

ANALYSIS OF COLLAGEN IX GENES FOR MUTATIONS IN JUVENILE DISCOGENIC DISEASE

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Introduction

Juvenile discogenic disease (JDD) is characterized by lumbar disc degeneration and thoracolumbar Scheuermann's disease. Since genetic factors have been implicated in disc disease involving disc herniation and degeneration, they may also be important in JDD. Moreover, recent studies have shown an association of the tryptophan alleles in COL9A2 (Trp2) and COL9A3 (Trp3) with lumbar disc disease in the Finnish population.

Methods

Sixty-one patients with JDD were studied. The patients were referred to Center for Diagnostic Imaging for MRI imaging to evaluate symptoms of back and leg pain. The MRI examination of these patients revealed evidence of moderately severe Scheuermann's Disease and associated advanced degenerative disc disease in the lower lumbar spine consisting of dehydration, disc space narrowing, disc herniation and stenosis. Genomic DNA was extracted from blood samples and analyzed for sequence variations in the COL9A1, COL9A2, and COL9A3 genes that code for the α 1, α 2 and 3α chains of collagen IX. All 102 exons were amplified by PCR and scanned for mutations by CSGE. Samples containing heteroduplexes in CSGE analysis were sequenced.

Results

The analysis of the collagen IX genes in the 61 JDD patients resulted in an identification of 100 sequence variations. Most of them were likely to be neutral because they were found in equal frequencies in the controls. One patient had the Trp2 allele, and four had the Trp3 allele. Two new mutations that resulted in a substitution of an obligatory glycine residue (G302S in the α 1 chain and G102S in the α 2 chain) were identified. In addition, one patient had two unique variations that resulted in amino acid substitution in the α 3 chain, P61L and Q420R. Also, a putative branch-point mutation (IVS10-35A/T) was detected in COL9A1 in one patient. Furthermore, frequencies of two alleles in COL9A3, IVS6-22G/A ($p=0.002$) and E30+137C/T ($p=0.033$) differed significantly between the patient and control group.

Discussion

The results suggest that genetic factors may contribute to JDD. The study provided evidence for the role of collagen IX in this disease.