CREST Syndrome; A Changing Clinical Significance

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CREST syndrome was initially described by Frayha et al in 1973 (1). He stressed a high frequency of esophageal dysmotility in the CRST syndrome which was reported by Winterbauer (2) in 1964 and consisted of the associated findings of calcinosis, Raynaud’s phenomenon, sclerodactyly and telangiectasia. He concluded that CREST syndrome was a more informative designation than the CRST syndrome. Rodnan (3) used CREST syndrome as a subset of systemic sclerosis (SSc). Moroi et al (4) described anticentromere antibody (ACA) as a specific autoantibody for CREST syndrome in 1980. However, recently CREST syndrome falls within the limited cutaneous subset of scleroderma and the disease association of ACA is not only with CREST syndrome, but also with collagen vascular diseases including Raynaud’s phenomenon.

Most Japanese patients with CREST syndrome do not satisfy all 5 symptoms. In this issue of the Journal, Akiyama et al (5) defined the CREST syndrome as a form showing at least any 3 of 5 symptoms. Only 5 of 30 patients (17%) had all 5 symptoms, but 29 patients (97%) had ACA. See also p 451.

CREST syndrome is sometimes associated with primary biliary cirrhosis (PBC). During the past decade, the clinical interest of CREST syndrome has moved to PBC-CREST overlap syndrome from a variant of limited cutaneous scleroderma. In the article of Akiyama et al (5), 8 patients were diagnosed as overlapping with PBC confirmed by the liver biopsy. In 1971, Reynolds et al (6) proposed a new syndrome consisting of PBC together with scleroderma, Raynaud’s phenomenon, calcinosis cutis and telangiectasia, which was compatible with CRST syndrome. Patients with PBC often have another immune-related disease such as Sjögren’s syndrome, Hashimoto’s disease, or SSc including CREST syndrome. Twenty of 113 patients with PBC (18%) reported from the Mayo Clinic (7) had SSc and related syndromes including 9 with Raynaud’s phenomenon, 8 with CREST syndrome and 8 with diffuse scleroderma.

Shoji et al (8) reported that clinical and serological features of ACA-positive PBC-CREST overlap syndrome were different from ACA-negative PBC-CREST and PBC-non CREST patients. The frequencies of Raynaud’s phenomenon and asymptomatic PBC in ACA-positive patients were higher than ACA-negative PBC patients. The predominant HLA type in Japanese patients with PBC-CREST overlap syndrome is a controversial subject between this issue and another paper (9). The postulated autoimmune mechanisms behind these conditions are poorly understood. Recently, Mayo et al (10) reported that overrepresentation of one T cell receptor beta chain variable region, TCRBV3, was documented in patients with PBC and/or CREST. This study demonstrated that the T cell repertoire of patients with PBC and CREST was characterized by expanded clonal populations of CD8 (+) T cells. CREST syndrome is a unique variant of SSc because of high frequencies of ACA and PBC.

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References