SUPPLEMENTAL MATERIAL

Additional clinical information:

Patient 1

The propositus is an African-American male born at 38 weeks by cesarean section with vacuum suction because of fetal bradycardia. Birth weight was 2,330 g (<10th %centile), length 69.5 cm (50-75th %centile), head circumference 30 cm (<10th %centile), and Apgar scores were 7 and 8. The infant had low-set ears, proptosis, hypertelorism, and the skull bones were not palpable. A radiographic survey of the skeleton showed an ossification defect in the superior portion of the skull but no other skeletal abnormalities. At 2 mo the patient had a ligation of a patent ductus arteriosus. A CT scan of the skull with three-dimensional reconstruction performed at 9 mo showed lack of ossification in the superior portion of the frontal, parietal, and occipital bones. At 14 mo, his length and head circumference were below the 3rd centile, and his weight was at 10th %centile. A MRI showed thinning of the splenium of the corpus callosum and severe cortical dysplasia. At 8 yrs he had microcephaly, brachycephaly, downslanting palpebral fissures, bilateral ptosis, flat nasal bridge, low-set ears with pre-auricular pit in the right ear, undescended right testicle, and short stature. His ophthalmologic exam showed amblyopia and severe myopia. He also had generalized seizure disorder and ADHD. At 10 yrs he developed psoriasis involving the arms and legs.

His sister, mother and maternal grandmother all have tall foreheads, brachycephaly, hypertelorism, and a history of a “soft skull” at birth. His sister has ADHD and microcephaly. His sister and mother have myopia. Review of the mother’s medical report showed that the mother had parietal bone atresia. His mother reported that her fontanel closed spontaneously during childhood. Both the mother and the grandmother have normal growth and intelligence. The grandmother had unilateral breast cancer at age 35.

Lawson-Yuen *et al*. (2006) described a patient who had a small unique interstitial deletion of the long arm of chromosome 3 spanning 3q13.1q13.3. This patient had agenesis of corpus callosum, global developmental delay, and distinctive facial features of a small nose, anteverted nares, and broad nasal root. Deletions involving the proximal segment of 3q have been previously reported in only 8 patients. Considering the small number of cases and the fact that each had different breakpoints and deletions of different sizes, it is difficult to synthesize a common phenotype for proximal 3q deletions (Lawson-Yuen et al. 2006). Because four patients have agenesis of the corpus callosum and one has holoprosencephaly, Lawson-Yuen et al. (2006) suggested a possible locus for a gene involved in neuronal migration or formation of the corpus callosum in a minimal region of overlap among the affected patients with 3q13.2q13.3 deletion. The proband in our family (individual III-4) (Fig. 4) has thinning of the splenium of the corpus callosum.

Distinctive head shapes are described in four cases previously reported in the literature (2 with plagiocephaly, one with brachycephaly, and one with dolicocephaly) (Jenkins et al. 1985; Okada et al. 1987; Mackie Ogilvie et al. 1988; Genuardi et al. 1994); individuals III-4, III-5, II-5 and I-1 in our pedigree have brachycephaly. The delayed ossification of the skull present in individuals III-4, III-5, II-5 and I-1 is not described in other patients previously reported in the literature.

Interestingly, a previous descried patient with a similar 3q deletion also had a PDA (Arai et al. 1982), as was the case in individual III-4. Two other previously described patients with 3q deletion had PFO and Tetralogy of Fallot (Jenkins et al. 1985; Simovich et al. 2008).

Patient 3

Campomelic dysplasia, MIM 114290, is an osteochondrodysplasia caused by point mutations in *SOX9* on 17q24.3 or by chromosomal aberrations with breakpoints primarily centromeric of *SOX9* (Gordon et al. 2009). About 10% of the cases do not exhibit campomelia (angulations of the long bones), acampomelic campomelic dysplasia. Acampomelic campomelic dysplasia is more frequent in patients who survive neonatal period and is associated with translocations and breakpoints centromeric of *SOX9*. A diagnostically important aspect of campomelic dysplasia is male-to-female sex reversal that occurs in about two-thirds of affected 46,XY males. The published campomelic dysplasia/acampomelic campomelic dysplasia translocation breakpoints

centromeric of *SOX9* fall into two clusters: a proximal cluster 50-375 kb and a distal cluster 789 kb to 932 kb centromeric of *SOX9*. In a single CD case with a complex but balanced translocation, the 17q breakpoint is exceptional and maps ~ 1.3 Mb telomeric of *SOX9* (Gordon et al. 2009; Lecointre et al. 2009; Leipoldt et al. 2007).

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FIG. LEGENDS

Supplemental Fig. S1, 3;2 translocation - 4;2 junction fragment on der chr2

Supplemental Fig. S2, 3;2 translocation - 3;2 junction fragment on der chr3

Supplemental Fig. S3, 5;17 translocation - junction fragment on der chr5

Supplemental Fig. S4, 5;17 translocation - junction fragment on der chr17