Menkes Disease

Alternative Names
MK
MNK
Menkea Syndrome
Kinky Hair Disease
Steely Hair Disease
Copper Transport Disease

WHO International Classification of Diseases
Endocrine, nutritional and metabolic diseases

OMIM Number
309400

Mode of Inheritance
X-linked recessive

Gene Map Locus
Xq12-q13

Description
Menkes disease is a neurodegenerative, recessive X chromosome linked disease of copper imbalance. The impaired copper transport leads to deficiencies in intestinal absorption of copper and in intracellular processing of copper in the central nervous system and connective tissues, where enzymes requiring copper as a cofactor no longer function properly. Clinical manifestations usually begin within the first 1–2 months of life and include abnormal kinky hair, eyebrows, and eyelashes, progressive cerebral deterioration, abnormal faces, ocular manifestations, connective tissue abnormalities, vascular defects, skeletal changes, bleeding diathesis, and a life span of three years. Menkes disease occurs worldwide at a rate of 1 individual per 100,000-250,000 live births.

Molecular Genetics
Menkes disease is caused by mutation in the gene encoding Cu (2+)-transporting ATPase, alpha polypeptide (ATP7A), which is a 1500 amino acid P type adenosine triphosphatase (ATPase). Structurally, it contains 17 domains - 6 copper binding, 8 transmembrane, a phosphatase, a phosphorylation, and an ATP binding, and is expressed in virtually all non-hepatic tissues. The ATP7A gene spans about 150 kb of genomic DNA, contains 23 exons, and is located on the long arm of the X chromosome at Xq13.3. Mutations in the ATP7A gene also cause the occipital horn syndrome.

Epidemiology in the Arab World

United Arab Emirates
Sztriha et al. (1994) reported two brothers who had typical clinical symptoms and laboratory findings of Menkes disease. The older one, 11 months old at the time of diagnosis, showed an EEG pattern of low amplitude and slow waves. Visual evoked potentials (VEPs) were absent; brainstem auditory evoked potentials (BAEPs) were abnormal. Regional cerebral blood flow (rCBF) studied by hexamethylpropyleneamine oxime single photon emission computed tomography (99mTc-HMPAO-SPECT) revealed reduced blood flow in both frontal and the right temporal regions. The younger boy, followed from birth, started seizures at the age of three months and had a hypsarrhythmia-like EEG. BAEPs were abnormal with prolongation of the latencies at the age of 12 months, while VEPs were near normal at 6 months, but disappeared by the age of 18 months. In addition, 99mTc-HMPAO-SPECT revealed an unexpected left parietal hyperperfusion.

References

Contributors
Ghazi O. Tadmouri: 11.5.2005