Myocardial disease in systemic vasculitis and autoimmune disease detected by cardiovascular magnetic resonance

Sir, Cardiovascular disease is a major cause of morbidity and mortality in patients with inflammatory autoimmune and vasculitic diseases such as systemic lupus erythematosus (SLE) and Wegener’s granulomatosis (WG) [1, 2]. An increased prevalence of subclinical atherosclerotic disease on carotid ultrasound [3] and coronary Electron Beam Computed Tomography (EBCT) [4] has led to the suggestion that accelerated atherosclerotic disease may account for the high cardiovascular mortality and morbidity. In keeping with these observations, SPECT-myocardial perfusion imaging has identified abnormalities of perfusion in almost one-third of subjects with SLE but no history of coronary artery disease [5]. Non-atherosclerotic disease processes may also be important. Cardiovascular risk in systemic vasculitic disease is not well predicted by Framingham risk scores [6] and non-atheromatous cardiac abnormalities including valvular, myocardial and pericardial disease are frequently present on echocardiographic and post-mortem studies [7–9]. This suggests a more complex aetiology and a significant contribution from the alterations in immune function and inflammation.

We have performed contrast-enhanced cardiac magnetic resonance (CMR) imaging on 100 patients as part of a double blind randomized controlled trial investigating premature cardiovascular disease in early chronic kidney disease (CKD). All patients recruited into this study had no history of ischaemic heart disease and well controlled 24 hour ambulatory blood pressure (<130/80). The protocol was approved by South Birmingham Local Research Ethics Committee and patients gave written informed consent.

In participants with SLE and WG, we have identified a high prevalence of myocardial abnormalities. In 11 patients (7 females, 4 males, mean age 51 years) with quiescent SLE (7) or WG (4) there were five patients with late gadolinium enhancement (LGE) within the left ventricular (LV) myocardium. The appearance of enhancement was consistent but did not correspond to the pattern expected in ischaemic damage and was not specific to coronary artery territories. The LGE was mid-wall, with a diffuse distribution indicative of regional areas of fibrosis. One patient also had a confluent area of LGE in a sub-epicardial location typical of myocardial inflammation (Fig. 1). In all five patients, LV function, dimensions and mass were all within normal limits. In the remaining cohort of 89 patients with early CKD from other, non-vasculitic/autoimmune aetiologies, only two had evidence of LGE. One was sub-endocardial in distribution, typical of myocardial infarction. In the other case, a patient with focal segmental glomerulosclerosis (FSGS) had mid-wall LGE as seen in SLE and WG.

To our knowledge, this is the first report of mid-wall LGE on CMR in systemic vasculitic and autoimmune disease. The pattern and distribution of scarring suggests fibrosis rather than infarction, which might have been expected in view of previous SPECT data. The superior spatial resolution of MRI allows detection of scarring and myocardial characterization on contiguous 7 mm slices, which is not possible with SPECT and may explain why this observation has not been reported previously by other imaging techniques. It is, however, consistent with reports of myocardial fibrosis based on post-mortem observations [7, 8].

These observations raise the possibility that myocardial damage in SLE and WG is due to a combination of subclinical inflammatory and immunological processes rather than ‘conventional’ coronary artery disease alone. The distribution of scarring supports post-mortem studies, which have shown patchy myocarditis and myocardial fibrosis in both SLE and WG [2, 7]. Acute presentation with myocarditis is rare and is thought to occur only in those with active disease, usually in association with pericardial change. Our findings suggest that subclinical myocarditis in these conditions may be much more common than previously thought and may contribute to the high incidence of clinical cardiovascular events.

Mid-wall LGE has been reported in other myocardial diseases including hypertrophic cardiomyopathy, dilated cardiomyopathy and amyloidosis. There is no evidence that any of our patients had these disease processes including the single patient with FSGS.

Mid-wall LGE has recently been reported as present in a small proportion of patients with end-stage kidney disease [10]. The associated cardiovascular comorbidities of such patients make the significance of this finding unknown but an association with underlying inflammatory disease cannot be excluded.

In summary, while markers of atherosclerosis are well recognized in systemic vasculitis and autoimmune disease, we report the first case series of myocardial fibrosis using CMR in these conditions. This raises the possibility that immune mediated damage as well as atherosclerotic disease may contribute to myocardial injury in these patients.

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Does cardiovascular risk factor profile influence prescribing of non-steroidal anti-inflammatory drugs in a rheumatoid population?

SIR, There has been much recent debate on the cardiovascular (CVS) risks associated with the long-term use of traditional non-steroidal anti-inflammatory drugs (tNSAIDs) and selective cyclooxygenase 2 inhibitors (coxibs), and particularly whether the increased CVS risk associated with the use of rofecoxib [1] applies equally to the other coxibs and tNSAIDs [2–4]. As discussed in the recent editorial by Singh [5], while the American FDA has taken the clear step of treating the cardiovascular risk of all anti-inflammatories as equal [6], the EMEA and MRHA have not [7, 8]. Careful selection of patients without significant CVS disease or risk factors appears vital, especially in diseases such as rheumatoid arthritis (RA) with an inherent increase in CVS disease [9, 10].

In this study, we asked whether age, disease duration or risk factors for CVS disease influenced use of tNSAIDs and coxibs among RA patients. No distinction was made between initial prescription by a rheumatologist or a general practitioner. We reviewed the charts of 176 RA patients randomly selected from our nurse-led RA cardiovascular risk clinic, noting established risk factors and by data interrogation and telephone interviews with the patients, established an exact record of current and past use of tNSAIDs and coxibs.

176 RA patients (45 male, 131 female, median age 61.0 yrs (IQR 52.3–69.0), median duration of disease 11.5 yrs (4.0–21.0) were assessed. Forty (22.7%) had never taken any NSAID or COX-2, almost all, due to a history of peptic ulcer disease and were generally prescribed codeine-based analgesia instead. Sixty three (35.8%) were currently using a tNSAID, 47 (26.7%) a coxib and 66 (37.5%) were taking no prescribed anti-inflammatory drugs. Of those patients currently receiving tNSAID therapy, 22 (34.9%) had previously taken a coxib but had been ‘switched back’ to a tNSAID following the withdrawal of rofecoxib. Of the patients who had ever taken coxib therapy, 17 had taken rofecoxib, 52 celecoxib and 31 etoricoxib. Patients currently not taking any tNSAID or coxib were significantly older (66.0 yrs (59.5–72.0) vs 60.0 yrs (50.0–66.0) P < 0.01 than those currently using either coxib or tNSAID. They also had greater disease duration.

Risk factors for cardiovascular disease were defined as hypercholesterolaemia, hypertension, diabetes mellitus, family history of CVS disease in a first-degree relative, obesity (BMI > 30), smoking and having had a past history of ischaemic heart disease or stroke. The number of patients possessing each number of risk factors, compared with their present use of any anti-inflammatory drug, tNSAID or coxib is shown in Table 1.

Patients currently receiving no anti-inflammatory therapy had a higher number of CVS risk factors as compared with those taking either coxibs or tNSAIDs (median 3.0 vs 2.0, P = 0.06). There was, however, no significant difference between coxibs or tNSAID groups in terms of CVS risk, age, disease duration or any individual CVS risk factor.

These results underline the high frequency of cardiovascular risk factors in RA patients and the widespread use of tNSAID and coxibs in this group. The 22 patients in whom a switch back was made from coxibs to tNSAIDs represent a cross-section of the group in terms of CVS risk factors (11 had three or more risk factors, 11 had two or less), suggesting that perceived CVS risk did not always figure in the decision to change medication, even at a time when there was a perception (and indeed advice given from some sources to GPs) that tNSAIDs might be safer than coxibs. Finally, 19 of the 38 patients with four or more CVS risk factors remain on treatment with a tNSAID or coxib.

Following this audit and in light of current opinion on the CVS risks of tNSAID and coxibs, it has been our practice to re-assess all patients on anti-inflammatory medication at routine reviews. Alternatives, such as codeine-based products, or alterations to doses of disease-modifying drugs or corticosteroids are not always given.

TABLE 1. Cardiovascular risk factors in RA patients, compared with current use of any NSAID, traditional NSAID and selective COX-2 inhibitors

<table>
<thead>
<tr>
<th>Number of CVS</th>
<th>Number of RA patients</th>
<th>Number (%) of patients taking any anti-inflammatory</th>
<th>Number (%) of patients taking traditional NSAID</th>
<th>Number (%) of patients taking coxib</th>
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