SWISS SOCIETY OF NEONATOLOGY

Oro-facial-digital syndrome type II (Mohr-Claussen syndrome)

August 2014

Lustenberger A, Bär W, Scharrer B, Mann C, Neonatal and Pediatric Intensive Care Unit, Cantonal Hospital of Graubünden, Chur, Switzerland

Oro-facial-digital syndromes are a heterogeneous group of disorders characterized by oral, facial, and digital anomalies. At least nine variants have been described with differences in dysplastic features and genetic inheritance. Oro-facial-digital syndrome type-II (OFDS-II), also called Mohr-Claussen syndrome, is an autosomal recessive disorder (1). Facial and oral features include frontal bossing, facial asymmetry, broad nasal bridge, cleft upper lip, cleft palate, and a lobulated tongue (2). Digital anomalies include clinodactyly, syndactyly, brachydactyly, pre- and post-axial polydactyly and duplication of the first toe (2, 3). Additional features are conductive hearing loss, congenital heart defects, and renal abnormalities (4). Mental development appears to be normal (5). The diagnosis is based on clinical findings (6).

We report on a female neonate with Mohr-Claussen syndrome and compare the clinical findings with those of the more common oro-facial-digital syndrome type-I (OFDS-I) as well as other syndromes with similar features.

CASE REPORT

This full term female neonate was born to a G1/P1 at 39 weeks of gestation by spontaneous vaginal delivery. The parents are non-consanguineous. Pregnancy had been uneventful except for colonization with Group B streptococcus. The Apgar scores were 9, 10, and 10 at 1, 5, and 10 minutes, respectively. During the first 24 hours, repetitive cyanotic episodes were noted when bottle-feeding was initiated. Distinct facial features and 6 digits on both hands and feet indicated a syndromal disorder. The girl was referred to our neonatal intensive care unit for closer monitoring and further investigations.

Family history was positive for an atrial septal defect and mitral valve prolapse in the mother as well as an atrial septal defect in the maternal uncle and grandfather. The parents also reported that a cousin of the father suffered from polydactyly, an anomaly of the pharynx and mental retardation. No specific diagnosis had been made.

Clinical examination revealed polysyndactyly on both hands with broad thumbs as well as polysyndactyly on both feet with a broad first toe (Fig. 1, 2). Facial dysmorphisms included micrognathia, a cleft tongue and uvula, a thick frenulum, an angular form of the alveolar process of the mandible, hypertelorism, antimongoloid slanting and a broad nasal bridge (Fig. 3).

At this point, our clinical differential diagnoses in-

cluded Rubinstein-Taybi and Pallister-Hall syndrome. Broad thumbs and the prominent facial features were in line with Rubinstein-Taybi syndrome, whereas additional fingers and toes and cutaneous syndactyly are typical features of Pallister-Hall syndrome. For the latter, additional characteristics would have been a structural abnormality of the brain (i.e., hypothalamic hamartoma), as well as a bifid epiglottis, an imperforate anus, and kidney abnormalities.

MRI of the brain revealed no cerebral anomalies, especially no hamartomas. Laryngoscopy showed a bifid uvula, a thick epiglottis resulting in insufficient closure of the glottis and a discreet laryngitis. Ultrasound examinations of the kidneys and hips were normal. Conventional X-rays revealed post-axial polydactyly on both hands with short, broad, and partly dysplastic phalanges, as well as pre-axial polysyndactyly on both feet with duplication of the first toes (Fig. 4, 5). Echocardiography demonstrated a large secundum atrial septal defect. Genetic analyses revealed a normal female karyotype (46, XX) and molecular genetic testing was unremarkable. Based on genetic and clinical findings, OFDS-II was diagnosed.

The baby's subsequent clinical course was without complications. Despite structural abnormalities of the palate and tongue as well as the laryngeal malformation, normal feeding was possible with adequate weight gain. The laryngitis was felt to be a consequence of

persistent irritation from saliva and/or regurgitated gastric contents due to impaired function of the dysplastic epiglottis. Proton pump inhibitors were administered to avoid acidic reflux into the larynx. Cardiology follow-up confirmed moderate right ventricular volume overload secondary to left-to-right shunting across the ASD. The baby was discharged home on day of life 13. Follow-up visits with pediatric neurology were scheduled to assess the baby's neurodevelopment.

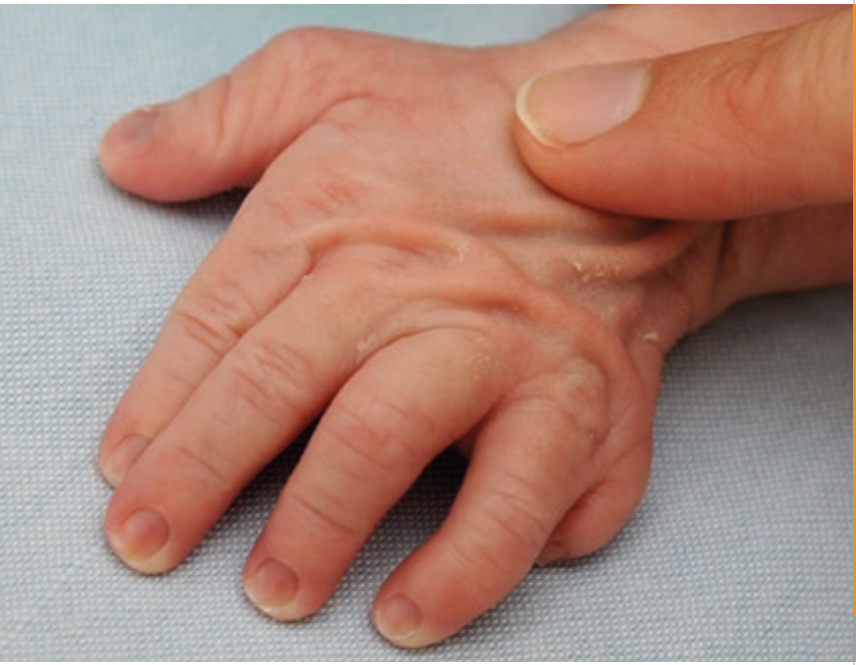

Fig. 1

Polysyndactyly of the left hand with a broad thumb.

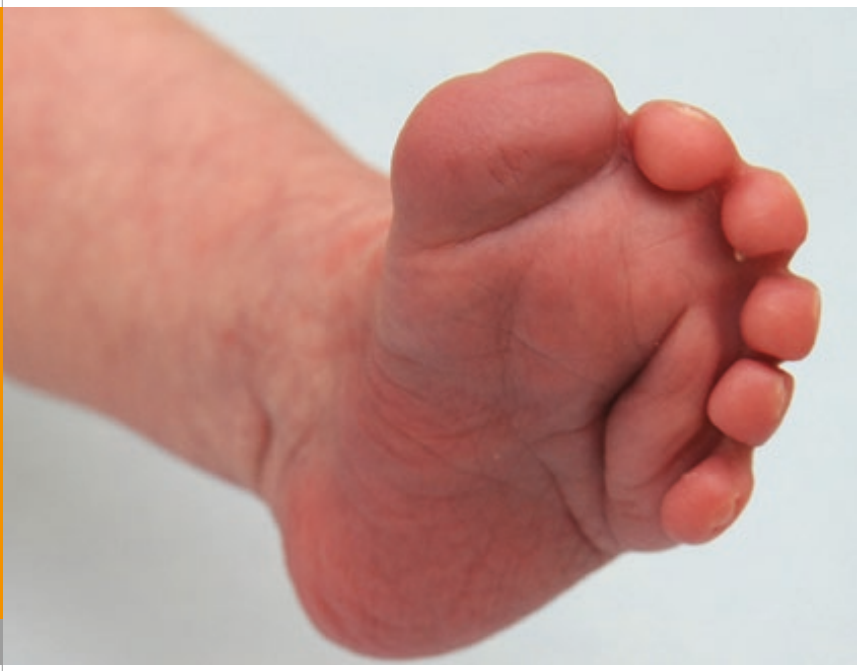

Fig.2

Polysyndactyly of the left foot with a broad first toe.

Fig. 3

Typical facial dysmorphisms: micrognathia, cleft tongue, thick frenulum, hypertelorism, antimongoloid slants and broad nasal root.

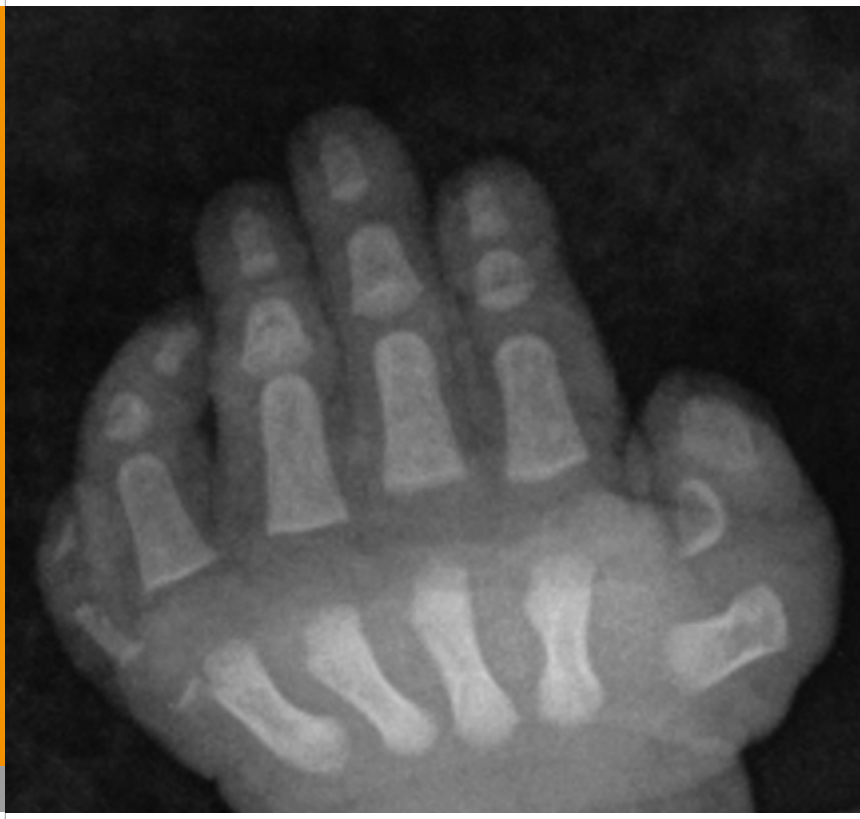

Fig. 4

Post-axial polydactyly on the left hand (extra digit is on the ulnar side of the hand) with short, broad and partly dysplastic phalanges.

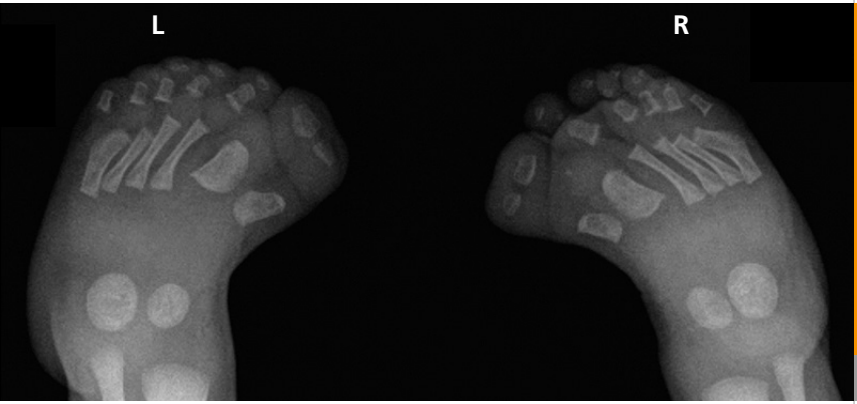

Fig. 5

Pre-axial polysyndactyly with duplication of the first toes on both feet (extra digit is on the side of the first toe).

DISCUSSION

Oro-facial-digital syndromes (OFDS) comprise a variety of different genetic disorders characterized by malformations of the oral cavity, maxillo-facial region, hands and feet. Mohr first described such phenotypes in 1941 (7). Based on different modes of inheritance and various phenotypes, at least nine different forms of OFDS can be distinguished; OFDS-I is the most common form and inherited as an X-linked dominant trait (8). In contrast, Mohr-Claussen syndrome (i.e., OFDS-II) is a rare autosomal recessive disorder (9), and its diagnosis is based on clinical findings (Table) (10). Patients with Mohr-Claussen syndrome have normal intelligence. Plastic surgery is indicated for cleft lip or palate, hypertrophic frenula and partial duplication of the hallux. Reconstruction of the auditory ossicles is indicated in order to improve conductive hearing impairment (6).

Because of variable clinical expression, even within an affected family, defining the specific form of OFDS can be difficult. Therefore, in order to make a correct diagnosis and offer appropriate genetic counseling, it is necessary to search carefully for any abnormalities typically associated with a specific form of oro-facial-digital defects (11).

In conclusion, any newborn or infant with structural abnormalities of face, oral cavity and digits should be evaluated for oro-facial-digital syndrome. OFDS implies a one in four risk of recurrence. Given the varia-

Nomenclature	Inheritance	Clinical manifestations
OFDS-I (Papillon-Léage-Psaume)	X-linked dominant (lethal in males)	**Oral** cleft lip and palate lobulated tongue tongue nodules (hamartomas) **Facial** hypertelorism **Digital** brachydactyly, syndactyly, clinodactyly reduplicated hallux **Others** cerebral abnormalities renal dysplasias mental retardation
OFDS-II (Mohr-Claussen)	autosomal recessive	**Oral** cleft lip and palate lobulated tongue micrognathia **Facial** broad nasal bridge frontal bossing **Digital** brachydactyly, syndactyly, clinodactyly, polydactyly reduplicated hallux **Others** conductive hearing loss congenital heart disease normal intelligence

Table

OFDS Type I and II: Inheritance pattern and main clinical characteristics.

bility of clinical features with possible involvement of internal organs, we suggest that every neonate with features attributable to OFDS are referred to a neonatal unit for further evaluation.

REFERENCES

1. Sakai N, Nakakita N, Yamazaki Y, Ui K, Uchinuma E. Oro-facial-digital syndrome type II (Mohr syndrome): clinical and genetic manifestations. J Craniofac Surg 2002;13:321-326

2. Ghossaini SN, Hadi U, Tawil A. Oral-facial-digital syndrome type II variant associated with congenital tongue lipoma. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2002;94:324-327

3. Biswas AA, Ghosh JKJ, Sinha MKRM, Basu KK, Chatterjee SS. Mohr-Claussen syndrome or oro-facial-digital syndrome (OFDS) type-II. J Pak Med Assoc 2009;59:484-486

4. Naiboglu B, Oysu C, Gokceer T. Orofaciodigital syndrome. Ear Nose Throat J 2012;91:E8-E9

5. Kalyan M, Kanitkar S, John R, Gireesh G, Bhate A, Mithun M. Oro-facial-digital syndrome type II. J Assoc Physicians India 2012;60:50-52

6. Martinot VL, Manouvrier S, Anastassov Y. Orodigitofacial syndromes type I and II: Clinical and surgical studies. The cleft palate (1994)

7. Mohr OL. A hereditary sublethal syndrome in man. Nor Vidensk Akad Oslo I Mat Naturv Klasse 1941;14:3-18

8. Hosalkar HS, Shah H, Gujar P, Kulkarni A, Yagnik MG. Mohr syndrome: a rare case and distinction from orofacial digital syndrome 1. J Postgrad Med 1999;45:123-124

9. Panigrahi I, Das RR, Kulkarni KP, Marwaha RK. Overlapping phenotypes in OFD type II and OFD type VI: report of two cases. Clin Dysmorphol 2013;22:109-114

10. Melnick M, Shields ED. Orofaciodigital syndrome type I: a phenotypic and genetic analysis. Oral Surg Oral Med Oral Pathol 1975;40:599-610

11. Gurrieri F, Franco B, Toriello H, Neri G. Oral–facial–digital syndromes: review and diagnostic guidelines. Am J Med Genet 2007;143A:3314-3323

concept & design by mesch.ch

SUPPORTED BY Takeda

CONTACT Swiss Society of Neonatology
www.neonet.ch
webmaster@neonet.ch