Case report

IgA nephropathy associated with ankylosing spondylitis: occurrence in women as well as in men

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SUMMARY Two patients (one male, one female) with ankylosing spondylitis (AS) and IgA nephropathy are described. The female patient is the first reported case to have AS and IgA nephropathy concurrently. Contrary to previously reported cases, her renal manifestation preceded her rheumatic symptoms. It is suggested that women with IgA nephropathy and AS may be overlooked as the severity of spondylitis and joint involvement is less than in men.

Key words: sex ratio, HLA-B27.

Ankylosing spondylitis (AS) is characterised by chronic inflammation of vertebral articulations and adjacent soft tissue. Classical AS occurs predominantly in men with a male:female ratio of 3–4:1, though sacroiliitis itself occurs with a sex ratio of approximately 1–2:1.^{1–3} Glomerulopathy associated with AS is uncommon, but it has recently been recognised that IgA nephropathy may be associated with AS. To our knowledge 22 men with AS and IgA nephropathy have been reported, yet no female patient has been described. In this report we describe the clinical findings in two patients (one male, one female) who had both AS and IgA nephropathy and review the other 22 cases previously reported.^{4–14}

Case reports

CASE 1

A 33 year old hypertensive Chinese housewife was referred for investigation of proteinuria (2 g/day). She had experienced two attacks of pharyngitis and macroscopic haematuria eight years previously.

Investigations showed microscopic haematuria with dysmorphic red blood cells and a glomerular filtration rate of 20 ml/min. Serum cryoglobulin, anti-nuclear factor, and hepatitis B surface antigen were not detected. The anti-DNA antibody and serum complement components were normal and the serum IgA concentration was raised (4.6 g/l). An intravenous urogram showed bilaterally smooth and shrunken kidneys. The tissue type was HLA-A11, Aw33, B17, B27, DR5, DRw6.

Renal biopsy showed global sclerosis in 50% of glomeruli. Of the remaining glomeruli, 20% had segmental sclerosis and 30% had segmental mesangial proliferation with cellular crescent formation. The tubules showed widespread foci of atrophy and the vessels demonstrated medial proliferation and thickening. Immunofluorescence studies showed intense staining for IgA (3+) and C3 (3+) with weaker reaction for IgM and IgG. Subsequent immunofluorescence studies with fluorescein conjugated human anti-HLA-B27 antiserum failed to demonstrate positive mesangial fluorescence. Electron microscopy showed electron dense deposits in the mesangial areas.

Two years later she developed accelerated hypertension and end stage renal failure requiring regular haemodialysis. During the 24 months before her dialysis she noticed frequent low back pain. Later

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she had increased right sacroiliac and left hip pain. The serum concentrations of calcium, phosphate, alkaline phosphatase, and parathyroid hormone were normal, and radiological skeletal examination did not indicate hyperparathyroidism or osteomalacia. There were, however, grade III changes in the right sacroiliac joint and grade I changes in the left sacroiliac joint (New York criteria).¹⁵ A radionuclide scan showed increased uptake in the right sacroiliac joint.

CASE 2

A 22 year old normotensive male Chinese student with a history of AS was referred for investigation of painless macroscopic haematuria. He had low back pain and left sacroiliac pain resulting in limping for two years. A Schober test suggested decreased spinal mobility. Radiological examination showed grade III changes in the left sacroiliac joint and grade II changes in the right sacroiliac joint.

Investigations showed microscopic haematuria with dysmorphic red blood cells, no proteinuria, and a glomerular filtration rate of 75 ml/min. Serum cryoglobulin, antinuclear factor, and hepatitis B surface antigen were not detected. The serum complement components were normal and the serum IgA concentration was raised (4.2 g/l). An intravenous urogram showed normal sized kidneys. HLA-B27 antigen was identified.

Renal biopsy showed diffuse mesangial proliferative glomerulonephritis with normal tubulointerstitial and vascular structure. Immunofluorescence studies demonstrated strong staining for IgA (3+) and C3 (3+). Immunofluorescence studies with fluorescein conjugated human anti-HLA-B27 antiserum failed to demonstrate positive mesangial fluorescence. Electron microscopy showed electron dense deposits in the mesangial areas.

The rheumatic symptoms were treated with non-steroidal anti-inflammatory agents, and the renal function remained unchanged in the 12 months following the renal biopsy.

Discussion

An association between the seronegative spondyloarthropathies, particularly AS, and IgA nephropathy has been suggested.^{6 11 16} The concurrence of IgA nephropathy and AS is unlikely to be caused by chance alone. A selective increase in serum IgA during clinical exacerbation of arthropathy^{12 17} and an increased incidence of recurrent haematuria have been observed in patients with AS. Furthermore, raised levels of circulating immune complexes have been recorded in both AS and IgA nephropathy.^{18 19}

Our two patients with primary IgA nephropathy proved by biopsy, had clinical and radiological evidence of sacroiliitis. Definite AS according to the New York criteria was met in the male patient while the female patient was classified as probable AS. Bone pain in patients undergoing haemodialysis is often interpreted as a symptom of renal osteodystrophy or β_2 microglobulin related erosive arthropathy.²⁰ As AS in women tends to present with peripheral joint involvement and is associated with less dramatic spinal changes²¹ its diagnosis is more difficult, especially when the women is receiving maintenance haemodialysis.

IgA nephropathy associated with AS is uncommon. Table 1 summarises the pooled data of 22 previously reported cases.⁴⁻¹⁴ IgA nephropathy associated with AS is characterised by a higher incidence of raised serum IgA (93%), a higher incidence of renal impairment at presentation (27%) and a lower incidence of macroscopic haematuria.

Table 1 Clinical features of 22 patients with IgA nephropathy and ankylosing spondylitis*

Clinical feature		Remarks
Mean age (years)	30 (range 15-55)	Five adult patients, age not specified
Sex (M:F)	22:0	
Positive HLA-B27	14/14	Not mentioned in eight patients
Raised serum IgA	14/15	Not mentioned in seven patients
Impaired renal function	6/22	One receiving dialysis
Renal manifestations		
Proteinuria and microscopic haematuria	14	
Proteinuria	4	
Microscopic haematuria	3	
Macroscopic haematuria	1	
Onset of ankylosing spondylitis		
Antedated renal manifestation	19	
Coincided with renal manifestation	2	
Developed after renal manifestation	1	

*Data collected from references 4-14.

compared with other IgA nephropathy without AS.¹⁹ All patients are positive for HLA-B27 and AS antedates the renal manifestation of IgA nephropathy in most. All previously reported patients are male despite the fact that the prevalence of AS in men is only three times that in women.¹⁻³ Our female patient is the first reported woman with concurrence of IgA nephropathy and AS. A possible explanation for the rarity of women with IgA nephropathy and AS may be that the diagnosis of AS is often missed as the severity and spinal involvement are less than in men; these clinical differences could make the diagnosis of AS more difficult in women.¹⁻³ Furthermore, in women with AS rheumatic symptoms are apparent about 10 years later than in men (peak 30-40 years).²¹ Hence, instead of presenting with AS, as do most male patients, our female patient first presented with haematuria rather than rheumatic symptoms as the peak age of manifestation of IgA nephropathy is usually between 20 and 30 years.²²

We suspect that women with IgA nephropathy associated with AS may often be overlooked as the initial rheumatic symptoms are mild. It is important to recognise this condition in patients undergoing dialysis as the symptoms may often be misinterpreted as renal osteodystrophy or erosive arthropathy. The management and prognosis of these diseases are quite different.

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