LETTERS TO THE EDITOR

Anophthalmia with cleft palate and micrognathia: a new syndrome or an unusual presentation of Rubinstein-Taybi syndrome?

In the December 1994 issue of this journal I read with interest the brief paper "Anophthalmia with cleft palate and micrognathia: a new syndrome?" by Phadke et al. The authors described a male neonate with bilateral anophthalmos in association with Pierre-Robin anomaly, abnormal genitalia, and normal chromosomes. They discussed the differential diagnosis of X linked Lenz syndrome and proposed that their patient "represents a new syndrome of anophthalmia, cleft palate, and micrognathia". They also considered the possibility of a microdeletion of 14q as 14q22-23 deletions reported by Bennett et al and Elliott al presented similar clinical manifestations.

During the past few years an increasing number of other syndromes with clefting and microphthalmos/anophthalmos/micrognathia have been reported.1-10 The syndrome of macrosomia, microphthalmos ± cleft palate, and early infant death delineated by Teebi et al is an autosomal recessive multiple congenital anomalies syndrome. The association of uveal colobomata, cleft lip and palate, and mental retardation described by Kingston et al is apparently inherited as an autosomal dominant trait, and also Edwards et al documented vertical transmission of ocular defects, clefting, and dysmorphic features in a family.

In the past we have had the occasion to examine two unrelated male newborns shortly after their birth with an identical pattern of malformations (bilateral anophthalmos, Pierre-Robin sequence, hypoplasia grade II-III). They were referred with the possible diagnosis of X linked Lenz syndrome and caused us serious difficulties in final diagnosis and genetic counselling. Both were children of healthy, unrelated parents and were born after normal, term pregnancies. Birth weights were 2100 g and 2200 g, lengths 46 cm and 44 cm, and head circumferences 33 cm and 33.5 cm, respectively. CT scans of the brain were normal. The clinical suspicion of true anophthalmos without associated CNS malformations. High resolution chromosome studies showed a normal 46,XY male karyotype in both boys. We were not able to establish a final diagnosis in the neonatal period and followed them at regular intervals. Only after the age of 1 year did it become evident that both two patients shared a significant ocular and cleft palate anomalies and an early infant death: a new autosomal recessive syndrome. Clin Genet 1989;36:174-7.

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Pallister-Hall and McKusick-Kaufman syndromes

In their article Unniss et al describe a patient who, in addition to typical manifestations of Pallister-Hall syndrome (PHS) (hypothalamic hamartoblastoma, "central" polydactyly with Y shaped metacarpals), had hydrocolpos caused by vaginal atresia with vagino-urethral fistula. The authors proposed that their patient had McKusick-Kaufman syndrome (MKKS) and hypothesised that PHS and MKKS might be one entity.

Before genetic testing for verification of the specific diagnosis is available, the analysis of clinical manifestations in familial cases of any syndrome remains the best way for the precise delineation of its phenotypic characteristics. Familial cases of MKKS2 showed that neither preaxial nor central forms of polydactyly have been reported. I do not remember vaginal atresia in the familial cases of PHS.

These two manifestations in the patient of Unniss et al suggest another syndrome than MKKS.

Although anal atresia is one of the clinical manifestations of MKKS, the data by Reed and Grinscon do not confirm this because these authors described 26 patients with hydrodromocotropes, but only one or two of them had MKKS.

Virtually any defect may be a component of different syndromes. Hypothalamic hamartoblastoma, for example, has been described in cases with Varadi, Beemer-Langer, Meckel, distal monosomy 7q, and other syndromes.4-6 The same is true for hydrocolpos.7 Some syndromes overlap considerably with PHS, and MKKS is one of these.8 The patient reported by Unniss et al confirms this overlap, which "reflects similarity in chronology and topography of the primitive event".9 Although brain investigations in the patients with suspected MKKS should be done, there are no data confirming that PHS and MKKS may be one entity.
