Vascular Disease in Mixed Connective Tissue Disease (MCTD)

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Sharp et al first described mixed connective tissue disease (MCTD) in 1972 as a distinct entity of connective tissue disease (1). MCTD is a disease entity characterized by overlap symptoms of systemic lupus erythematosus (SLE), systemic sclerosis (SSc) and polymyositis/dermatomyositis (PM/DM), as well as by the presence of antibody to U1RNP. However, it has been suggested that rather than being regarded as a distinct disease entity, MCTD should be designated as undifferentiated connective tissue syndrome (2). On the other hand, several recent reports showed that MCTD was a distinct disease entity (3–5). Regarding a genetic markers, MCTD-associated HLA is distinct from the SLE- and SSc-associated HLA in Japanese and Caucasian patients (3, 6, 7). Furthermore, as a clinical feature of this disease, pulmonary hypertension (PH) is a characteristic organ involvement and is the most frequent cause of death, especially in Japan (8–10).

In MCTD patients with PH, the muscular type pulmonary arteries and arterioles exhibit fibrous intimal thickening and medial muscular hypertrophy. Some show marked luminal stenosis or fibrin thrombi (9, 10). A considerable number of flexiform lesions are present in some cases (10). These findings are similar to those of PH in SSc, which consist of concentric intimal proliferation, medial hypertrophy and a variable degree of myxomatous degeneration (11).

However, renal crisis with malignant hypertension and a high level of plasma renin activity is clinically very rare in MCTD as a SSc symptom. Renal crisis is the most severe organ involvement in SSc. The primary process is injury of the endothelial cells, which results in intimal thickening and intimal proliferation of renal intralobular and arcuate arteries. Inflammatory cells are conspicuously absent in the pathologic examination of these arteries. Renal crisis is clinically rare in MCTD, but Sawai et al (12) described renal histopathological findings of 25 autopsy cases of MCTD, in which obvious renal intimal thickening of interlobular artery was observed.

In this issue of the Journal, Yamaguchi et al report an interesting case of MCTD with renal crisis and PH (13).

See also 1250.

In this case the pathological findings of renal biopsy revealed severe renal intimal hyperplasia with mild glomerular changes, which was compatible to SSc renal crisis. It is very impressive that these vascular lesions, renal crisis and PH were clinically

improved by combining high-dose corticosteroid with cyclophosphamide infusion. In general SSc renal crisis and MCTD PH are not improved by these immunotherapy treatment.

This case may suggest that the pathogenesis of the vascular lesions of MCTD is different from that of SSc, although the pathological findings are similar. The vascular disease of MCTD may have a wide variety of pathogenesis. This speculation is very exciting.

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