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Article *in* Indian Journal of Clinical Biochemistry · September 2007

DOI: 10.1007/BF02913328 · Source: PubMed

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Indian Journal of Clinical Biochemistry, 2007 / 22 (2) 118-122

X-LINKED ADRENOLEUKODISTROPHY: PROFILES OF VERY LONG CHAIN FATTY ACIDS IN PLASMA AND FIBROBLASTS IN EIGTH SERBIAN PATIENTS

Sanja Grkovic, [1]Rajko Nikolic, Maja Djordjevic, Ljubomir Stojanov, [2]Snezana Zivancevic-Simonovic, [3]Gordana Djordjevic-Denic, Bozica Kecman

Department of Pediatrics , Department of Gynecology [1], Mother and Child Health Care Institute of Serbia, Belgrade, Serbia and Montenegro, [2]Institute of Pathological Physiology Medical Faculty Kragujevac, [3]Institute of Pathological Physiology Medical Faculty Belgrade

ABSTRACT

X-linked adrenoleukodistrophy is a severe neurodegenerative disorder with impaired very long chain fatty acid metabolism. The disease associated ABCD1 gene encodes a peroxisomal membrane protein which belongs to the superfamily of ATP-binding cassette transporters.We investigated eight male X-ALD patients diagnosed among 142 suspected patients referred for investigation. Plasma levels of very long chain fatty acids were measured at our laboratory using capillary gas chromatography. Eight cases of childhood X-ALD were diagnosed. This is the first published series of Serbian patients with X-ALD. In addition, diagnosis identifies carriers, which could be benefit for genetic counselling and prenatal diagnosis.

KEY WORDS

X-linked adrenoleukodistrophy, peroxisome disorders, very long chain fatty acids, capillary gas chromatography

INTRODUCTION

X-linked adrenoleukodistrophy (X-ALD; McKusick 300100) is the most frequent peroxisomal disorder, with an estimated frequency of 1:20,000 in males (1,2). It should be differentiated clinically and biochemically from neonatal ALD, an autosomal recessive disorder of peroxisome biogenesis in which the function of at least five peroxisomal enzymes is impaired.

The accumulation of VLCFA's in tissues of X-ALD patients results from their impaired capacity to degrade these substances. This reaction normally take place in a peroxisome as a part of the cell. The plasma concentration of very long chain fatty acids (VLCFA) is elevated in more than 99 % of males with X-ALD of all ages regardless of the presence or absence of symptoms. This assay is extremely specialized and therefore is perfomed only in a few laboratories worldwide.

Address for Correspondence :

Dr. Sanja Grkovic
Mother and Child Health Care Institute of Serbia ,
Ljeska 55, 11030 Belgrade,
Serbia and Montenegro,
E-mail: metlab@sezampro.yu

Patients with X-ALD lack one of the proteins required for this degradation. The protein that is missing or defective is called ALDP (X-ALD protein). X-ALD is due to mutations or defects in the gene that codes for ALDP. This gene is located on the X-chromosome (ABCD1 gene). Molecular analysis of the ABCD1 gene is available clinically (3). It is used primarily for genetic counseling for determination of carrier status in at risk female relatives and for prenatal diagnosis (4). Here we report the results of our study on the VLCFA profiles in specimens from controls and patients affected by X-ALD.

MATERIALS AND METHODS

Chemicals : Organic solvents such as chloroform, methanol, n-hexane, toluene and diethylether were the highest available grade including the standards of fatty acids were obtained from Sigma-Aldrich.

Biological samples : Plasma or serum: venous blood (with or without anticoagulant) 2-5 ml, is centrifugated for 10 min at 800 g, preferably within 1 h of collection to avoid hemolysis, and the plasma or serum is separated. The sample is stored at –4 °C or lower temperature until analysis can be performed.

Cultured fibroblasts: human skin fibroblasts were cultured in