A rare renal involvement in a patient with axial Spondyloarthritis: don’t miss focal segmental glomerulosclerosis and hyalinosis

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Abstract
Renal involvement in spondyloarthritis is dominated by amyloidosis, IgA nephropathy and urolithiasis. Other nephropathies are rare. A patient followed for SpA consults with edema, hydrocele and a pleural effusion. A FSGS was confirmed by renal biopsy and the etiological investigation has ruled out the causes of secondary FSGS.

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Key words:
Spondyloarthritis; Renal involvement; Focal segmental glomerulosclerosis and hyalinosis

Key Clinical Message:
Renal involvement in SpA should not be missed, screening these patients during follow-up allows early detection of any impairment and helps guide early nephroprotection and treatment measures. AA amyloidosis, IgA nephropathy and urolithiasis are the most reported, however, other rare involvement can be described.

Author Agreement
I, Tbini Houssem, here by certify that all named authors have seen and approved the final version of the manuscript being submitted. I on behalf of all authors warrant that the article is the authors’ original work, hasn’t received prior publication and isn’t under consideration for publication elsewhere. I confirm that the order of authors listed in the manuscript has been approved by all of them.
Authors understand that the Corresponding Author is the sole contact for the Editorial process. He is responsible for communicating with the other authors about progress, submissions of revisions and final approval of proofs.

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Renal involvement in SpA should not be missed, screening these patients during follow-up allows early detection of any impairment and helps guide early nephroprotection and treatment measures. AA amyloidosis, IgA nephropathy and urolithiasis are the most reported, however, other rare involvement can be described.

Abstract
Renal involvement in spondyloarthritis is rare and it is dominated by AA amyloidosis, IgA nephropathy and urolithiasis. Other nephropathies are rare and are limited to few case reports. Description of the case: we report a case of a patient followed for axial SpA who developed a focal segmental glomerulosclerosis and hyalinosis. Indeed, he consults after being lost to follow-up for 3 years with edema of the 2 lower limbs associated with a hydrocele and a bilateral pleural effusion of low abundance. A FSGS was confirmed by renal biopsy and the etiological investigation has ruled out the causes of secondary FSGS. Conclusion: Although renal involvement is rare in SpA, screening those patients in order to early detect any renal impairment is important during disease monitoring.
Key words:
Spondyloarthritis; Renal involvement; Focal segmental glomerulosclerosis and hyalinosis

Introduction:
Spondyloarthritis (SpA) is a chronic inflammatory rheumatism most commonly affecting young men. It is characterized by pelvic-spinal involvement which may be isolated or associated with peripheral joint and/or enthesitic involvement and by association with the human leukocyte antigen B27 (HLA-B27) haplotype (1). Among the extra-articular manifestations of SpA, renal involvement is rare and mostly severe. AA amyloidosis, IgA nephropathy and urolithiasis are the most common causes. However, other nephropathies could be seen in SpA; they are rare and limited to case reports (2,3). Thus, we report the case of a focal segmental glomerulosclerosis and hyalinosis (FSGS) in a patient with axial SpA.

Case:
A 49-year-old man with a history of retrobulbar optic neuritis was diagnosed with axial SpA since 2017. The diagnosis was made according to ASAS 2009 criteria (inflammatory chronic back pain over one year, positive C-Reactive-Protein (CRP) at 164mg/l and bilateral sacroiliitis on X ray (grade II)) (4). There was no extra-articular manifestation at the time of the disease diagnosis. He was treated with Non-Steroidal Anti-Inflammatory Drugs NSAIDs (diclofenac and indomethacin) for a period of two months. This treatment was quickly stopped upon the discovery of proteinuria at 0.3 g/24h. The patient was put on corticosteroid therapy (10 mg of Prednisone) and we decided to put him on biotherapy (Adalimumab).

The patient was lost to follow-up from 2017 to 2020. He consulted in December 2020 with edema of lower limbs, a hydrocele, and a bilateral pleural effusion of low abundance. His blood pressure was high (180-200 mmHg systolic). On osteoarticular examination, there were back stiffness and limitation in hips mobility. Moreover, there were no other articular involvement or abnormalities in the general examination.

Laboratory investigations showed: CRP at 51mg/l, normal level of urea and creatinine, the 24-hour urine protein was at 5.9 g/24h, the proteinemia was at 46g/l and the albuminemia was at 14.4g/l and there was not hématuria. In front of those clinical and biological data; we retained the diagnosis of impure nephrotic syndrome with arterial hypertension. Regarding SpA activity, the Bath Ankylosing Spondylitis Disease Activity score (BASDAI) was at 6.3, the Ankylosing Spondylitis Disease Activity Score (ASDAS CRP) was at 4.95. By questioning the patient, he affirmed that he self-administrated paracetamol and NSAIDs occasionally in case of pain.

To explore the impure nephrotic syndrome, a renal biopsy was indicated and the anatomopathological examination concluded to a FSGS involvement (Figure 1). After ruling out the causes of secondary FSGS (human immune-deficiency virus, hepatitis B virus, parvovirus B19, and Cytomegalovirus infections, drug / toxic origin, adaptive FSGS by nephronic reduction and glomerular hyperfiltration) we put the patient on corticosteroid therapy (prednisone) at a dose of 1 mg/kg/day in association with diuretics (furosemide and spironolactone) and an ACE inhibitor (ramipril) for a period of 3 months, five albumin infusions were also prescribed.

After three months of treatment, the edema as well as the nephrotic syndrome have almost disappeared. Regarding his SpA, the patient is currently awaiting a support agreement for Adalimumab from the social insurance funds. He only receives analgesic treatment.

Discussion:
SpA is a chronic inflammatory rheumatism predominantly affecting young men. Its prevalence is estimated between 0.3 and 2% of the general population (1). It can be responsible for axial, peripheral articular and enthesitic involvement.

Renal involvement is rare in SpA, its frequency varies between 4.3 and 35%(2). This impairment is often underestimated because of its late onset (with an average of 6.6 to 19.4 years) (2) and the decrease in its...
incidence mainly explained by the reduction in the use of NSAIDs after the introduction of biotherapies in management of SpA (3).

The main circumstances of discovery of renal involvement during SpA are edema, proteinuria, hematuria, increased blood pressure, urolithiasis, deterioration of renal function and nephrotic syndrome (2,5,6).

Data from the literature report renal involvement in SpA to three main etiologies represented by AA amyloidosis, IgA nephropathy and urolithiasis. These different etiologies vary according to studies. Ninety per cent of kidney damage are explained by amyloidosis (62%) and IgA nephropathy (30%) (2,5–7). Literature data on other etiologies (less than 8%) are limited to case reports. Cases of extra-membranous glomerulonephritis, mesangial glomerulonephritis with C3 and IgM deposits, and membrano-proliferative glomerulonephritis have been reported rarely (8–11). Rare cases of SpA-FSGS association have also been reported, including 3 cases in 3 Tunisian series (2,6,12,13). To the best of our knowledge, the present case is the fourth reported one with no other identifiable cause of secondary FSGS.

Given the paucity of data in the literature, it seems difficult to determine whether this association is etiological or a simple coincidence. In our patient, before adopting an association between SpA and FSGS, we excluded the causes of secondary FSGS (viral infections, drug / toxic origin, adaptive FSGS by nephronic reduction and glomerular hyperfiltration). Knowing that our patient had NSAIDs to control his SpA activity, the presence of FSGS could be either due to previous medication with NSAIDs or associated with his SpA.

A review of the literature showed that renal damage due to NSAIDs are mainly acute interstitial nephritis (AIN), acute tubular injury (ATI), minimal change disease (MCD), papillary necrosis (PN) and, rarely membranous nephropathy (MN) (13,14). Literature data about the relationship between NSAIDs and FSGS are controversial, an association has been reported by some authors even in topical NSAIDs (15,16). However Markowitz et al and Pauksakon et al in more recent study assert that available data do not support a relationship between NSAIDs and FSGS (14,17). Those data may support that FSGS in our patient can be related to SpA. In summary, there is no study, as well as epidemiologic evidence, that directly demonstrate the causal relationship between SpA and FSGS. The role of NSAIDs, which are the main treatments for SpA, as the cause of FSGS remains unclear. Since that, having eliminated the other possible causes is in favor of SpA and FSGS association.

Our patient will be put on Adalimumab. This later has been used since 2006 for the treatment of SpA (18). It has also been used in refractory cases of FSGS since 2014, it reduces proteinuria and protect kidney function from degradation, it has also been reported as an alternative in cases of resistance or allergy to rituximab in FSGS (19,20).

**Conclusion:**

We report a rare case of FSGS in a patient with SpA. Recognition of renal impairment in SpA is important in order to guide necessary nephroprotection measures and appropriate therapy before significant renal damage occurs. The diagnosis should be made by renal biopsy which in the majority of cases reveals amyloidosis or IgA nephropathy, however, in rare cases, some rare associations can be discovered.

**References:**


Figure 1. (a) Glomerulus in a renal biopsy image with focal segmental glomerulosclerosis lesion (arrow). Light microscopy (Trichrome x 400). (b) Glomerulus in a renal biopsy image with focal segmental glomerulosclerosis lesion (arrow). Light microscopy (Trichrome x 200).