Reviewer's report

Title: Case report: Scleroderma with crescentic glomerulonephritis

Version: 4 Date: 13 September 2007

Reviewer: PETER HEWINS

I am familiar with the literature and believe that this case meets one of the 7 criteria for evaluation in the journal: An unexpected association between diseases or symptoms

Has the case been reported coherently?: Yes

Is the case report authentic?: Yes

Is this case worth reporting?: Yes

Is the case report persuasive?: Yes

Does the case report have explanatory value?: No

Does the case report have diagnostic value?: No

Will the case report make a difference to clinical practice?: Yes

Comments to authors:

General
The authors present an unusual case of crescentic glomerulonephritis complicating systemic sclerosis. This is an uncommon concurrence and the case demonstrates that presumptions about the cause of impaired kidney function can be misleading, even where there is ‘classical’ associated renal syndrome (scleroderma renal crisis in this instance). Consequently, adequate investigation is paramount in patients with renal failure, especially those with rapidly deteriorating kidney function. As such this report should be of interest to a general audience, particularly those involved in the care of patients with systemic sclerosis.

Revisions necessary for publication
I believe that at present, the explanatory and diagnostic value of this case report is limited and that the following deficiencies should be addressed by the authors to correct this:

1) It would be helpful to briefly outline and/or reference diagnostic criteria for scleroderma and systemic sclerosis. Given the presence Raynaud’s phenomenon, acroosteolysis and Scl 70 autoantibodies in this patient, limited
cutaneous systemic sclerosis may more accurately describe her condition. Diagnostic precision is especially relevant here since one might speculate that this patient has some form of overlap syndrome with features of systemic sclerosis and SLE. It would also be useful to mention or reference features of systemic sclerosis which are associated with scleroderma renal crisis (e.g. prednisolone usage). For example see Vonk MC et al Ann Rheum Dis 2007;66;1129-1131 and Penn H et al Q J Med 2007; 100:485–494.

2) Blood pressures (at initial presentation and 11 months later when presenting to the nephrologist) and the presence or absence of fundoscopic evidence of accelerated phase hypertension should be described.

3) It would be opportune to emphasize the utility of estimated GFR (eGFR) which is becoming widely reported alongside serum creatinine. Although the MDRD formula was not designed with reference to an Asian population, it is probably still useful: eGFR in this instance was 38 ml/min at presentation, demonstrating that in fact the patient already had significant kidney dysfunction at that time. Accordingly, it would worth pointing out that there were good grounds for performing a kidney biopsy at presentation (after controlling BP) and to have done so might well have altered the outcome. eGFR formulas are not intended for use in acute renal failure.

4) I assume that further autoantibody tests were not performed, however, it would very helpful to briefly discuss additional tests that could have assisted diagnosis in this instance. Anti-dsDNA antibody testing would be particularly informative since these autoantibodies are closely associated with proliferative lupus nephritis and although the patient does not fulfil diagnostic criteria for SLE, it is clear that some patient’s present with lupus nephritis in the absence of other features. Again this raises the possibility of an overlap syndrome involving systemic sclerosis and SLE. Furthermore, anti-PR3 and anti-MPO antibody testing (by immunoassay) would have helped to clarify the inconclusive results of the ANCA immunofluorescence. I appreciate that these tests may have been unavailable in this instance but it appropriate to indicate that supplemental immunoassay testing is recommended for all patients with suspected small vessel vasculitis and in particular for all sera with an antinuclear antibody (ANA) that could mask an ANCA. (See “International consensus statement on testing and reporting of antineutrophil cytoplasmic antibodies (ANCA)” Savige J et al. Am J Clin Pathol 1999; 111:507–13 or Paspaliaris B et al J. Clin. Pathol. 2000;53:774-777). Additionally, testing for circulating anti-glomerular basement membrane antibody is important in patients presenting with acute renal failure that may be due to glomerulonephritis.

5) Crescentic glomerulonephritis describes the pathological correlate of the clinical syndrome rapidly progressive glomerulonephritis but neither term defines the immunopathogenesis which it is essential in define in order to select appropriate therapy (Jennette JC Nephrol Dial Transplant 2001 16(suppl 6): 80-82 and Jennette JC Kidney International 2003 63: 1164–1177). Pathologically the lesion can be categorized as pauci-immune, immune complex mediated or anti-GBM (linear glomerular staining) mediated. I recommend that the authors
briefly describe or tabulate important causes of crescentic nephritis. In the developed world, ANCA-associated vasculitis is the leading cause followed by anti-GBM nephritis with other causes including lupus nephritis and crescentic IgA nephritis (Henoch-Schoenlein purpura). It might be helpful for the authors to indicate to what extent they believe this pattern is representative in their country. One anticipates that post infectious GN and MPGN/cryoglobulinaemic GN associated with hepatitis C infection may be more prevalent in some regions.

6) Furthermore, the current histopathologic description is rather inadequate making it difficult to determine the precise diagnosis. It is conventional (and informative) to describe the % of glomeruli affected by crescents and it would be particularly helpful to describe the presence or absence of glomerular hypercellularity and its composition (mesangial proliferation is mentioned in the legend), glomerular thrombosis or necrosis, subepithelial deposits (crescentic variants of membranous nephropathy) and the pattern of immunostaining (e.g. linear or granular). Are the glomerular lesions predominantly segmental or global?

7) There should be some additional short comment about the treatment of crescentic nephritis. The isolated use of methylprednisolone is rarely successful except possibly in post-infectious GN. For diseases such as ANCA-vasculitis, anti-GBM disease and proliferative lupus nephritis, combination therapy with corticosteroids and cyclophosphamide is typically required. Plasma exchange is used as an adjuvant therapy in selected cases (anti-GBM disease and severe ANCA-vasculitis) and newer alternatives including mycophenolate mofetil and Rituximab (ANCA-vasculitis and lupus nephritis) are currently being assessed in randomized trials.

8) Another important differential diagnosis to mention in this case is bilateral renal artery stenosis (RAS) which should be considered in all patients presenting with deteriorating kidney function after ACEI therapy. Indeed acute renal failure due to RAS but mistaken for scleroderma renal crisis, has been described (Morris K et al Nephrol Dial Transplant (1994) 4: 1489-1491).

9) Finally, it would be appropriate to mention nephrogenic systemic fibrosis (nephrogenic fibrosing dermopathy) a recently described condition with features of systemic sclerosis that develops in patients with advanced kidney disease, apparently in association with gadolinium exposure. The risk appears to be greatest in individuals with a GFR <30 ml/min and restricted use of gadolinium enhanced MRI has been recommended.


The current background could be revised and abbreviated to accommodate some of these points.

What next?: Revise and resubmit
Quality of written English: Acceptable