

ANKYLOSING SPONDYLITIS – A RARE CAUSE OF AA AMYLOIDOSIS WITH RENAL AND CARDIOVASCULAR ALTERATIONS

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Abstract. *Ankylosing spondylitis (AS) is a relatively rare chronic inflammatory condition that affects axial spine and extraarticular structures – the eyes, the skin, the lung, the kidney, etc. AS is more common in males and the majority of patients are HLAB27 positive. The most common clinical manifestations of AS are chronic persistent pain and stiffness in the axial spine and sacroiliac joints and enthesitis. The chronic inflammation of articular and periarticular structures can lead to the development of secondary (AA) amyloidosis with deposition of amyloid beta-fibrils in parenchymal organs – the kidney, the heart, the skin and in periarticular spaces. We present a 78-year-old male patient with more than 30 years history of ankylosing spondylitis and systemic (AA) amyloidosis.*

Key words: *ankylosing spondylitis, secondary AA amyloidosis, histological detection of amyloid, treatment*

INTRODUCTION

Ankylosing spondylitis (AS) is a relatively rare chronic inflammatory condition that affects axial spine and extraarticular structures – the eyes, the skin, the lung, the kidney, etc. [1, 2, 3, 4, 5]. AS is a rare disease, affecting approximately 1% of the population worldwide. It is more common in males and the majority of patients are HLAB27 positive. The most common clinical manifestations of AS are chronic persistent pain and stiffness in the axial spine and sacroiliac joints and enthesitis. The typical radiological features of AS include bone ankyloses (bamboo spine), syndesmophytes and ligamentum calcifications [3]. AS is characterized with lack of antinuclear antibody and rheumatoid factor positivity and is therefore referred to as a seronegative spondyloarthropathy. AS is known to cause different types of renal involvement, including glomerular changes, AA amyloidosis and tubulointerstitial changes [6]. The chronic inflammation of articular and periarticular structures can lead to the development of secondary systemic (AA) amyloidosis with deposition of amyloid beta-fibrils in parenchymal organs – the kidney, the heart, the skin and in periarticular spaces. In many patients the development of amyloidosis is a major determinant of survival and disability and depends mainly on the disease activity, duration and the presence of adequate treatment.

Systemic AA amyloidosis is a rare condition characterized by abnormal, extracellular deposition of β 1-fibrils composed of insoluble fragments of serum

amyloid A protein (SAA) [7]. It can develop as a complication of any type of chronic inflammatory disease, including chronic bacterial infections (tuberculosis, leprosy, osteomyelitis), chronic fungal infections, autoimmune diseases (rheumatoid arthritis, ankylosing spondylitis), and in some genetic diseases with recurrent inflammatory attacks and autoinflammatory syndromes (familial Mediterranean fever, Muckle-Wells and TRAPS, etc.) [7, 8]. The deposition of beta-fibrils in the tissues leads to progressive organ dysfunction, parenchymal organ failure (e.g., cardiac, renal and hepatic), hemorrhagic diathesis (when amyloid is deposited in the vascular walls), autonomic dysfunction and development of severe orthostatic hypotension (when deposited in the sympathetic ganglia), progressive heart failure with rhythm and conduction disturbances, in patients with renal amyloidosis – to nephrotic syndrome and its complications (increased thromboembolic risk, decreased immune response and dyslipidemia) [7, 8].

We present a 78-year-old male patient with more than 30 years of history of ankylosing spondylitis and systemic (AA) amyloidosis.

CASE PRESENTATION

A 78-years-old male patient was admitted to the Clinic of Nephrology in June 2022 for diagnostic evaluation of nephrotic-range proteinuria (3.21 g/l) and renal failure (serum creatinine of approximately 320 μ mol/l). At the admission the patient reported fatigue, shortness of breath and limitations in anterior and lat-

eral spinal flexion. In 1986 the patient was diagnosed with a central form of Ankylosing spondylitis, he was later proven to be HLAB27 positive. The patient has been treated with non-steroid anti-inflammatory drugs (NSAIDs), short courses of oral corticosteroids. The patient had undergone X-ray therapy for skin cancer on the scalp and curative X-ray therapy for prostatic cancer 10 years before the first admission to our clinic.

At the admission the patient had marked increase in serum creatinine (322 $\mu\text{mol/l}$) and urea (25.7 mmol/l), anemia (hemoglobin 93 g/l), low serum albumin (29 g/l) and normal total protein (67 g/l) levels, and urinalysis revealed positive dip-sticks test for albuminuria, negative dip sticks test for glucose, blood, leukocytes, normal urinary sediment; proteinuria was 3.21 g/l . Serum electrophoresis showed decreased gamma-globulin levels without M-gradient – nephrotic syndrome. The investigated autoantibodies (antinuclear, anti-dsDNA and antinephrophil cytoplasmic) and HBC and HCV markers were negative, and C3 and C4 complement fractions were within the normal limits.

Abdominal ultrasound showed decreased renal (80-85 mm) and renal parenchymal size (10-12 mm) with increased parenchymal echogenicity and renal parenchymal size and small parenchymal renal cysts (Fig. 1).

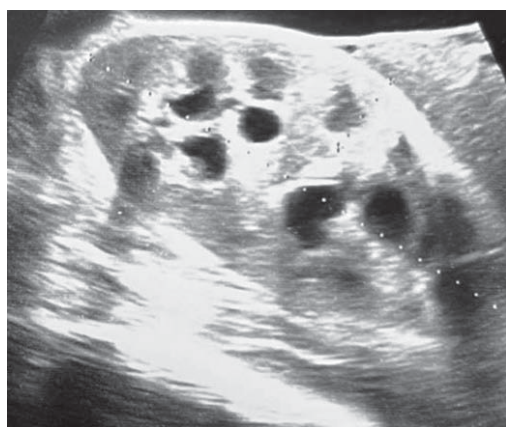


Figure 1. Abdominal ultrasound – bilateral nephrosclerosis: decreased renal and parenchymal size with marked increase in parenchymal echogenicity, visible renal pyramids and small renal parenchymal cysts

Echocardiographic examination revealed left ventricular hypertrophy with septal and posterior wall thickening (19 and 15 mm), decreased ejection fraction of 45%.

X-ray investigation of the abdomen showed syndesmophytes and bilateral sacroiliitis (Fig. 2).

The patient was considered contraindicated for renal biopsy due to the marked spinal ankyloses, de-

creased renal and parenchymal size and increased renal parenchymal echogenicity. Therefore, due to the presence of both renal failure and nephrotic syndrome, the patient underwent subcutaneous tissue biopsy with specific staining for amyloid.

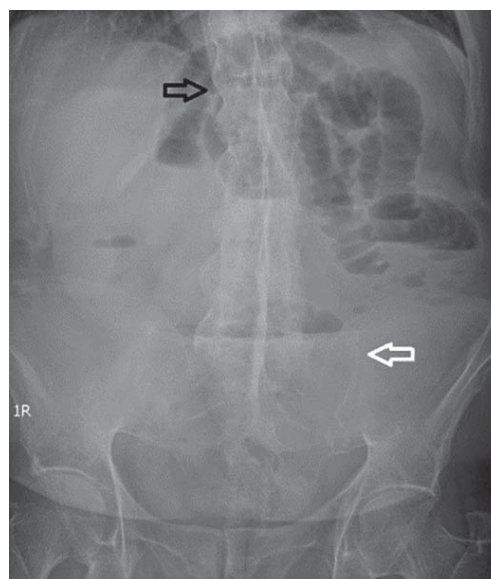


Figure 2. Abdominal X-ray – visible syndesmophytes (black arrow) and sacroiliitis (white arrow)

The subcutaneous fat tissue biopsy revealed deposition of eosinophilic matter on light microscopy that showed apple-green birefringence by polarized light with Congo red stain (Fig. 3). Immunochemical investigation detected deposition of AA amyloid.

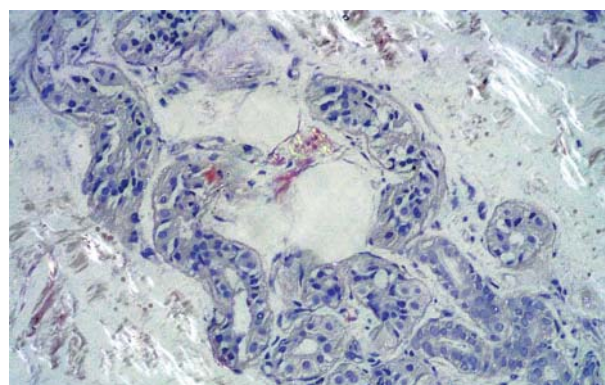


Figure 3. Congo red stain of amyloid depositions and apple-green birefringence by polarized light

After the subcutaneous fat tissue biopsy result was available, the patient was presented to rheumatologist and was considered not indicated for biological treatment and was therefore started on low dose corticosteroids (methylprednisolone 2 tablets) and colchicine 1 tablet b.i.d. in combination with gastroprotection and treatment of renal anemia and renal bone disease.

DISCUSSION

Ankylosing spondylitis is a rare immune mediated disease associated with persistent and progressive inflammation of the articular and periarticular structures, predominantly affecting the axial spine and sacroiliac joints. Due to the chronic inflammation, secondary (AA) amyloidosis can develop. The presented patient has classical manifestations of AS, including typical X-ray changes, in combination of both renal and cardiac involvement – high-grade proteinuria plus renal failure and decreased left ventricle ejection fraction with marked increase in left ventricle wall thickness, suggesting systemic amyloidosis. The patient was investigated for paraproteinemia and no M protein was detected in serum, therefore primary AL amyloidosis could be excluded.

AS can cause several types of renal involvement, including [6]:

- Glomerular changes: minimal change nephropathy (especially in patients on anti-TNF treatment), membranous nephritis, focal and segmental glomerulosclerosis, mesangiocapillary glomerulonephritis and IgA nephropathy (especially if inflammatory bowel disease is present).

- AA amyloidosis.

- Tubulointerstitial nephritis (associated with NSAIDs treatment and/or secondary Sjogren's syndrome).

- Renal vascular disease – rare, usually as a complication of accelerated atherosclerosis and/or concomitant vasculitis.

- Renal changes due to comorbidities, i.e., diabetic or hypertensive nephropathy, chronic tubulointerstitial nephritis in patients with pyelonephritis, etc.

Biopsy investigations have crucial role in the diagnosis of renal involvement in AS. As the patient had advanced renal changes with marked decrease in kidney and parenchymal size and increase in renal parenchymal echogenicity in combination with axial spine ankyloses that significantly impedes both the ability to lie in bed and breathing excursions, we undertook subcutaneous fat tissue biopsy that detected the deposition of AA amyloid [9]. The deposition of amyloid in renal structures can explain the presence of both renal failure and high-grade, nephrotic-range proteinuria in combination with cardiac amyloidosis (marked thickening of left ventricular

myocardium and decreased ejection fraction) [10]. Therefore, low dose corticosteroid in combination with colchicine was initiated.

CONCLUSION

In conclusion, systemic AA amyloidosis is a possible complication of AS and should be considered in all AS patients with cardiac and/or renal involvement. As renal biopsy could be difficult in AS due to spinal ankyloses and/or contraindicated in advanced renal disease, subcutaneous fat tissue biopsy, along with intestinal and gingival biopsy, remains a method of choice for the detection of amyloidosis in these patients.

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