miller syndrome;
Genée–Weidemann syndrome;
Postaxial acrofacial dysostosis syndrome;
Corneal opacity

Abstract *Background:* Miller syndrome is one of the acrofacial dysostosis syndromes, which are characterized by malformations of the craniofacial region and limbs.

Case report: A 26 month old male child, the product of healthy nonconsanguineous parents has many typical features of Miller syndrome. He has cleft lip and palate, malar hypoplasia, left crumpled cup shaped ear, and prominent nose together with the absence of the fifth ray in feet (postaxial) and fixation of interphalangeal joints of both thumbs (preaxial). However the limb affection is bilateral and symmetrical against what is usually reported (bilateral with more affection of one side) and the micrognathia is very mild. Our patient has also bilateral corneal opacities as well as underdeveloped external genitals.

Conclusion: There is phenotypic variability in Miller syndrome, and our patient may represent a new distinct subgroup in postaxial acrofacial dysostosis.

1. Introduction

The acrofacial dysostosis syndromes, which are characterized by malformations of the craniofacial region and limbs, are a clinically heterogeneous group of disorders. Based primarily on the pattern of limb defects, two major groups have emerged: Nager syndrome with predominantly preaxial malformations plus mandibulofacial dysostosis (severe micrognathia and malar hypoplasia) and Miller syndrome with predominantly post axial malformations plus mandibulofacial dysostosis [1].

Miller (Genée–Weidemann) syndrome represents a clinically and biochemically distinct subgroup of postaxial acrofacial dysotosis (POADS). The facies can be strikingly similar to Treacher Collins syndrome [2].

Ng et al., reported that the pattern of malformations observed in individuals with Miller syndrome is similar to those in individuals with fetal exposure to methotrexate. Methotrexate is a well-established inhibitor of de novo purine biosynthesis, and its antiproliferative actions are thought to be due to its

* Corresponding author. Tel.: +20 2 22585577.
E-mail address: shawkyrabah@yahoo.com (R.M. Shawky).
Peer review under responsibility of Ain Shams University.

ELSEVIER Production and hosting by Elsevier

1110-8630 © 2014 Production and hosting by Elsevier B.V. on behalf of Ain Shams University.
http://dx.doi.org/10.1016/j.ejmhg.2013.12.004

inhibition of dihydrofolate reductase and folate-dependent transmethylations. Accordingly, defects of both purine and pyrimidine biosynthesis appear to be capable of causing a similar pattern of birth defects [3].

We report an Egyptian patient who has many typical features of Miller syndrome with subtle facial changes, and few associated congenital malformations after taking consent of the parents.

2. Case report

The patient was a 26–month old male child, the third in order of birth of healthy non consanguineous Egyptian parents. The patient was delivered at full term by cesarean section. His birth weight was appropriate for gestational age. No history of drug intake by the mother during pregnancy. The patient was referred to the Genetics Clinics, Pediatric Hospital, Ain Shams University because of abnormal features.

On examination the skull circumference is 47 cm (−1.65 SDS), height is 86.5 cm (−0.15 SDS), weight is 10 kg (−2.41 SDS), BMI is 13.36 kg/m^2 (−3.07 SDS) [4,5]. The patient has an open anterior fontanel 2 × 2 cm, and there is hypertelorism. The eyes show transverse slant as well as small corneal opacity. The patient has broad bulbous nose, with broad nasal tip, and wide nares. The right ear is low set, malformed, cup shaped, and posteriorly rotated. The left ear lobule is small and slightly everted upwards. Also he has long philtrum which shows a scar of cleft lip operation, thin upper lip, and high arched palate (Figs. 1 and 2). The upper limbs show that the interphalangeal joints of both thumbs were fixed in extension, with clinodactyly of the little fingers. The lower limbs show bilateral postaxial oligodactyly (the fifth toes are absent), long second toe, and medial deviation of the third and forth toes (Fig. 3).

The patient has normal mentality. Genital examination shows small uncircumcised penis measuring 3.1 cm in full stretched length (−2.3 SDS) [6], with bilaterally undescended small testes both felt in the inguinal canal, (left testes < 1 ml and right testes 1.5 ml in volume), and underdeveloped scrotum (Fig. 4). Chest, cardiac, abdominal, and neurological examinations are normal. Hearing and vision are also normal.

Figure 1 Facial features including transverse slant of palpebral fissures, broad bulbous nose, with broad nasal tip, and wide nares, bilateral corneal opacities at the medial lower quadrant, long philtrum which shows a scar of cleft lip operation, and thin upper lip.

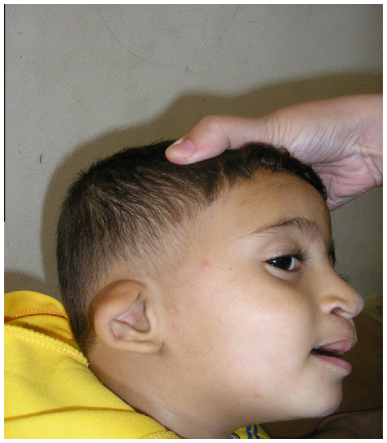


Figure 2 The right ear is low set, malformed, cup shaped, and posteriorly rotated.

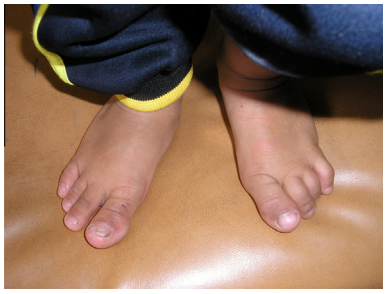


Figure 3 Bilateral postaxial oligodactyly (absence of the fifth toe), long second toe, and slight medial deviation of third and forth toes.

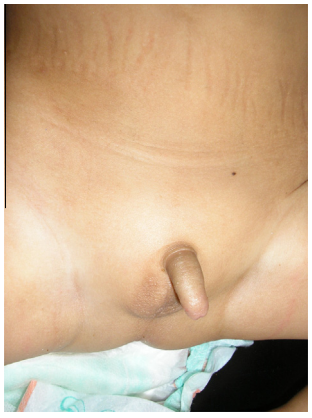


Figure 4 Small uncircumcised penis, with underdeveloped scrotum, bilaterally undescended small testes both felt in the inguinal canal.

There was suboptimal testosterone response to the HCG test (Human Chorionic Gonadotropin 5000 IU intramuscular, with serum testosterone measured after 72 h). Peak testosterone level was 0.3 ng/ml, and there was absence of three fold rise of serum testosterone from baseline level. Also the test did not result in testicular descent. Skeletal survey was normal apart from bilateral absence of the fifth metatarsal, and fifth