Pericardial involvement in systemic sclerosis

R J Byers, D A S Marshall, A J Freemont

Abstract

Objective—To determine the frequency and histological characteristics of pericardial involvement in systemic sclerosis.

Method—Necropsy sections of pericardium from 44 patients with systemic sclerosis were studied, together with sections from 19 age/sex matched controls. Sections were stained with haematoxylin and eosin, acid toluidine blue, and elastic van Gieson. Mast cells were counted in 10 random high power fields and the degree of fibrosis was quantified using a Chalkley count.

Results—Chronic pericarditis was seen in 31 (77.5%) of the systemic sclerosis cases, but in only one of the controls. The characteristic changes of uraemic pericarditis were not seen. The degree of fibrosis was greater in those with systemic sclerosis, though numbers of mast cells, thought to be important in fibrogenesis, were similar in both groups. Myocardial fibrosis was seen in 15 (37.5%) of systemic sclerosis cases but in none of the controls.

Conclusion—The incidence of pericarditis and myocardial fibrosis is much greater than in controls. The results indicate that pericarditis is a primary disease (rather than secondary to uraemia).

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count of 21.1 of 250 compared with 11.8 of 250 (p<0.05). The incidence of mast cells was also greater in those with systemic sclerosis, with a mean of 4.1 mast cells/10 hpf in the index group and 2.9/10 hpf in the controls, but the difference was not significant (p>0.05). Acute myocardial infarction was seen in three cases. Detailed postmortem reports were available in 16 cases, of which eight had confirmed renal failure, with uremia, at death.

Discussion

Systemic sclerosis causes visceral fibrosis and frequently results in cardiac failure caused by myocardial fibrosis. Pericardial involvement has been reported in between 33% and 72% of cases in necropsy series, and includes fibrinous pericarditis, chronic fibrous pericarditis, pericardial adhesions, and pericardial effusions. Most cases are asymptomatic, with premorbid symptoms being reported in only 7% to 20% of patients, though echocardiographic studies demonstrate the higher prevalence of subclinical pericardial involvement in systemic sclerosis. None of the previous reports has included histological assessment of the pericardium. Furthermore, though in most cases the pericardial changes seem to be primary, it has been suggested that in some cases they are secondary to uremia, which is frequently seen in end stage systemic sclerosis.

This study confirms the high incidence of pericardial disease reported previously. The inflammation was chronic in all the cases, with an additional neutrophilic infiltrate in two cases, and was accompanied by a significant increase in fibrous tissue compared with controls, in keeping with macroscopic reports of an increase in pericardial adhesions. The characteristic fibrinous exudate and acute inflammatory response seen in uremic pericarditis was seen in only two cases, one of whom had reported evidence of renal failure, and, in the subgroup of patients for whom necropsy reports were available, the degree of fibrosis was similar in those with reported renal failure and in those without (mean Chalkley counts of 15.3 and 14.5 respectively). This suggests that in most cases the changes seen resulted from primary pericardial involvement by systemic sclerosis rather than uremia.

Mast cells are thought to be important in the development of fibrosis in systemic sclerosis, via release of basic fibroblast growth factor and histamine, which may promote fibroblast proliferation, though other cells including lymphocytes also play a part. Increased numbers of mast cells have been reported in toluidine blue stained tissue sections of dermis of early skin lesions in systemic sclerosis, though the number was equal to controls in late cases, suggesting that the primary role is in the early phase of the disease. Toluidine blue detects only undegranulated mast cells. Recently a study using immunofluorescence to detect degranulated, ‘phantom’, mast cells demonstrated large numbers of degranulated mast cells in the dermis in systemic sclerosis. The same study found that mast cell degranulation precedes fibrosis, and indicated that degranulation is not specific for systemic sclerosis, but may occur in several other diseases. Although we found an increase in pericardial mast cells in those with systemic sclerosis compared with controls the increase did not reach statistical significance. The cases in this study were obtained at necropsy and had longstanding disease. Thus changes in mast cell number in early disease may no longer have been present. Alternatively, as the method used detected only granulated mast cells, it is possible that the number has been underestimated, and that larger numbers of degranulated mast cells are present, degranulation being precipitated by severe illness before death or the process of systemic sclerosis.

While our patients are a selected cohort of systemic sclerosis patients we believe this postmortem study has emphasised a comparatively common feature of the pathology of systemic sclerosis. That antemortem echocardiography has also shown a high incidence of pericardial involvement suggests that this finding is not restricted to those dying with the disorder. The pericardial changes are those of fibrosis and chronic inflammation, while mast cell numbers were not significantly different compared with normal controls. The pericardial changes are not typical of uremia and we believe they reflect primary involvement in the disease process rather than those secondary to uremia. The lack of increase in mast cells may reflect the late stage of the disease, or degranulation caused by severe illness in these cases.

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