Tenascin-C and prolifeative arteriosclerosis in flexor tenosynovium of idiopathic carpal tunnel syndrome

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Introduction: Carpal tunnel syndrome (CTS) is the most common entrapment neuropathy. However, little is known about the pathophysiology. In contrast, recent MRI findings demonstrate that tenosynovial swelling within the carpal tunnel is the most common cause of CTS. Actually, researches to flexor tenosynovium in CTS have increased. Our previous study demonstrated proliferative arteriosclerosis with a breakdown of internal elastic membrane and neointimal formation in small arteries in the tenosynovium of CTS [1]. The purpose of the present study is to carry out a biochemical and histological study of the flexor tenosynovium so as to identify the roles of tenascin-C which has been often found to be involved both in tissue remodeling and in vascular hypertrophy in the pathogenesis.

Materials and Methods: Subjects: All patients signed an informed consent document, and the study was approved by the institutional review board. The study group consisted of 40 patients (12 men and 28 women) who underwent open surgical treatment for CTS. The patients' mean age was 53.2 years (range, 31 to 79 years). Patients with a history of diabetes mellitus, inflammatory arthritis, autoimmune disorders, thyroid abnormalities, or renal failure, were excluded. The patients were divided into 4 groups based on duration of disease: group A (n=9; <3 months); group B (n=12; 4-6 months); group C (n=6; 7-12 months); and group D (n=13; ≥12). Most of the patients in group D had had mild numbness in the median nerve distribution for years, however, abrupt worsening of their symptoms had led them to choose surgery.

Histological analysis: The specimens were cut into 5μm-thick sections, and stained with hematoxylin and eosin (HE) and elastica van Gieson. Immunohistochemical studies were performed with a polyclonal rabbit anti-tenascin-C antibody (MBL, Nagoya, Japan).

Morphometric analysis

Specimens were viewed using a BX50 microscope (Olympus, Tokyo, Japan) equipped with a video camera. Digitized images were provided on the screen of a computer and morphometric analysis was performed using Lumina Vision version 1.11 software for Windows (Mitani Shoji Co., Fukui, Japan).

A total of 40 fields containing small arteries with diameters of 50–400 μm were selected in specimens stained with anti-tenascin-C antibody in blind to clinical data of specimens. The percentage of tenascin-C-expressing areas in the arterial wall and connective tissue was calculated as the sum total of stained areas divided by the total area of arterial wall or connective tissue.

Statistical analysis

StatView 5.0 for Windows software (SAS Institute, NC, USA) was used for statistical analysis. Data were analyzed using Kruskal-Wallis Analysis and Mann-Whitney U test. Values of p<0.05 were deemed statistically significant.

Results: Histological abnormalities were noticed in the vessels, synovial lining, and loose connective tissue. Vessels were characterized by medial and intimal hyperplasia, changes that are similar to the proliferative arteriosclerosis associated with conditions such as malignant hypertension. Elastica van Gieson staining clearly revealed breakdown of internal elastic membrane and neointimal formation in small arteries in the tenosynovium of CTS (Fig. 1).

Tenascin-C expression by the vessels was correlated with disease duration in the morphometric analysis (Fig. 2a). In group A, although most vessels displayed normal architecture, diffuse and intense immunostaining for tenascin-C was noted in vessel walls (Fig. 3a). In group B, many small arteries displayed luminal narrowing due to hypertrophic remodeling and anti-tenascin-C staining was strongly confined (Fig. 3b). In group C, most vessels displayed marked medial and intimal thickening with severe luminal narrowing. Furthermore, tenascin-C staining was observed only in the hypertrophied intima (Fig. 3c). Although specimens from group D exhibited histological findings similar to group C, a noticeable difference in the anti-tenascin-C staining pattern was present between the two groups. In contrast to the uniformly low immunostaining for tenascin-C in group C, a fraction of small arteries in group D showed high and diffuse tenascin-C deposition.

Discussion: Our previous study showed that both tenascin-C are expressed intensely by the coronary artery after percutaneous transluminal coronary angioplasty and strongly induce neointimal formation [2]. These indicate that proliferative arteriosclerosis and vascular stenosis is caused by similar mechanism in CTS. On the other hand, tenascin-C's expression in the connective tissue was not found to be correlated with CTS duration. This indicates that the production of tenascin-C is regulated differently in different tissues. Gelberman et al. have demonstrated that in CTS intra-carpal tunnel pressure increases up to 30 mmHg, considered that the median nerve and the tendons including the tenosynovium are placed under high hydrodynamic pressure [3]. Jones et al. have demonstrated that tenascin-C gene expression can be mechanosensitive and that it occurs on most occasions at the level of the gene promoter [4]. Taken together, tenascin-C production in the connective tissue may be affected by mechanical stress.

References: