Clinical and genetic features of Japanese patients with the vascular-type of Ehlers-Danlos syndrome


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Objectives: Vascular-type Ehlers-Danlos syndrome (EDS) is the most serious among the major types of EDS recognized. Vascular-type EDS (vEDS) is an autosomal dominant inherited disorder resulting from mutations within the α1 type III collagen gene (COL3A1) [1]. Recently, we analyzed the clinical characteristics, type III collagen production levels from cultured dermal fibroblasts, and identified mutations of COL3A1 in 16 Japanese patients with vEDS.

Methods: For quantification of the type III collagen production, fibroblasts were cultured with 3H-proline and the radio-labeled proteins were separated by SDS-PAGE, and the radioactive bands were detected by fluorography. Mutations in the COL3A1 were detected by cDNA analysis and subsequently by genomic DNA analysis.

Results: As for mutations of the COL3A1, glycine-substitution mutations were demonstrated in 8 patients (50%), and splice-site mutations of exon junctions, such as exon skips, in the remaining 8 patients (50%). The type III collagen production level in the cultured fibroblasts was 12.05% of the normal value, on average. In regard to the clinical manifestations, thin, translucent skin in 92.8% of the patients, extensive bruising in 87.5%, the characteristic facies in 78.5%, acrogeria in 40.0%, hypermobility of the small joints in 92.8%, pneumothorax in 50.0%, a positive family history in 46.6%, arterial rupture or dissection in 18.7%, and rupture of the gastrointestinal tract in 25.0%.

Conclusions: Half of mutations in the COL3A1 were splice-site mutations of exon junctions and the rest of those were glycine-substitution mutations. The analysis in the present series revealed a low frequency of cases presenting with serious clinical findings, such as rupture of the arteries or gastrointestinal tract. As these serious complications have been shown to increase with advancing age [2], future development of these serious complications among the patients of this series is very possible, because the mean age of the patients was relatively low (27.2 years) at the time of the analysis.

References