Adrenoleukodystrophy

Alternative Names
ALD
Addison Disease and Cerebral Sclerosis
Adrenomyeloneuropathy
AMN
Siemerling-Creutzfeldt Disease
Bronze Schilder Disease
Melanodermic Leukodystrophy

WHO International Classification of Diseases
Endocrine, nutritional and metabolic diseases

OMIM Number
300100

Mode of Inheritance
X-linked

Gene Map Locus
Xq28

Description
X-linked adrenoleukodystrophy is both the most frequent genetically inherited demyelinating disorder and the most frequent peroxisomal disorder. It affects about 1 in 20,000 males and shows extreme clinical heterogeneity, even within the same kindreds. The more severe form of cerebral adrenoleukodystrophy in 50% of the cases is associated with multifocal demyelination of the brain leading to death within a few years.

Adrenal insufficiency (Addison’s disease) is probably the only clinical manifestation of adrenoleukodystrophy while the main biochemical abnormality of adrenoleukodystrophy is an impairment of very long chain fatty acid (VLCFA) b-oxidation in the peroxisomes, which results in the accumulation of VLCFA cholesterol esters in the adrenal gland and in the white matter of the brain.

Molecular Genetics
The adrenoleukodystrophy locus has been mapped to Xq28, about 650 kb upstream from the color pigment genes. The adrenoleukodystrophy gene extends over 21 kb and comprises 10 exons. It encodes a 745 amino acid-long protein that has been found by immuno-electron microscopy to be present in the peroxisomal membrane and that might be involved in the import of VLCFA CoA synthase into the peroxisomal membrane.

Epidemiology in the Arab World

Lebanon
Sawaya et al. (1999) reported a case of adrenoleukodystrophy in a 26-year-old man, who developed adrenal insufficiency (Addison’s disease) at the age of 7, vitiligo at the age of 13 and severe ulcerative colitis at the age of 25 years, 1 year before the neurologic manifestations of adrenoleukodystrophy appeared. On presentation, the neurologic exam revealed an intact mental status with a refined intelligence and humor. Sawaya et al. (1999) reported that the development of ulcerative colitis was surprising considering its rare association with Addison’s disease. Sawaya et al. (1999) also noted that their patient’s brother and sister had VLCFA in their serum.

Saudi Arabia
Al-Essa et al. (2000) conducted a retrospective study to evaluate the data of 10 patients from Saudi Arabia with X-linked adrenoleukodystrophy regarding the clinical, biochemical, neuroradiological, and neurophysiological findings. Al-Essa et al. (2000) noted that the common presenting symptoms were deterioration in school performance, vision and hearing, behavioral changes, and seizures. Eight patients survived 1-4 years and one patient 12 years after the initial presentation, while one patient expired. Six
patients had the childhood form, 3 had the adolescent form and one had the adrenomyeloneuropathy form. Six are in an advanced stage of the disease and 3 have mild to moderate spasticity. All except 2 manifested moderate to severe dementia with variable degrees of visual loss. Decreased hearing and features of adrenal insufficiency were seen in 7 patients. Very long chain fatty acids were significantly increased in seven and mildly elevated in 2 patients, however the C26 to C22 ratio was increased in all. The characteristic high-signal intensity of parieto-occipital white matter on brain magnetic resonance imaging T2-weighted images was observed in all patients. Two patients had functional study of the brain, which showed hypometabolic activity in gray and white matter of the occipital lobes. Various neurophysiological abnormalities were detected. The response to different treatment modalities was not promising. Al-Essa et al. (2000) suggested that the disease is more common in Saudi Arabia than had been previously recognized due to phenotypic variability and a wide spectrum of presentations.

References

Contributors
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