Isolated postaxial polydactyly is an autosomal dominant hereditary trait that can be a feature of more than 80 mendelian or chromosomal disorders [Gorlin et al., 2001]. Polydactyly, in association with mental retardation, occurs in a number of syndromes, while the combination of these two features in the absence of other symptoms is rare [Castilla et al, 1998]. Here we report on two sibs manifesting mental retardation, postaxial polydactyly, and epilepsy, an association suggesting the diagnosis of Oliver syndrome [Oliver, 1940; Stevenson and Wilkes, 1983].

Patient 1 was a 19 year-old boy, the firstborn of healthy non-consanguineous parents. The mother had three spontaneous abortions, but the family history was otherwise unremarkable. The pregnancy was complicated by intrauterine growth retardation (IUGR). Delivery at term was normal, with a birth weight of 2350 g (<3rd centile), length 47 cm (3rd centile), OFD 32 cm (3rd centile). APGAR scores were 6 and 9 at 1 and 5 minutes, respectively. At 2 months of age, he developed generalized seizures, which were controlled by anticonvulsant drugs. Developmental milestones were delayed with an I.Q of 70 (Terman-Merril scale) at the age of 9 years. Since the age of 3 years he has undergone developmental and speech therapies.

The patient was first evaluated by us at the age of 18 years, when the family requested genetic counseling (Fig. 1). His height was 165 cm (3rd centile) (similar to the midparental height of 166 cm), weight was 67 kg (50th centile), and OFD 53 cm (10th centile). Slight body asymmetry was apparent, with a underdeveloped right side. Facial features were generally similar to those in his parents. However, he also had
prominent, thick eyebrows, malocclusion, high-arched palate, and rounded and prominent jaw. There was also a thoracic left convex lateral scoliosis. The hands showed postaxial scars. His clinical records noted that bilateral postaxial fingers had been surgically removed at the age of 8 years (rudimentary right finger and a left cutaneous appendix). He also had bilateral cutaneous syndactyly of fingers 2 through 5, clinodactyly of the fifth fingers, and fingertip pads. His lower limbs were normal.

Laboratory tests, including extensive metabolic studies, karyotype and FRAXA analyses were normal. A skeletal radiograph survey was unremarkable. A cerebral MRI disclosed thinning of the cerebral cortex in front of the ventricular collateral trigone.

Patient 2 was the 13 year-old sister of patient 1 (Fig. 2a). Pregnancy was uncomplicated, and delivery at term was normal. Her birth weight was 2850 g (10th centile), length 47 cm (3rd centile), and OFD 33 cm (10th centile). Her APGAR scores were 8 and 9, at 1 and 5 minutes, respectively. At 4 months she developed seizures, which were controlled by anticonvulsant drugs. Her psychomotor development was delayed, with an I.Q 68 (Terman-Merril scale) at age of 7 years. On physical examination, her height was 137 cm (3rd centile), weight 34 kg (10th centile), and OFD 50 cm (<3rd centile). Her body asymmetry was more marked compared to her brother. The left leg was 1 cm shorter compared to the right. She also had malocclusion, high-arched palate, thoracic right convex lateral scoliosis. She had postaxial polydactyly of the left hand, with a camptodactylyous extra digit, bilateral clinodactyly of the fifth fingers, cutaneous syndactyly of fingers 2 to 5, and fingertip pads (Fig. 2b). Postaxial polydactyly was also present on the right foot, with bilateral
brachydactyly of toes 3 to 5 (Fig. 2c). The speech was indistinct, faltering and scanty in expression.

Laboratory tests, including metabolic studies, karyotype and FRAXA analyses were normal. Skeletal X-ray disclosed postaxial polydactyly type A of the left hand and right foot, bilateral dysplasia of the fifth fingers and of the extra finger, bilateral symphalangism of proximal interphalangeal joints of fifth fingers, fusion of two phalanges and aplasia of distal phalanges of sixth finger, brachydactyly of toes 3 to 5 and fusion of two phalanges of sixth toe (Fig. 3). A cerebral MRI disclosed thinning of the cerebral cortex in front of the ventricular collateral trigone. The pattern profile analysis of the hand radiographs was unremarkable in both patients (data not shown).

The two sibs reported in the present study manifest a distinct and unusual syndrome of body asymmetry, postaxial polydactyly, mental retardation, and seizures. Although polydactyly is a feature of many recognized disorders, its association with mental retardation and convulsions as an accompanying major manifestations is rare. In 1940, Oliver described a family in which three of 11 children, including two females and one male, born to first cousin parents, had postaxial polydactyly of the hands and feet associated with mental retardation and indistinct, faltering and scanty speech [Oliver, 1940]. Regrettably, the clinical report was rather incomplete, thus precluding the possibility to determine if other minor features were present. Stevenson and Wilkes [1983] have described two sisters presenting with prominent jaw, severe mental retardation, postaxial polydactyly of hands, cutaneous syndactyly of fingers, and epilepsy. They concluded that these sisters had the same condition as that described by Oliver [1940].
Together with the two sibs reported here, not less than seven individuals in three families, including two consanguineous pedigrees, point to the existence of the Oliver syndrome of polydactyly and mental retardation. However, the review of published data suggests that the spectrum of features occurring in these subjects could be wider than originally recognized (Table I). Concordant features in all subjects were postaxial polydactyly, which in four individuals affected also the feet, and mental retardation, which is usually severe, with absent or indistinct speech. Similarly to isolated polydactyly, the polydactyly in Oliver syndrome demonstrates substantial interindividual and intrafamilial variability. Cutaneous syndactyly was noted in at least three patients, and occasional camptodactyly and clinodactyly of fingers have been recorded. Furthermore, the two sibs reported here had prominent fingertip pads. Brachydactyly and syndactyly of the toes was noted in three subjects. In general, facial features were not characteristic. Nevertheless, a prominent jaw was reported in the offspring of Stevenson and Wilkes [1983] and in the two sibs reported here. Based on the records of the family reported here, it seems that this feature is progressive. The two patients reported here and the affected sibs in the family reported by Stevenson and Wilkes [1983] manifested seizures with onset in the first months of life or in early childhood. We suggest that, together with polydactyly and mental retardation, seizures should be regarded as a feature of Oliver syndrome. We are unable to conclude if other characteristics, recorded less frequently, such as microcephaly (case 2), body asymmetry and malocclusion (cases 1 and 2) should be considered minor components of this syndrome. We suggest that the most likely mode of inheritance is autosomal recessive, based on parental consanguinity in the two previously reported families, and recurrence in offspring of unaffected parents, as
reported here.
REFERENCES


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