Mental retardation, distinct craniofacial dysmorphism, and central nervous system malformation: confirmation of a syndrome

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Abstract

We present a child with severe mental retardation, a central nervous system malformation, signs of ectodermal dysplasia, and a distinct craniofacial dysmorphism. Similar but less pronounced craniofacial features were present in the mildly mentally retarded mother. This observation confirms a previous report of a boy with the same MCA-MR syndrome and suggests X linked or autosomal dominant inheritance.

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Key words: mental retardation; craniofacial dysmorphism; CNS malformation.

Case report

At a gestational age of 20 weeks, a large biparietal diameter was noted on ultrasound. Delivery was at 32 weeks after premature rupture of the membranes. Birth weight was 2000 g (50th centile), length 46 cm (75th centile), and head circumference 35 cm (97th centile = 34.2 cm). Except for severe feeding problems, no other major problems occurred in the neonatal period. Multiple dysmorphic features were apparent at birth, including marked macrocephaly, with a large anterior fontanelle and frontal bossing. He had maxillary hypoplasia with a high palate, deep set eyes, and ptosis of the eyelids, more pronounced on the left (fig 1). The nasal septum was very short, the ears

were low set, and there was retrognathia. Later in life, retracted nipples were observed, with supernumerary nipples, two on the left and one on the right side. He had very long and slender fingers and toes and a pectus excavatum. The scrotum was hypoplastic with bilateral cryptorchidism and a normal penis. He had small teeth with severe enamel defects. The skin was thin and dry and he had dry, soft scalp hair. Nails and sweating were normal. At the age of 5 months, a perception deafness with 40 dB loss on the left side and 60 dB loss on the right side was recorded by means of brainstem evoked auditory responses. At the age of 14 months, a bilateral inguinal hernia was surgically corrected. Ultrasound of the kidneys was normal.

Swallowing difficulties persisted with marked drooling and recurrent aspiration pneumonia. Nasogastric tube feeding was needed until the age of 2 years. At the age of 3.3 years, there was failure to thrive, with weight 11.6 kg (3rd centile = 12.5 kg), length 91 cm (3rd centile = 93 cm), and macrocephaly with head circumference 55.3 cm (97th centile = 53.2 cm). The child is severely mentally retarded with absence of speech development and he is very hypotonic with little head control.

A CT scan of the brain at the age of 14 months showed a central nervous system malformation with agenesis of the corpus callosum, mildly dilated ventricles, and a small cerebellum (fig 2). Eye fundus was normal. Metabolic screening including plasma amino acids, lactate, ammonia, and pyruvate was normal. Thyroid function was normal. A karyotype on peripheral white blood cells was normal 46,XY after high resolution banding. X rays of the

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Figure 1 Craniofacial features of the patient at the age of 3.5 years.

Figure 2 CT scan of the brain showing agenesis of the corpus callosum and mildly dilated ventricles.

Figure 3 X rays of the legs showing the very thin, bowed fibulae.

Figure 4 Craniofacial features of the mother at the age of 28 years.

Figure 5 Craniofacial appearance of the patient reported by Fryns *et al.*¹

limbs showed a very thin fibula bilaterally, bowed on the left side (serpentine fibula) (fig 3).

This child is the first child of non-consanguineous parents. The mother is mildly mentally retarded. Her facial expression is hypotonic and she has similar but less pronounced dysmorphic features to her son (fig 4). She is also macrocephalic (head circumference 56.6 cm (97th centile), with frontal bossing and contrasting midfacial hypoplasia. The eyes are

deep set and she has retrognathia. The fingers are long and slender. Skin and hair are normal. Karyotype on peripheral white blood cells is normal 46,XX. The mother has five older brothers. One brother died accidentally and her father died from chronic bronchopulmonary disease. Her mother functions at a low-normal intellectual level. The four brothers are employed as unskilled labourers. They are not mentally retarded. These family members could not be examined personally, but judging from photographs they do not have similar dysmorphic features to the proband or his mother. The father of the child is mentally and physically normal.

Discussion

We present a boy with severe mental retardation, a distinct craniofacial dysmorphism, a central nervous system malformation, including agenesis of the corpus callosum, and signs of ectodermal dysplasia. The mother has the same facial dysmorphism, but less pronounced, and is mildly mentally retarded. Other family members do not have similar features nor mental retardation.

These features are identical to the patient reported by Fryns *et al.*¹ (fig 5), sharing the severe mental retardation, agenesis of the corpus callosum, ectodermal dysplasia, and craniofacial dysmorphism. Another patient was reported by Soekarman and Fryns² who also had severe mental retardation, hypotonia with feeding difficulties, and central nervous system malformations (dilated ventricles and partial hypoplasia of the cerebellum). Facial features were similar including a relative macrocephaly.

In the present patient, the clinical picture was dominated by the severe mental retardation with hypotonia and dysmorphic features. The signs of ectodermal dysplasia were less pronounced compared to the other reported patients.

Whereas these patients share major features, some variable associated findings are present. The present child has very thin and bowed fibulae, a finding absent in the other patients. Serpentine fibula is a rare finding, and has been reported in association with polycystic kidney disease as an apparently variable expression of Melnick-Needles syndrome.^{3,4} Hypothyroidism was present in the patient of Fryns,¹ but not in the present patient nor in the boy reported by Soekarman and Fryns.² The aetiology of this disorder is not known. The patient reported by Fryns *et al.*¹ was sporadic, whereas the mother of the second patient² possibly had minor signs of ectodermal dysplasia. In this family, the mother clearly shows the same facial dysmorphism as her son. She also has the same long and slender fingers and is mildly mentally retarded. The present observation of a disorder in both the mother and her son is compatible with a genetic disorder, either autosomal dominant (with variable expression) or X linked inheritance (with mild expression in a female carrier). In the present family, neither the maternal grandparents nor maternal uncles are

mentally retarded or have similar dysmorphic features, and therefore the family history does not help to distinguish between these two possibilities. The fact that the three reported patients are boys might be in favour of an X linked disorder. In conclusion, this observation confirms the existence of a specific syndrome with a distinct craniofacial dysmorphism, mental retardation, and agenesis of the corpus callosum.

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- 4 Majewski F, Enders H, Ranke MB, Volt T. Serpentine fibula-polycystic kidney syndrome and Melnick-Needles syndrome are different disorders. *Eur J Pediatr* 1993;**152**: 916-21.