Measuring serum aminoterminal type III procollagen peptide, 7S domain of type IV collagen, and cardiac troponin T in patients with idiopathic dilated cardiomyopathy and secondary cardiomyopathy

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Abstract

Objective—To identify new prognostic indicators in idiopathic dilated cardiomyopathy (DCM) and secondary cardiomyopathy.

Design and patients—Serum concentrations of aminoterminal propeptides of type III procollagen and the 7S domain of type IV collagen (7S collagen)—which have recently been used as indicators of collagen matrix turnover in other diseases—and of cardiac troponin T were measured in 17 consecutive patients with DCM and in four patients with secondary cardiomyopathy (one associated with hyperthyroidism, two with chronic renal failure, one with amyloidosis), confirmed by endomyocardial biopsy. The correlation of these variables with short term prognosis was then assessed prospectively.

Results—11 of the patients were positive for type III procollagen, 7S collagen, or troponin T even though their creatine kinase concentrations were within the normal range. These patients had a poor short term prognosis (p < 0.001).

Conclusions—Within the DCM and secondary cardiomyopathy groups, there was a subgroup of patients with raised concentrations of serum collagen and troponin T, for whom short term prognosis was poor. Although it is unclear whether these serum peptide levels reflect ongoing myocyte degeneration and interstitial fibrosis, they may serve as useful new prognostic indicators for cardiomyopathy.

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Idiopathic dilated cardiomyopathy (DCM) is a primary myocardial disease of unknown cause characterised by ventricular dilatation and impaired myocardial contractility. Although characteristics such as ventricular enlargement, New York Heart Association (NYHA) functional class, and haemodynamic abnormalities are helpful in determining the risk of cardiac events, the assessment of prognosis for an individual patient with cardiomyopathy remains difficult, so a more accurate marker reflecting the pathogenesis of DCM is needed.

Microscopic changes associated with DCM and secondary cardiomyopathy can be roughly divided into interstitial changes and myocyte degeneration. Although there has been little study of interstitial matrix turnover and ongoing myocyte degeneration in patients with cardiomyopathy, serum aminoterminal propeptides of type III procollagen (type III procollagen) and the 7S domain of type IV collagen (7S collagen) have recently been used as indicators of collagen matrix turnover in other diseases, while cardiac troponin T is thought to reflect myocyte degeneration. In this study, serum concentrations of type III procollagen, 7S collagen, and troponin T were measured, and correlations between these variables and cardiac event prognosis were assessed prospectively in patients with DCM and secondary cardiomyopathy.

Methods

Seventeen consecutive patients with DCM and four with secondary cardiomyopathy (one associated with hyperthyroidism, two with chronic renal failure, and one with amyloidosis) admitted to Hyogo Prefectural Amagasaki Hospital between September 1995 and February 1997 were included in the study. Cardiac catheterisation including coronary angiography, left ventriculography, haemodynamic studies, and endomyocardial biopsy was performed in all patients. No significant coronary stenosis was found in any of them. The criteria used for the diagnosis of DCM were based on the definition of the WHO/ISFC task force. None of our DCM patients had a history of infective myocarditis, metabolic disease,
ALT, alanine aminotransferase; AST, aspartate aminotransferase; BUN, blood urea nitrogen; left ventricular end diastolic volume index; EF, left ventricular ejection fraction.

Eleven of the 21 patients had significantly raised serum concentrations (shown in bold) of type III procollagen, 7S collagen, and troponin T (table 2). None of these patients had significantly raised serum creatine kinase. There was no correlation between haemodynamic variables and serum collagen concentrations.

Clinical follow up was performed for all 21 patients. Patients were treated with conventional diuretics, digoxin, or vasodilators. Use of angiotensin converting enzyme inhibitors did not appear to affect short term prognosis in this small group of patients. Patient 4 died unexpectedly six months after first being admitted to our hospital. Patient 6 developed heart failure requiring the addition of diuretic treatment after four months and was readmitted to hospital 16 months after her first admission. Patient 8 developed heart failure and required diuretic treatment or hospital admission after five months. Patient 10, with amyloidosis, died of cardiogenic shock nine months after his first admission. Patient 11 was admitted to hospital three times during the previous 12 months. Patient 14 died after seven months, just after ascending the stairs in her home. Patient 15, with cardiomyopathy secondary to chronic renal failure, was admitted to hospital three times during the previous 6 months.

The 10 patients who were seronegative for type III procollagen, 7S collagen, and troponin T were stable during the follow up period and required no additional drug treatment. The cardiac event-free rate for these seronegative patients was significantly higher than for the seropositive patients on day 216 (p < 0.001) (fig 1).
Troponin T in dilated cardiomyopathy

507

studies are needed to determine the pathological significance of serum type III procollagen and 7S collagen in patients with cardiomyopathy. The determination of serum creatine kinase concentration is a well established and widely accepted method for the laboratory diagnosis and follow up of myocardial infarction. Troponin T is a tropomyosin binding protein of the troponin regulatory complex located on the thin myofilament of the contractile apparatus. In our study, no patients with DCM or secondary cardiomyopathy were positive for creatine kinase. However, five patients were positive for troponin T. We previously demonstrated indium-111 antимyosin antibody uptake in patients with DCM, suggesting ongoing myocyte degeneration. Interestingly, the son of patient 6 was recently diagnosed as having hypertrophic cardiomyopathy, and patient 6 herself may have end stage hypertrophic cardiomyopathy resembling DCM. A rise in serum troponin T in patients with cardiomyopathy may suggest ongoing myocyte degeneration.

Discussion

DCM and secondary cardiomyopathy are characterised histologically by myocyte degeneration and interstitial changes. Although extracellular matrix turnover and ongoing myocyte degeneration in DCM have yet to be established and characterised, we measured serum type III procollagen and 7S collagen—recently developed markers of collagen matrix turnover, especially in patients with liver disease—along with serum troponin T concentrations in this study of patients with primary and secondary cardiomyopathy. Within the DCM and secondary cardiomyopathy groups, there was a subgroup of patients whose serum peptide concentrations were raised and for whom the short term prognosis was poor.

The procollagen type III aminoterminal peptide is an extension peptide of collagen type III. During the conversion of procollagen type III to collagen type III, type III procollagen is cleaved in a stoichiometric fashion and liberated into extracellular fluid. Type IV collagen, which is one of the major constituents of basement membranes and fibrous tissue, is composed of a 7S collagen domain formed by four aminoterminal ends linked together in an antiparallel arrangement, and a globular carboxyterminal cross linking domain.

Raised serum type III procollagen concentrations have been reported in patients with acute myocardial infarction and essential hypertension. In our study, 11 patients were positive for type III procollagen or 7S collagen.

These peptides are not tissue specific, and their cardiac origin remains speculative. However, none of our patients with DCM had significant lung, liver, or renal disease, nor was any relation found between pulmonary capillary wedge pressure, liver enzymes, serum creatinine, or blood urea nitrogen concentration and changes in serum type III procollagen (data not shown). It is unlikely that lung, liver, or kidney is the source of extracellular matrix proteins in our patients with DCM. Whether the serum levels of type III procollagen or 7S collagen reflect collagen matrix turnover is still unclear. However, we recently investigated a case of acute myocarditis following common cold symptoms with raised serum troponin T in the acute stage and raised serum type III procollagen in the chronic stage. Further studies are needed to determine the pathological implications of serum type III procollagen and 7S collagen in patients with cardiomyopathy.

Several patients showed evidence of ongoing or recurrent myocarditis in this small group of consecutive patients. Follow up serum samples from patient 1 (after eight months), patient 2 (after 12 months), patient 9 (after seven months), patient 19 (after two months), and patient 21 (after two months) remained negative for these peptides.

CONCLUSIONS

In summary, our prospective study revealed a subgroup of patients with DCM or secondary cardiomyopathy with raised serum type III procollagen, 7S collagen, or troponin T, whose short term prognosis was poor. It was notable that some patients had significant serum levels of troponin T, though theirCreatine kinase was within the normal range. These serum peptides may be useful additional prognostic indicators in patients with cardiomyopathy.

2 Risteli L, Risteli J. Noninvasive methods for detection of collagen matrix turnover, especially in patients with liver disease—along with serum troponin T concentrations in this study of patients with primary and secondary cardiomyopathy. Within the DCM and secondary cardiomyopathy groups, there was a subgroup of patients whose serum peptide concentrations were raised and for whom the short term prognosis was poor.

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