Hydrocephalus due to Congenital Stenosis of Aqueduct of Sylvius

**Alternative Names**
HSAS
HSAS1
Hydrocephalus, X-Linked
HYCX
Aqueductal Stenosis, X-Linked
XLAS
Hydrocephalus, X-Linked, with Congenital Idiopathic Intestinal Pseudoobstruction

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

**OMIM Number**
307000

**Mode of Inheritance**
X-linked recessive

**Gene Map Locus**
Xq28

**Description**
Hydrocephalus comes from the Greek: "hydro" means water, "cephalus" means head. It is a condition marked by dilatation of the cerebral ventricles, most often occurring secondarily to obstruction of the cerebrospinal fluid pathways and accompanied by an accumulation of cerebrospinal fluid within the skull. Hydrocephalus is typically characterized by enlargement of the head, prominence of the forehead, brain atrophy, mental deterioration and convulsions. The disease may be congenital or acquired and may be of sudden onset or be slowly progressive.

X-linked hydrocephalus is the most common form of inherited, congenital hydrocephalus, with an incidence 1 in 30,000 male births. It is characterized by aqueductal stenosis, severe mental retardation and half of the affected individuals have flexion deformities of thumbs.

**Molecular Genetics**
X-linked hydrocephalus is caused by mutation in the gene encoding the L1 cell adhesion molecule, expressed in the developing central and peripheral nervous system. L1 is important in neuronal migration, axon growth, guidance, fasciculation, and synaptic plasticity. L1 is also expressed in nonneuronal cells such as the immune system, kidney, pigment cells, and a variety of cancers. It is a member of the Ig superfamily and binds to several extracellular ligands, as well as binding to itself in a homophilic manner. L1 is an integral membrane protein with six Ig domains, five fibronectin type III domains, and a highly conserved cytoplasmic tail. The first Ig domain supports binding to neurocan. The sixth Ig domain, which contains a RGD sequences, is capable of promoting neurite growth for some neurons by binding to an integrin or homophilically to L1 itself. The third FN domain also has an integrin-binding site. L1 also functions in repellent cell interactions with the first Ig domain binding to neuropilin to form a coreceptor for sema3a.

**Epidemiology in the Arab World**

**Kuwait**
Teebi et al. (1989) described an Arab child of consanguineous parents with the characteristic 'inverted' facial expression, i.e., when smiling or laughing, he appeared to be crying. Investigations at age 6 showed minor changes, indicating the probable importance of detecting the abnormality through the facial expression at an early age. In 1991, Teebi and Hassoon indicated that at age 8 the child still showed the inverted facial expression upon laughing, but also had renal changes as a consequence of a
neurogenic bladder in addition to hydrocephalus due to stenosis of the aqueduct of Sylvius. Teebi and Hassoon (1991) suggested that the association is not fortuitous and probably widens the spectrum of urofacial syndrome or represents a distinct entity mimicking the urofacial syndrome.

**Saudi Arabia**
Addar and Babay (2005) reported for the first time in the literature two families with recurrent congenital hydrocephalus each for the fourth time. The first showed evidence of X-linked recessive form, while the second was an autosomal recessive form.

**United Arab Emirates**
Al Talabani et al. (1998) studied the pattern of major congenital malformations in 24,233 consecutive live and stillbirth at Corniche hospital, which is the only maternity hospital in Abu Dhabi, between January 1992 and January 1995. A total of 401 babies (16.6/1,000), including 289 Arabs, were seen with major malformation. Single gene disorders accounted for 24% of the cases of which 3% were due to sex linked disorders. In their study, Al Talabani et al. (1998) observed two cases of Fabry disease in families from the United Arab Emirates. Recurrence was reported in the families. Al Talabani et al. (1998) concluded that their study was very close to representing the true incidence of congenital abnormalities in the whole United Arab Emirates, as they investigated over 98% of deliveries in Abu Dhabi, the capital of United Arab Emirates.

**References**

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