The Egyptian Journal of Medical Human Genetics (2012) 13, 363–365

Ain Shams University

The Egyptian Journal of Medical Human Genetics

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

CASE REPORT

Microcephalic osteodysplastic primordial dwarfism (MOPD) type I with lissencephaly and brain cyst

Reda A. Abolila *, Rima M. Alsawan, Mohamed T. Alrefaie

Neonatal Department, Farwanya Hospital, Kuwait

Received 6 February 2012; accepted 10 May 2012
Available online 12 July 2012

KEYWORDS

MOPD III;
Lissencephaly;
Brain cyst;
Primordial dwarfism;
Extreme low birth weight;
MOPD I;
MOPD II

Abstract We are reporting a very rare case of primordial dwarfism associated with lissencephaly and brain cyst, in a full term (37 weeks) girl, who had extreme low birth weight (580 g), delivered vaginally with good APGAR score (6 and 7) at 1 and 5 min, respectively. The mother was healthy, para 0 + 1, 20 years old, had previous abortion and had no risk factors for severe intra uterine growth retardation (IUGR). Parents were non consanguineous. Although the baby had extreme low birth weight (ELBW) she did not need any ventilatory support till discharge from the hospital and was discharged home sucking well with weight on discharge 1.2 kg. The baby had typical features of primordial dwarfism MOPD type I and to our knowledge this is the first time to report such a rare case from Kuwait. Also the patient had lissencephaly and brain cyst which were not reported previously.

1. Introduction

There are around 200 types of dwarfism; most of them are due to skeletal or endocrine disorders [1]. Primordial dwarfism is a very rare form of dwarfism beginning in early stages of intrauterine life (primordial stage) and results in a smaller body size in all stages of life [2]. It is responsible for the most severe forms of dwarfism, and it was estimated that there are only around 100 individuals in the world affected with this disorder [3]. Primordial dwarfism includes specific types of profoundly proportionate dwarfism, in which individuals are extremely small for their age, even as a fetus and can be detected as early as 13 weeks of intrauterine life by antenatal ultrasonography [2]. After birth, growth continues at a stunted rate, leaving affected individuals perpetually years behind their peers in stature and weight [3]. It is rare for the individuals affected by primordial dwarfism to live past the age of 30 years. In microcephalic osteodysplastic primordial dwarfism (MOPD) II there is an increased risk of vascular problems, which may cause death at earlier age [4]. Differential diagnosis of primordial dwarfism includes: Seckel dwarfism, MOPD I, II and III, Russel–Silver syndrome, Meier–Gorlin syndrome [3–7]. People with Seckel dwarfism have; characteristic facial appearance, with beaked nose, microcephaly, scoliosis, hip dislocation, delayed bone age, radial head dislocation, and seizures [5]. Majewski osteodysplastic primordial dwarfism (also called microcephalic osteodysplastic primordial dwarfism and Majewski was the first one to describe it) [7]; this form of primordial dwarfism has three subtypes which are shortened to MOPD I, MOPD II and MOPD III. In MOPD I patients usually have corpus callosum agenesis, seizures, attacks of apnea,

* Corresponding author. Mobile: +965 665410.
E-mail address: redaabolila@yahoo.com (R.A. Abolila).
Peer review under responsibility of Ain Shams University.

Production and hosting by Elsevier

1110-8630
http://dx.doi.org/10.1016/j.ejmhg.2012.06.005

hair thinness including scalp hair, eye lashes and eyebrows. They also have short vertebrae, elongated clavicles, bent femurs, hip displacement, and microcephaly [7]. In MOPD II; patients have further medical issues including: squeaky voice, microdontia, widely spaced primary teeth, poor sleep patterns, delayed mental development, frequent sickness breathing problems, eating problems, hyperactivity, farsightedness, brain aneurysms, delayed bone age in addition to microcephaly [2–4]. MOPD III was reported by Majewiski et al. in 1982. Patients have an intrauterine dwarfism with platyspondyly and anomalies of pelvis and clavicles [8]. In MOPD patients will not reach the size of an average newborn until they are between the ages of 3–5 years [3]. In Russel–Silver syndrome the final height often exceeds the height of others with primordial dwarfism, and they are quite different having webbed toes, non-descended testicles, hypospadias, weak muscle tone, delayed bone age, thin upper lip, high pitched voice, small chin, delayed closure of the fontanel, hypoglycemia, and a broad forehead which may appear to be triangular shaped and large for their small body size, and some patients have hemi-hypertrophy [9]. Meier–Gorlin syndrome is characterized by small ears, variable degrees of deafness and absence of knee caps and patients also have curved clavicles, deformed ribs, and elbow dislocation and like Russel–Silver syndrome, those patients usually exceed the height of those with Seckel syndrome and MOPD [10,11]. The lack of normal growth in primordial dwarfism is not due to a deficiency of growth hormone. So, administering growth hormone has limited role on the growth of the affected individuals and no other effective treatment [1]. The management includes social support for the affected individuals and their families.

2. Case presentation

Our patient was a full term female, delivered vaginally, after an uneventful 37 weeks of pregnancy, for p 0 + 1, 20 year old mother with one previous abortion and had no risk factors for severe IUGR. There was severe oligohydramnios and the mother had regular antenatal follow up. Parents were non consanguineous. Although the girl was the product of full term pregnancy (37 weeks), her growth parameters were far away below the 3rd centile. Her weight was 580 g, length was 28 cm and head circumference was 22.5 cm giving the picture of a very severe symmetrical IUGR newborn. These parameters were plotted on the 50th centile of growth chart for 22–23 weeks. In spite of the severe LBW the baby was born active and recorded good APGAR score (6 and 7) at 1 and 5 min, and she needed only routine respiratory support in the form of suction and O2 hood. In NICU she was weaned of oxygen rapidly over a period of 2 days. In addition to severe symmetrical IUGR the baby had the following dysmorphic features: no scalp hair, no eye lashes and eyebrows, sloping forehead, prominent occiput, protruding eyes with no corneal opacities or cataract, prominent nose, small dysplastic ears, narrow anterior fontanel (about to close), single umbilical artery, small hands with bilateral single palmer crease, small dysplastic nails, and contractures at the elbow joints. The knee joints were dislocated and there was hyperlaxity at both ankle joints with edema on the dorsum of the feet (Figs. 1 and 2).

The following photos (1 and 2) in Farwanya hospital NICU, showing the baby at the age of 5 days; very small (compare it to the authors hand), pink in room air, has no eye lashes, no eyebrows and no scalp hairs, and photo (3) at the age of 4 weeks after recovery from klebsiella septicemia showing protruding eyes, deformed left knee joint and edema of the dorsum of the feet.

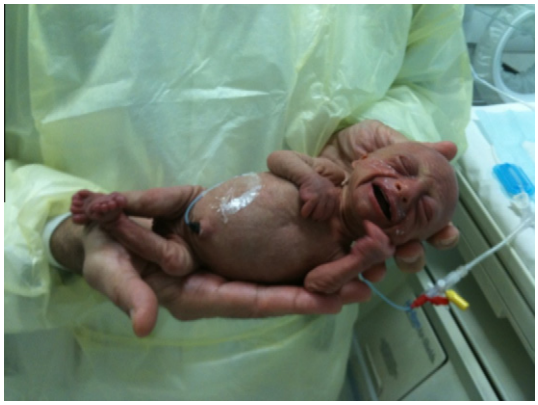

Figure 1 Photo of the baby at the age of 5 days. The baby was very small, with no eye lashes, no eyebrows and scalp hair.

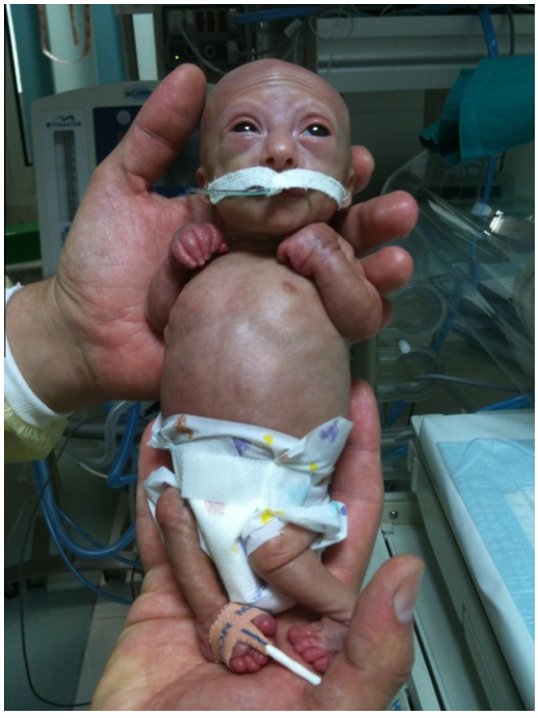

Figure 2 Photo showing the baby at the age of 4 weeks after recovery from klebsiella septicemia. There was clear left knee deformity with edema of the dorsum of both feet.

The baby had a stable course in NICU. She was weaned of O2 after 2 days. There was jaundice in the 2nd day of life, with border line exchange transfusion bilirubin level which responded to phototherapy. First line antibiotics (ampicillin and gentamycin) were stopped after 5 days according to our unit antibiotic policy and baby was on full oral tube feeding by the age of 2 weeks. By this age she developed klebsiella septicemia which was treated by antibiotics for 2 weeks and was

supported with O2 hood only without any need for mechanical ventilation. Investigations: included CBC, kidney and liver function tests, serum electrolytes all were within normal values. Metabolic screening by filter paper blood spot was also normal. Skeletal survey was reported by radiologist as normal (apart from clear joint deformities). Abdominal U/S: was normal. MRI brain showed: corpus callosum agenesis, large interhemispheric cyst measuring ($40 \times 12 \times 23$ mm) compressing the lateral ventricles and bilateral frontal areas of lissencephaly. Karyotype result was normal (46 XX). Torch screening for the baby and mother was negative.

3. Discussion

We reported this case because it is a very rare condition of MOPD I in which we found lissencephaly in association with interhemispheric brain cyst. Also the baby did not need any ventilatory support in spite of extreme low birth weight which was 580 g only. As mentioned in the literature the correct diagnosis of primordial dwarfism may not be made until time has been elapsed and it becomes apparent that the child has severe dwarfism [1]. The first impression when we saw this baby after birth was that she had progeria (with this senile facies and loss of scalp hair) although progeria is rarely presented in the neonatal period. After thorough examination and investigations we found that the baby has typical features of MOPD I which were mentioned in literatures [3]. Skeletal survey of our baby did not show bony changes found in primordial dwarfism, such as thinning of bones and widening of the ends of the long bones but clinically there was clear joint deformities in the knees. MRI brain showed corpus callosum agenesis and this is one of the findings in MOPD I in the previous reported cases but there was no brain aneurysms. The additional abnormalities which we found in the brain were the large interhemispheric cyst and lissencephaly. In 2002 Klinge et al. reported one case of micro lissencephaly in a case with MOPD syndrome [12]. In our baby we found also single palmer crease and single umbilical artery. In January 2008, Rauch Anita reported that mutations in the pericentrin gene (PCNT) were found to cause primordial dwarfism [13]. Pericentrin has a role in cell division, proper chromosomal segregation, and cytokinesis suggesting that this gene is important for normal growth. We could not do this genetic study; however the clinical findings in the baby were enough to give us diagnosis. As mentioned before some families have more than one child with MOPD type I [7]. This suggests that the disorder is inherited as an autosomal recessive pattern but our patient was the first baby for non consanguineous parents raising the possibility that it may be a sporadic case but this did not exclude the autosomal recessive pattern of inheritance.

References

[1] Fima Lifshitz. Pediatric endocrinology: growth, adrenal, sexual, thyroid, calcium, and fluid balance disorders; 2007 [Retrieved 07.01.11].
[2] Hall JG et al. Majewski osteodysplastic primordial dwarfism type II (MOPDII): natural history and clinical findings. Am J Med Genet 2004;130A(1):55–72.
[3] Bober MB et al. Primordial dwarfism type II (MOPD II): expanding the vascular phenotype. Am J Med Genet A 2010;152A(4):960–5.
[4] Majewski F, Ranke M, Schinzel A. Studies of osteodysplastic primordial dwarfism II: the osteodysplastic type II of primordial dwarfism. Am J Med Genet 1982;12:23–35.
[5] Sugio Y, Tsukahara M, Kajii T. Two Japanese cases with microcephalic primordial dwarfism: classical Seckel syndrome and osteodysplastic primordial dwarfism type II. Jpn J Hum Genet 1993;38:209–17.
[6] Shanske A et al. Central nervous system anomalies in Seckel syndrome: report of a new family and review of the literature. Am J Med Genet 1997;70:155–8.
[7] Microcephalic osteodysplastic primordial dwarfism types 1 and 3. Orphanet; November 2008.
[8] Majewski F, Stoeckenius M, Kemperdick H. Studies of osteodysplastic primordial dwarfism III: an intrauterine dwarf with platyspondyly and anomalies of pelvis and clavicles – osteodysplastic primordial dwarfism type III. Am J Med Genet 1982;12:37–42.
[9] Bongers EMHF et al. Meier–Gorlin syndrome: report of eight additional cases and review. Am J Med Genet 2001;102:115–24.
[10] Boles RG et al. Further delineation of the ear, patella, short stature syndrome (Meier–Gorlin syndrome). Clin Dysmorphol 1994;3:207–14.
[11] Russell A. A syndrome of intra-uterine dwarfism recognizable at birth with cranio-facial dysostosis, disproportionately short arms, and other anomalies (5 examples). Proc R Soc Med 1954;47(12):1040–4 [PMID 13237189].
[12] Klinge L et al. Microlissencephaly in microcephalic osteodysplastic primordial dwarfism: a case report and review of the literature. Neuropediatrics 2002;33:309–13.
[13] Rauch Anita et al. Mutations in the pericentrin (PCNT) gene cause primordial dwarfism. Science 2008;319:816–9.