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*Brief Clinical Report*

# Detection of a Rare Wilson Disease Mutation Associated With Arylsulfatase A Pseudodeficiency

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**We have studied a patient with Wilson disease (WD), belonging to a family segregating late-onset, dominant cerebellar ataxia. Analysis of the WD gene showed that the patient is a compound heterozygote, carrying the 14His1069Gln mutation from the father and the 8Gly710Ser mutation from the mother. The 8Gly710Ser is a mutation described previously only in a Swedish patient. Our patient is also homozygous for arylsulfatase A pseudodeficiency. This genetic defect, which has been reported in association with other neuropsychiatric syndromes, has not been described in WD. Am. J. Med. Genet. 85:175–178, 1999.**


**KEY WORDS: Wilson disease; neurological/psychological impairment; arylsulfatase A pseudodeficiency**

## INTRODUCTION

The Wilson disease (WD) disease locus, encoding a copper transporting P-type ATPase (ATP7B), has been assigned to chromosome 13 and several mutations have been identified [Tanzi et al., 1993]. The metabolic defect consists of insufficient biliary copper excretion with a gradual accumulation of copper, primarily in the liver and secondarily in the brain, kidneys, and other organs. The age of onset varies from childhood to early adult, with large variability of clinical manifestations. In some patients the main sign is early liver involvement, while in others neuropsychiatric changes may be evident, consisting of tremor or behavior abnormalities [Akil and Brewer, 1995].

We report on the clinical and molecular genetic analysis of a new case of WD with neurological/psychiatric involvement, belonging to a family in which several members had a late-onset, dominant cerebellar ataxia. DNA analysis of the patient demonstrated three different mutations, resulting in a compound heterozygosity at the WD locus and homozygosity for arylsulfatase A pseudodeficiency (ASA pd).

## CLINICAL REPORT

A 22-year old man with a 4-year history of behavior abnormalities, followed 2 years later by dysarthric speech and diffuse tremor, was admitted to our institute in July 1995.

There was no consanguinity in his family and both parents were of European origin. Several members on the maternal side of the family had a cerebellar disorder transmitted as a dominant trait, with onset in the fifth decade and death in the sixth decade of the life. They were followed elsewhere and had a diagnosis of Pierre Marie ataxia. Only two of them are still alive but unavailable for further clinical and molecular studies. The 46-year-old mother of the propositus is healthy.

The past medical history of the propositus was unremarkable. His initial symptoms were represented by psychological changes, treated elsewhere for 3–4 years with psychoactive drugs and psychoanalysis. On admission, the neurological examination showed mild ataxia, bradykinesia, dysarthria, generalized hypotonia, extrapyramidal tremor (greater on the right), and dysmetria. Neuropsychological evaluation showed anxiety with personality problems characterized by impulsivity and occasionally aggressive behavior.

Initially, we suspected a disorder similar to that de-

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