Stuve-Wiedemann Syndrome

Alternative Names
STWS
SWS
Schwartz-Jampel Syndrome Type 2
SJS2
Schwartz-Jampel Syndrome Neonatal
Stuve-Wiedemann/Schwartz-Jampel Type 2 Syndrome

WHO International Classification of Diseases
Congenital malformations, deformations and chromosomal abnormalities

OMIM Number
601559

Mode of Inheritance
Autosomal recessive

Gene Map Locus
5p13.1

Description
Stuve-Wiedemann syndrome, originally described in 1971, is a rare abnormality that belongs to the group of the bent-bone dysplasias and is characterized by bowing of the lower limbs, with internal cortical thickening, wide metaphyses with abnormal trabecular pattern, and campodactyly. Additional features include feeding and swallowing difficulties, as well as respiratory distress and hyperthermic episodes, which cause death in the first months of life. The rare survivors develop progressive scoliosis; spontaneous fractures; bowing of the lower limbs, with prominent joints and dysautonomia symptoms, including temperature instability; absent corneal and patellar reflexes; and smooth tongue.

This syndrome has been considered uniformly lethal until reports presented cases of patients surviving beyond three years. Some of these survivors were diagnosed as patients with Schwartz-Jampel type 2 syndrome. In addition to this, clinical and radiological overlap with Schwartz-Jampel type 2 syndrome has suggested that Stuve-Wiedemann syndrome and Schwartz-Jampel type 2 syndrome could be a single entity.

Skeletal abnormalities in Stuve-Wiedemann syndrome are so characteristic that an early post partum diagnosis can be made. However, a close cooperation between radiologists, clinicians, and geneticists is required for correlation of clinical and radiological findings.

Molecular Genetics
There is evidence that Stuve-Wiedemann/Schwartz-Jampel type 2 syndrome is caused by mutation in the leukemia inhibitory factor receptor gene. The leukemia inhibitory factor receptor gene encodes a 1,097-amino acid transmembrane protein that is composed of 6 different domains: 2 cytokine receptor homology domains, 1 immunoglobulin-like domain, 1 type III fibronectin domain with 3 modules, 1 transmembrane domain, and 1 cytoplasmic domain. The leukemia inhibitory factor is a polyfunctional cytokine that affects the differentiation, survival, and proliferation of a wide variety of cells in the adult and the embryo.

Epidemiology in the Arab World

Oman
Al-Gazali et al. (1996) reported 11 children in 5 families, four of Omani origin, with severe neonatal Schwartz-Jampel Syndrome. All presented at birth with skeletal abnormalities and feeding difficulties. Five had the typical pursed appearance of the mouth. Nine died from respiratory complications (5 in the neonatal period and 4 before 2 years of age). One (4 months old) remains hospitalized since birth requiring continuous oxygen supplementation and one (5 months old) requires nasogastric
tube feeding and has repeated attacks of aspiration. Al-Gazali et al. (1996) suggested that within the group of cases of neonatal Schwartz-Jampel Syndrome there is a subgroup with severe respiratory complications and early death. Brown et al. (1997) conducted linkage analysis in the two well-documented consanguineous families of Al-Gazali et al. (1996) for the critical region of 1p34-p36. No demonstrable linkage to chromosome 1 was found in either family. Although the markers were not fully informative in these families, it was clear that the affected subjects within each family had different haplotypes and that the results were not consistent with linkage to chromosome 1p34-p36. Brown et al. (1997) further extended their analysis to the ryanodine receptor gene (RYR) at the malignant hyperthermia locus on chromosome 19. Analysis of microsatellite markers covering chromosome 19 did not show any informative homozygosity. This was suggestive that patients in these two families had a disorder genetically distinct from the classical Schwartz-Jampel Syndrome.

Sudan
Al-Gazali et al. (2000) reported a Sudanese baby, born to first cousin parents, with congenital bowing of the long bones, camptodactyly, talipes equinovarus and radiological features resembling both Stuve-Wiedemann syndrome and Schwartz-Jampel syndrome type 2. There was a history of one miscarriage at two months gestation. The couple had two normal children. The affected baby had, in addition, agenesis of the corpus callosum and other non-specific dysmorphic features including microganthia, a short neck and low set ears. The baby developed respiratory distress after birth and died if respiratory complications. Al-Gazali et al. (2000) noted that the agenesis of the corpus callosum has not been reported in either Stuve-Wiedemann syndrome or Schwartz-Jampel syndrome type 2. They also suggested that the constellation of abnormalities in their case could represent a previously non-described syndrome.

United Arab Emirates
Al Gazali (1993) reported three sibs, two females and one male, of a family of United Arab Emirates origin with severe manifestation of Schwartz-Jampel Syndrome. The family consists of unrelated parents with a total of eight children. Two of these children survived until the age of three and four years respectively and one died at two years of age. The two older children, both females, died of overwhelming chest infections at 3-4 years of age. Both had, in addition to the shortening and flaring of the metaphyses, severe spinal deformity (kyphoscoliosis) and fragmented femoral epiphyses with rapid destruction on the right side in the older child. The younger male patient had multiple admissions because of failure to thrive and recurrent respiratory problems with laryngospasm. He died at the age of 2 years. In year 1996, the total number of children with neonatal Schwartz-Jampel Syndrome reported from the United Arab Emirates was estimated to be 14. Al-Gazali et al. (2003a) reviewed all cases of Stuve-Wiedemann/Schwartz-Jampel type 2 syndrome in the United Arab Emirates diagnosed over a period of 10 years (1993-2003) and said that 24 children from 13 families were seen in the Al-Ain Medical District. Most of these families were from either Oman [See also: Oman > Al-Gazali et al. (1996)] or Yemen [See also: Oman > Al-Gazali et al. (2003b)]. This was enough reason for Al-Gazali et al. (2003a) to indicate that Stuve-Wiedemann/Schwartz-Jampel type 2 syndrome is fairly common in the population of the United Arab Emirates and calculated the birth prevalence of this disorder as 0.52/10,000 births. In many of the families, a founder mutation in the Leukemia Inhibitory Factor (653_654 ins T) was identified (Dagoneau et al., 2004) [See also: Leukemia Inhibitory Factor Receptor > Epidemiology in the Arab World > United Arab Emirates > Dagoneau et al. (2004)].

Yemen
Al-Gazali et al. (2003b) reported three children from two inbred families from Yemen with Stuve-Wiedemann syndrome who had survived the first year of life; their ages were 6, 2.8, and 2 years. In all three children the skeletal abnormalities progressed to severe bowing of the long bones with prominent joints and severe spinal deformity. All exhibited neurologic symptoms including temperature instability with excessive sweating, reduced pain sensation with repeated injury to the tongue and limbs, absent corneal reflexes, and a smooth tongue. All three children had normal intelligence. Radiologic changes included undertubulation of the diaphyses, rarefaction and striation of metaphyses, destruction of the femoral heads, and spinal deformity. Al-Gazali et al. (2003b) confirmed that survival in this syndrome is possible and that the prognosis improves after the first year of life. It also supported the existence of a characteristic phenotype in Stuve-Wiedemann syndrome survivors which develops after the first year of life. This phenotype is characterized by progressive skeletal abnormalities, with distinct radiological
changes and characteristic neurological features similar to dysautonomia. Al-Gazali et al. (2003b) also noted that similar to all surviving cases of Stuve-Wiedemann syndrome, the three patients they described had an improved clinical course after the first year of life. The children were able to feed normally after the age of one year. However, these children exhibited temperature instability with either increased or decreased sweating associated with reduced pain sensation which resulted in repeated ulceration of the tongue and injuries to the limbs and associated secondary infection. Radiographs of the chest and skeleton of the three children were further reviewed by Langer et al. (2004) for classification of the underlying skeletal dysplasia. Skeletal radiographs revealed bowing of the long tubular bones, most pronounced at the lower extremities. The follow-up radiographs showed progressive bowing of the long tubular bones as well as progressive metaphyseal decalcification. Computed tomography was performed for further investigation of midface hypoplasia.

References

Contributors
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