Characterization of the epidemiology and genetic basis for Dupuytren contracture

Kerstin Becker, Sigrid Tinschert, Katja-Martina Eckl, Serena Torres, The Dupuytren Study Group, Peter Nürnberg, Hans Christian Hennies

Dermatogenetics, Cologne Center for Genomics, University of Cologne, Cologne, Germany
Institute of Clinical Genetics, Technische Universität Dresden, Dresden, Germany
Cologne Excellence Cluster on Cellular Stress Responses in Aging-associated Diseases, University of Cologne, Cologne, Germany

Abstract

Hypothesis
Dupuytren disease is a multifactorial fibromatosis that causes progressive and permanent contracture of the palmar fascia with subsequent flexion contracture of the fingers. A strong genetic predisposition exists but few is known about the epidemiology and the molecular etiology and pathogenesis of the disease.

Methods
We have embarked on a comprehensive study to unravel the genetic factors involved in Dupuytren contracture. Clinical and epidemiological data were collected using a standardized questionnaire. DNA was extracted from blood samples, and RNA and fibroblasts were isolated from fresh tissue samples. Cultured cells were analyzed for the expression of myofibroblast markers such as α-smooth muscle actin before and after stimulation with transforming growth factor β. Association analysis and expression profiling are done using Affymetrix SNP and gene arrays.

Results
To date we have collected tissue and blood samples from 440 German and Swiss patients. 77 (18%) of the patients were females. 176 patients (40%) had a positive family background. In cases with positive family history both hands were affected in 64% as compared to 45% with no known family history. The mean age at first surgical treatment was 58 ± 13 years of age and ranged from 22-86 years. It was 58 ± 13 years in male and 60 ± 13 years in female patients. 32 patients also had knuckle pads and 27 patients showed plantar fibromatosis. 12% of the patients also had diabetes, 3% rheumatoid arthritis, and 1% epilepsy. We did not observe a clear risk factor, since about one third of the patients were (former) smokers and an association with alcohol abuse was not seen.

Summary
A first whole genome association study is under way and further large scale genetic and cell biological analyses will be performed in order to gain insight into the genetics and pathogenesis of Dupuytren contracture. Our findings will also contribute to the understanding of stress-induced and age-dependent changes in myofibroblasts.