



Hennekam Lymphangiectasia-Lymphedema Syndrome

Alternative Names

Hennekam Syndrome

Lymphangiectasias Lymphoedema Type

Hennekam Type

Intestinal Lymphangiectasia-Lymphedema-
Mental Retardation Syndrome

WHO International Classification of Diseases

Diseases of the circulatory system

OMIM Number

235510

Mode of Inheritance

Autosomal recessive

Description

Hennekam syndrome is an autosomal recessive syndrome with lymphangiectasia, severe peripheral lymphedema, facial anomalies, seizures, mild growth retardation and variable mental retardation. Defective vascular and lymphatic development and consequent alteration in the fluid dynamics appear to disrupt critical events in craniofacial morphogenesis resulting in this phenotype.

Molecular Genetics

Several genes known to be involved in lymphangiogenesis have been excluded in Hennekam syndrome using linkage analysis. Among the important candidate genes for analysis, Prox-1 is expressed initially in a subpopulation of the vascular endothelial cells at the sites where the lymphatics bud off the veins and later becomes confined to the lymphatic endothelial cells. Prox-1 is required for both emergence of lymphatic endothelial cells from the veins and their differentiation towards the lymphatic phenotype.

Epidemiology in the Arab World

Oman

Al-Gazali et al. (2003) reported a male child of Omani first cousins with Hennekam syndrome. The pregnancy was normal and the delivery was by lower segment Cesarean section. At the age of two months he had abdominal swelling, edema and failure to thrive. Evaluation at seven years revealed a flat midface with a depressed nasal bridge, ascites and edema of the scrotum.

Palestine

Al-Gazali et al. (2003) described a male child born to inbred parents of Palestinian origin with Hennekam syndrome. The pregnancy was normal and delivery was by lower segment Cesarean section due to fetal distress. At the age of 2.5 years he presented dysmorphic features including a prominent forehead, flat occiput, mild ptosis, widely spaced and prominent eyes, epicanthic folds, down-slanting palpebral fissures, and a very flat midface with a depressed nasal bridge and a very small nose. At the age of six years he presented with generalized edema involving the face, scrotum, ankle, and feet. He also had delayed speech due to hearing impairment.

Tunisia

Al-Gazali et al. (2003) reported a female child born to Tunisian second cousins. She was the product of normal pregnancy and delivery. She had several dysmorphic features at birth including bossing of the forehead, a depressed nasal bridge, small dysmorphic ears and edema of the dorsum of hands and feet. At three months of age she presented with a wide anterior fontanelle, a prominent forehead with an open metopic suture, widely spaced eyes, a very flat and depressed nasal bridge, thin tented lips, small dysmorphic ears and preauricular skin tags. She was treated for diarrhea in the first two months of life and also had persistent vomiting. At 1 year of age she was hypotonic



with delayed milestones and had a bilateral severe conductive hearing loss.

United Arab Emirates

Al-Gazali et al. (2003) described a male child of first cousin parents from the United Arab Emirates with Hennekam syndrome. Both parents and all other children in the family were normal. He was the product of a normal pregnancy and normal term delivery. At birth he was noted to have puffy face with marked edema of the hands, lower legs, and dorsum of the feet, more on the left side than the right side. At two months of age he was admitted to hospital because of abdominal swelling. Since that time, he underwent repeated hospitalizations for shortness of breath and prolonged expiration on auscultation. At 9 years he presented a prominent occiput, widely spaced eyes, epicanthic folds, a flat face with a

depressed nasal bridge and a short nose, poor dental hygiene and a high, arched palate. Since anomalies of the veins and the consequent developmental abnormalities of the lymphatics might lead to alterations in the fluid balance of the embryo, Al-Gazali et al. (2003) hypothesized that altered fluid dynamics due to defective vascular and lymphatic development might disrupt critical events in craniofacial morphogenesis, resulting in Hennekam syndrome.

References

Al-Gazali LI, Hertecant J, Ahmed R, Khan NA, Padmanabhan R. Further delineation of Hennekam syndrome. *Clin Dysmorphol.* 2003; 12(4):227-32.

Contributors

Ghazi O. Tadmouri: 15.5.2005

