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CONGENITAL DEVELOPMENTAL DISORDERS

CLINICAL MANIFESTATIONS OF SOTOS SYNDROME

The major clinical criteria for the diagnosis of Sotos syndrome were evaluated by geneticists in a retrospective analysis of patients examined at the Children's Hospital, Goudi, Athens, Greece. These criteria were compared with those determined by meta-analysis of reports in the literature. Of a total of 22 patients (10 male and 12 female; aged between 2 months and 12 years) referred between 1996 and 2007 and initially enrolled in the study, 19 had typical Sotos syndrome; 3 with atypical facial characteristics were 'Sotos-like', (Douglas et al, 2003) and were excluded. All patients were re-evaluated regularly, including heart triplex ultrasonography and cranial MRI, and clinical findings were distinguished from those of similar overgrowth syndromes such as Weaver, and Beckwith-Wiedemann (Douglas et al, 2003). Molecular analysis was conducted later to confirm the diagnosis in some cases.

The criteria required for a diagnosis of Sotos syndrome in previous studies (Douglas et al, 2003) included a distinctive facial gestalt, height and head circumference >97th percentile, advanced bone age, and developmental delay. Of 19 patients in the present series, 6 met all required clinical criteria, 10 lacked one criterion, and 3 lacked two criteria. Facial features included prominent forehead, dolichocephaly, down slant palpebral fissures, hypertelorism, pointed chin, and premature teeth eruption. Typical facial gestalt and macrocephaly were present in all patients, overgrowth (>97th percentile) in 16, and advanced bone age in 12. MRI findings were abnormal in 14 patients, and included dilated ventricles (10/19), demyelination (5/19), and corpus callosum thinning (5/19). Genitourinary anomalies included cryptorchidism (4/19), and bladder diverticulae (2/19). Developmental delay was present in 16/19 cases, with severe mental retardation in 9. In the meta-analysis of 6 published series, facial gestalt was a constant finding, overgrowth and advanced bone age were strongly significant (P<0.001 and <0.009, respectively), and urinary malformations

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showed a slight increase in prevalence (P<0.042). The frequency of developmental delay, brain abnormalities, and congenital heart defect was not significant.

Sotos syndrome is a genetic disorder caused by NSD1 mutations or deletions. The diagnosis is based on two major clinical criteria, a typical facial gestalt and macrocephaly. Advanced bone age, height, and learning difficulties are not specific for Sotos syndrome, and occur in other overgrowth syndromes. (Leventopoulos G, Kitsiou-Tzeli S, Kritikos K, et al. A clinical study of Sotos syndrome patients with review of the literature. **Pediatr Neurol** May 2009;40:357-364). (Respond: Dr Leventopoulos, Fokidos 53, Goudi, Athens 11527, Greece. E-mail: levent2669@hotmail.com).

COMMENT. Sotos syndrome, or cerebral gigantism, was originally described as a syndrome of excessively rapid growth with acromegalic features and a non-progressive neurologic disorder (Sotos JF et al. **N Engl J Med** 1964;27:109-116). In early childhood, head circumference and height are >97th percentile, but after puberty, growth is normal. Neurologic defects include hypotonia, gait dyspraxia, developmental delay, mild mental retardation, and seizures, 50% febrile. NSD1 mutations, frequent in European-origin patients, and microdeletions, in Japanese, account for genotype-phenotype differences involving prevalence of overgrowth, and cardiovascular and urogenital malformations. (Nagai T et al. **J Med Genet** 2003;40:285-289). Clinically, the diagnosis of Sotos syndrome should be suspected in children born with typical facial features and macrocephaly, especially if these cardinal manifestations are associated with excessive growth, advanced bone age, mental retardation, congenital heart defect, or genitourinary anomaly.

DEVELOPMENTAL COORDINATION DISORDER IN SCHOOL-AGE CHILDREN

The prevalence of developmental coordination disorder (DCD) in children, at 7 years of age, in a large UK birth cohort was determined using DSM-IV criteria, in a study at the University of Bristol, UK; and Utrecht University, Netherlands. Children with neurologic disorders or IQ of <70 were excluded. By using tests that measured manual dexterity, ball skills, balance, handwriting skills and activities of daily living, 119 of 6990 children met criteria for DCD, with a prevalence of 1.7%, 17/1000 at a mean age of 7.5 years. The gender ratio was 1.8:1 male to female. When an additional 222 children with "probable DCD" were included, the risk of DCD was 4.9%. The risk of DCD was greater in children of lower socioeconomic backgrounds, birth weight <2500 g, and born at <37 weeks' gestation. DCD is an important often overlooked cause of disability in school age children. (Lingham R, Hunt L, Golding J, Jongmans M, Emond A. Prevalence of developmental coordination disorder using the DSM-IV at 7 years of age: a UK population-based study. **Pediatrics** April 2009;123:e693-e700). (Respond: Raghu Lingam MBChB, MRCPCH, University of Bristol, Dept Community-Based Medicine, Bristol B566JS, UK. E-mail: raghu.lingam@bristol.ac.uk).

COMMENT. A similar study using different measures of coordination was conducted in apparently normal schoolchildren born extremely preterm (<29 weeks or birth weight <1000 g) at Westmead Hospital, New South Wales, Sydney, Australia. (Goyen T-A, Lui K. **Arch Dis Child** April 2009;94:298-302). At age 8 years, the prevalence of DCD was 42% in