

## IgA nephropathy associated acute kidney injury with ankylosing spondylitis and HLA-B27 positive: a case report

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### Abstract

We are reporting a rare case with ankylosing spondylitis (AS), renal impairment with IgA nephropathy. Here, we discuss the course of diagnosis. A 32 year-old man with bilateral pain of the sacroiliac joints for 5 years and leg swelling for 10 days.

A Diagnosis of AS by HLA-B27 and pelvic X-ray tests, pathological diagnosis and IgA nephropathy based on renal biopsy. We administered methylprednisolone 500 mg/d for 3 consecutive days, followed by methylprednisolone 40 mg oral QD for a month. The patient was followed up once a month. In the sixth month, the patient's serum creatinine had decreased to 0.96 mg/dL, urine microalbumin creatinine ratio decreased to 173.3 mg/g, and albumin had risen to 33.1 g/L. Pain and morning stiffness were relieved. Although the causal relationship between AS and IgA nephropathy in this patient still needs to be established. In clinical practice, patients with AS need to be screened for renal complications.

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**Key words:** Ankylosing Spondylitis (AS), Acute Kidney Injury (AKI), Renal Biopsy, HLA B 27, IgA nephropathy.

### Introduction

Ankylosing Spondylitis (AS) is the major subtype and a main outcome of an interrelated group of rheumatic diseases, which is named spondyloarthritis now.<sup>1</sup>

Recent specialists believe AS is an advanced stage of axial spondyloarthritis, which can be identified by a combination of clinical symptoms and established radiographic changes.<sup>2</sup> Inflammatory back pain is the principal clinical feature of AS, caused by sacroiliitis and inflammation at other locations, including the axial skeleton, peripheral arthritis, and extra-arthritis organs, for instance, anterior uveitis, heart, and kidney.<sup>3</sup> Renal complication accounted for 8.1-21.7% in extra-arthritis events<sup>2</sup>, it can lead to chronic or end-stage renal disease.<sup>4</sup>

Recent studies investigated renal involvement in AS primarily according to urinary analysis. Clinicians observed that about 8.1-44.7% of AS patients were found abnormality in urinalysis, and microscopic hematuria was the most frequent finding in urinalysis for AS patients, but usually intermittent during follow-up, only in 10.5% patients were assumed glomerular hematuria.<sup>2,5</sup>

Therefore, abnormality in urinalysis has not always been the truth. Acknowledged, renal biopsy was the golden standard of diagnosis for the overwhelming majority of renal parenchyma disease, including nephropathy relevant to AS; meanwhile, it provided more information for physicians to choose an appropriate therapy plan and estimate the individual prognosis. However, considerably fewer reports have investigated the pathological characteristics and renal outcomes of AS patients with renal impairment. In addition, renal biopsy was performed in a handful of patients, while the

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observations were conflicting and controversial.

A 32-year-old male patient with concurrent IgA nephropathy and ankylosing spondylitis is described. He had HLA-B27 antigen. Renal involvement is considered to be very rare. Eighteen such cases reported are reviewed, and a possible common genetic or other pathogenesis discussed.

### Case report

A 32-year-old man presented with a 5 year history of recurrent pain in his cervical, thoracic spine and bilateral sacroiliac joint pain with bilateral leg swelling which was accompanied by high erythrocyte sedimentation rate (ESR), C-reactive protein, and gammaglobulin levels.

The joint disease progressed (low back pain, morning stiffness, restriction of spine mobility, asymmetric arthritis of low extremities), and bilateral sacroiliitis was detected by X-ray. Rheumatoid factor was negative. The condition was diagnosed as ankylosing spondylitis (AS), and the patient was treated with oral indomethacin, plaquenil, and sulfasalazine. Following respiratory infections, pain exacerbated and prompted the use of non-steroidal anti-inflammatory drugs (NSAIDs). There was no history of ocular and skin lesions, urethritis, and bowel disease.

At the time of admission, physical examination revealed a thin man (160 cm, 49 kg) of typical stooped posture, with increased thoracic kyphosis and cervical forward flexion, pitting edema (grade 2) in bilateral lower extremities and limited lumbar lateral flexion. His spinal motion was markedly limited in all directions: Schober's test 10-11.5 cm, maximal lateral flexion with only 2% decrease in body height and fingertip-floor distance of 55 cm. Chest expansion was 1 cm. Tenderness was discovered over the sacroiliac joints and along the thoracic and lumbar spine. Quick compression on both cristae iliaca elicited moderate pain in the sacroiliac region.

Patient presented with puffy face with bilateral leg swelling and his blood pressure was 160/95 mm Hg.

Laboratory examination showed that the erythrocyte sedimentation rate (ESR) was 109 mm/h, human leukocyte antigen (HLA)-B27 was positive, C-reactive protein was high. The antinuclear antibodies and rheumatoid factor were all negative. Urinalysis showed the presence of proteinuria (4+), with microscopic hematuria, urine protein quantitation (5.78 g/24 h), urinary microalbumin/creatinine (6,715 mg/g), serum creatinine (1.5 mg/dL), triglyceride was 2.04 mmol/L, cholesterol was 9.06 mmol/L, and uric acid was 523 umol/L. Hepatitis B/C and HIV serology were all negative. High immunoglobulin IgA and IgM with normal globulin, IgG, complement C3 and C4. Chest x-ray showed no pulmonary edema and cardiomegaly. The ECG revealed sinus tachycardia and left atrial enlargement. X-ray of sacroiliac joints and spine showed changes typical of ankylosing spondylitis. Serum concentrations of calcium, phosphate, and alkaline phosphatase were normal. Antinuclear antibodies, rheumatoid factor, and hepatitis B surface antigen were negative, ultrasound of renal systems revealed normal sized kidney with mild echogenic cortex.

A renal biopsy demonstrated mild mesangial proliferative glomerulonephritis with focal tubulointerstitial damage. There were three glomeruli of which two showed mild proliferation of mesangial cell and matrix and one moderate mesangial proliferation. The glomerular basement membranes were thin and smooth without shrinkage as is frequently seen in hypertensive patients. Focal tubular atrophy with mononuclear infiltrations was observed in the interstitium. Diffuse granular deposits of IgA(2 +), C3( +) and fibrinogen (±) were found in the mesangium by immunofluorescence microscopy; (fig. 1); deposits of IgG and C1q could not be identified.



Figure 1: Patient with ankylosing spondylitis



Figure 2: Chest X-ray showed that the thoracic vertebrae underwent a bamboo-like change, but there was no narrowing of the intervertebral space.

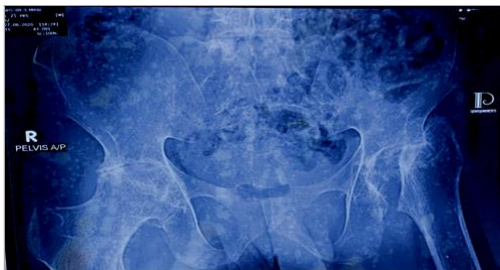


Figure 3: X ray pelvis with both hip joints (AP view ) showed old fracture left femoral head and posterior displacement, bilateral degenerative sacro-ileitis and obliterated joint spaces.

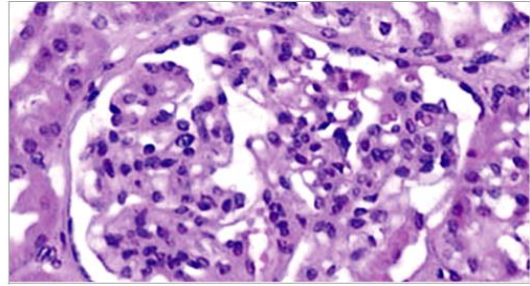


Figure 4: Glomerular tuft with mild global mesangial hypercellularity; direct immunofluorescence demonstrated diffuse mesangial IgA deposits.

During hospitalization, the patient's generalized edema became worse, Albumin decreased to 12 g/L, and creatinine rose to 2.1 mg/dL. Methylprednisolone (500 mg/d) was given for 3 consecutive days, followed by methylprednisolone 40 mg oral QD. One month later, the patient reported that her pain had disappeared completely. The microalbuminuria/creatinine ratio decreased to 4606 mg/g, while albumin increased to 26 g/L.

The patient was followed up once a month. In the sixth month, the patient's serum creatinine decreased to 0.96 mg/dL, urine microalbumin/creatinine decreased to 173.3 mg/g, and albumin rose to 33.1 g/L. Pain and morning stiffness were relieved, and the BASDAI score dropped to 4.0.

### Discussion

The clinicopathological features in the previously described patients and in our patient with nephritis associated with seronegative spondylarthropathies (18 cases) are summarized.<sup>6,7,8,9</sup>

Almost all patients were males between 20 and 55, and had HLA-B27, proteinuria (~14.4g/day), and complained of back problems 2-25 years prior to the diagnosis of nephritis. Four patients (22%) progressed to chronic or end-stage renal failure.<sup>6,7</sup>

Kidney biopsy was performed in all cases. Eleven cases were diagnosed as typical

IgA nephropathy, one as membranous glomerulonephritis, 3 by Malaviya et al. 2 by Shu et al. as mesangioproliferative glomerulonephritis without any IgA deposits by immunofluorescence microscopy.<sup>8,9,10</sup> No case was shown to have drug induced nephropathy or renal amyloidosis.

Cowling et al. have reported that elevated IgA levels were mostly seen in the active phase of ankylosing spondylitis as measured by ESR and CRP.<sup>11</sup>

IgA nephropathy associated with AS is uncommon. 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 compared with other IgA nephropathy without AS.<sup>12</sup>

Our patient with HLA-B27 positive 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.<sup>13,14,15</sup>

Although elevated IgA and IgA-immune complex levels were commonly observed in AS patients, the role of IgA in AS was controversial. Pathogenesis of IgAN in AS was unclear. However, combined with the fact that renal impairment could happen at any stage of AS, there possibly were some circulating subjects in AS patients that could cause both kidney disease and arthritis, and antibodies or inflammatory factors were the most likely suspects. Recently, a key character came to light to elucidate the pathogenesis in pIgAN, that is, deposits of glycosylation-deficient IgA1 (Gd-IgA1) and its immune complex in the glomerular mesangium. Eventually, a research team from Japan revealed antibodies against Gd-IgA1 were mainly IgG subtype in pIgAN.<sup>16,17</sup>

Few studies reported renal outcomes of AS patients with renal involvement. A recent study observed the renal outcomes of renal amyloidosis in AS, 6 patients (46.1%) reached ESRD when they were

diagnosed as renal amyloidosis, and 3 patients (23.1%) progressed to ESRD at the end of follow-up.<sup>18</sup>

Lee et al. showed a patient with amyloid A amyloidosis secondary to underlying AS achieved complete remission of nephrotic syndrome; however, re-biopsy revealed there was little change pathologically.<sup>18</sup>

The literature has rarely mentioned the renal outcomes of secondary IgAN in AS. Marocchi *et al.* studied a patient with AS and secondary IgAN, which progressed to chronic renal disease and required hemodialysis, in the course of treatment with infliximab.<sup>19</sup> In the present study, renal outcomes either clinical remission or the eGFR change performed well in both the IgAN and non-IgAN subpopulations. No patients progressed to ESRD or eGFR declined >50%, and eventually only 1 patients had an eGFR decline >30%.

A Strong association with HLA-B27 in patients with ankylosing spondylitis is well known. IgA nephropathy, on the other hand, has been shown to have an association with HLA-BW35 or HLA-B12, and more recently with HLA-DR4.<sup>20</sup> Since HLA antigens are known to be associated with several immunopathological diseases, both IgA nephropathy and seronegative spondylarthropathies might be related to certain HLA complexes, but this requires confirmation by further systematic research work.

### Conclusion:

In conclusion, this reported case had a 5 years history of AS. With intermittent NSAIDS treatment, the symptoms were only partially relieved, and the patient developed joint damage and renal complications. After treatment with glucocorticoids, joint pain, morning stiffness, and kidney function were significantly improved. In clinical practice, patients with AS should be screened for renal complications. The renal prognosis of kidney disease in AS was good, appropriately two-thirds of the patients achieved complete remission or partial

remission, and eGFR decline >30% happened in only 1 patient.

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