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IgA Nephritis in a Patient with Ankylosing Spondylitis: A Case Report and Mini Review

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ABSTRACT

Ankylosing Spondylitis (AS) is an inflammatory disease characterized by involvement of the spinal joints and adjacent structures leading to bone fusion. Although secondary amyloidosis is the most common renal involvement type in AS, there are few reports regarding to other glomerular disorders including association of IgA nephritis with AS. We present a 24-year-old male patient that admitted with intermittent hematuria and proteinuria while he was followed up for AS disease and diagnosed as chronic IgA nephritis by renal biopsy.

Key words: ankylosing spondylitis, IgA nephritis, renal biopsy

ANKİLOZAN SPONDİLİTLİ BİR HASTADA IGA NEFRİTİ: OLGU SUNUMU VE KISA LİTERATÜR TARAMASI

ÖZET

Ankilozan spondilit spinal eklemlerin inflamasyonu ile seyreden inflamatuar bir hastalıktır ve eklem yapışıklıkları kemiklerde birleşmeye neden olur. AS de izlenen renal hastalığın en yaygını sekonder amiloidoz olmasına rağmen diğer glomeruler tutulumlarda tanımlanmıştır. Maalesef literatürde yalnız çok az olguda AS li hastalarda IgA Nefriti rapor edilmiştir. Burada AS hastalığı nedeni ile takipteyken aralıklı hematüri ve proteinürinin tespit edildikten sonra, renal biyopsiyle kronik IgA Nefropatisi tanısı konulan 24 yaşında erkek hastayı sunduk.

Anahtar sözcükler: ankilozan spondilit, IgA nefropatisi, renal biyopsi

Immune mechanisms are considered to play a key role in Ankylosing Spondylitis (AS) (1). Seronegative spondylarthritis are frequently characterized by extra-articular manifestations (2). Type AA amyloidosis is a rare and late complication of AS and possible cause of death especially in patients with aggressive course (3). Additionally, other renal involvement types are mesangial IgA segmental and focal glomerulonephritis (3). In this report, we present a case of IgA nephritis in a patient with Ankylosing Spondylitis

Case report

Twenty-four-year-old male patienT admitted with dark urine while he was receiving indomethacin and sulfasalazine for AS. Laboratory parameters including whole blood count, sedimantation rate and biochemical analysis were in normal range. Urine analysis indicated proteinuria (++), hematuria and leukocyturia. Glomerular filtration rate was 98 mL/min/1.73 kg/m^2 and esbach was 1640 mg/day. Antinuclear antibody (ANA), anti-dsDNA, cANCA, pANCA, C3, C4, anticardiolipin IgM and Ig G and plasma immunoglobulins were within normal limits. Serum cryoglobulin and hepatitis B surface antigen were negative. Abdominal ultrasound and chest X-ray examinations exhibited no abnormality. Staining of rectal biopsy specimen with congo red was negative and consequent renal biopsy showed global sclerosis in 12% of glomeruli, and segmental sclerosis in 12% and segmental mesangial proliferation in 30% of the remaining glomeruli. Widespread atrophic focuses at the tubules and medial proliferation leading to vessel wall

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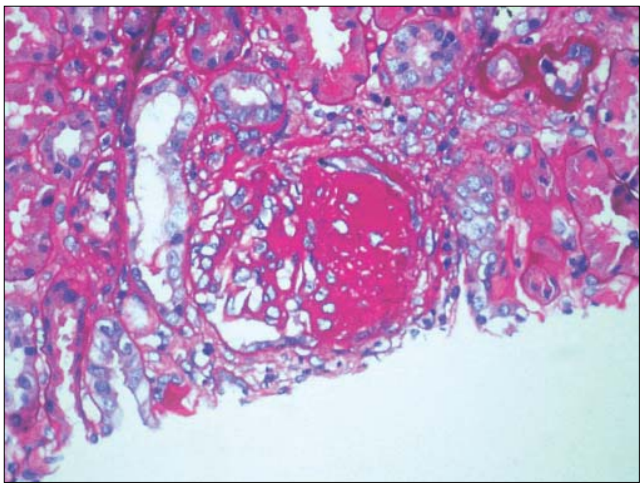

Figure 1. Glomerulus show mesangial hypercellularity and expanded mesangial matrix

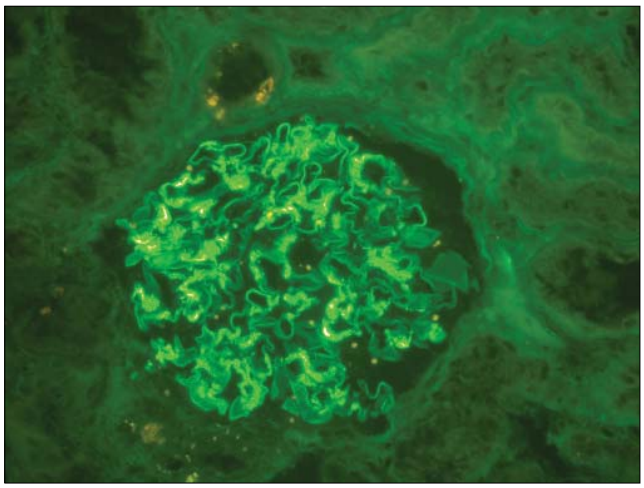

Figure 2. Immunofluorescence studies showed dense staining for IgA (3+) and C3 (2+) with poor reaction for IgM and IgG.

thickening were evident in the histopathologic examination. Immunofluorescence studies showed dense staining for IgA (3+) and C3 (2+) with poor reaction for IgM and IgG. Protein restricted diet was recommended, and treatment including ramipril, losartan potassium, and fish oil was initiated as well as etanercept for AS. At the 6th month of follow-up, patient was free of symptom, and proteinuria gradually decreased to 369 mg/day.

Discussion

The prevalence of IgA nephropathy in general population is estimated to be between 0-2 and 4% (4). Immunoglobulin A (IgA) nephropathy is the most common type of primary glomerulonephritis in patients with ankylosing spondylitis (3). The association of IgA nephropathy with seronegative spondyloarthropathies such as ankylosing spondylitis, Behcet's disease, psoriatic arthritis, Reiter's syndrome and the postenteritic arthritides have been previously reported, especially in cases of AS (5,6). However there are controversial reports about the association of AS and IgA nephropathy. Peeters et al stated that AS is associated with IgA nephropathy (7). In contrast, Swaak et al found no evidence of IgA nephropathy in any of 40 patients with ankylosing spondylitis (8). In an other cohort study, Wall et al described an increased incidence of recurrent haematuria in 32 patients with AS, but only one patient had histopathologically confirmed IgA nephropathy (9). Similarly, Calin reported the absence of an evidence of IgA nephropathy in 68 patients suffering from AS (10). As a result, it can be concluded that recurrent hematuria occurs in up to 20% of patients suffering from AS, whereas histopathologically confirmed IgA nephropathy is present in about 2% (11). The majority of previously reported cases are male in accordance with the fact that the prevalence of AS in men is three times higher than that in women (12).

AS and IgA nephropathy share some immunologic features, such as elevated serum IgA and IgA related immune complex (13). Although a linkage exist between these disorders, the physiopathological mechanism between each other remains unclear. IgA levels are reported to be high during the active inflammatory phases of spondylitis, and circulating IgA containing immune complexes may be found in the spondyloarthropathies (14). Reynolds et al have shown such a difference in HLAB27 positive and negative patients with AS (15).

Anti-TNF alpha agents have improved the outcome of axial forms of AS that are resistant to conventional anti-inflammatory therapies. Infliximab, a monoclonal anti-TNFalpha antibody, has greatly improved the evolution of AS although several adverse events have been described. On the other hand, infliximab has been demonstrated to reduce renal symptoms associated with chronic inflammatory rheumatological diseases, such as amyloid A (AA) amyloidosis, but few data are available on its efficacy in controlling IgA nephropathy associated with AS (16). The present case well responded to Anti-TNF based treatment.

In conclusion, the prevalence of IgA nephropathy in patients with AS is not greater than that of the general population. The majority of previously reported patients are male and IgA level was high in the HLA-B27 positive patients (15). Our case shows that amyloidosis is not only the

type of renal involvement in patients with AS. The exact relationship of these two entities; both etiological or coincidental still needs to be elucidated. The occurrence of this rare association needs to be recognized and differentiated from other more common causes of renal involvement in patients with AS. Kidney biopsy should be performed in patients with AS displaying micro- or macroscopic hematuria with or without proteinuria. Both congo red stain and immunofluorescence studies are necessary to establish a correct diagnosis in these patients. Further studies with large number of patients with AS are needed to judge the real prevalence of IgA nephropathy in this disease.

References

1 Calvo-Río V, Loricera J, Martín L, Ortiz-Sanjuán F, Alvarez L, González-Vela MC et al. Henoch-Schönlein purpura nephritis and IgA nephropathy: a comparative clinical study. Clin Exp Rheumatol 2013;31:45-51.

2. Jacquet A, Francois H, Frangie C, Yahiaoui Y, Ferlicot S, Micelli C. et al. IgA nephropathy associated with ankylosing spondylitis is not controlled by infliximab therapy. Nephrol Dial Transplant 2009;24:3540-2.

3. Singh G, Kumari N, Aggarwal A, Krishnani N, Misra R. Prevalence of subclinical amyloidosis in ankylosing spondylitis. J Rheumatol 2007;34:371–3.

4. World MJ. Review of cases of IgA nephropathy. JR Army Med Corps 2013;159:90-3.

5. Satko SG, Iskandar SS, Appel RG. IgA nephropathy and Reiter's syndrome. Report of two cases and review of the literature. Nephron 2000;84:177-82.

6. Matsuda M, Suzuki A, Miyagawa H, Shimizu S, Ikeda S. Coexistence of IgA nephropathy and undifferentiated spondyloarthropathy in a female patient. Clinical Rheumatology May 2006, Volume 25, Issue 3, pp 415-8.

7. Peeters A.J, van den Wall Bake AW, Daha MR, Breeveld FC. Inflammatory bowel disease and ankylosing spondylitis associated with cutaneous vasculitis, glomerulonephritis, and circulating IgA immune complexes. Ann Rheum Dis 1990;49:638-40.

8. Swaak A.J, Frankfort I, Menon RS, Pekelharing JM, Planten O. Absence of IgA nephropathy in patients with ankylosing spondylitis. Rheumatol Int 1986;6:145-9.

9. Wall BA, Agudelo CA, Pisko EJ. Increased incidence of recurrent hematuria in ankylosing spondylitis: a possible association with IgA nephropathy. Rheumatol Int 1984;4:27-9.

10. Calin A. Rarity of nephropathy in ankylosing spondylitis. Arthritis Rheum. 1982;25:1510.

11. Levy-Clarke G, Nussenblatt R. Does anti-TNF therapy decrease the incidence of anterior uveitis in patients with ankylosing spondylitis? Nat Clin Pract Rheumatol 2006;2:72–3.

12. Elewaut D, Matucci-Cerinic M. Treatment of ankylosing spondylitis and extraarticular manifestations in everyday rheumatology practice. Rheumatology (Oxford) 2009;48:1029–35.

13. Song IH, Appel H, Haibel H, Loddenkemper C, Braun J, Sieper J. et al. New onset of Crohn's disease during treatment of active ankylosing spondylitis with etanercept. J Rheumatol 2008;35:532–6.

14. Braun J, Baraliakos X, Listing J, Davis J, van der Heijde D, Haibel H. et al. Differences in the incidence of flares or new onset of inflammatory bowel diseases in patients with ankylosing spondylitis exposed to therapy with anti-tumor necrosis factor alpha agents. Arthritis Rheum 2007;57:639–47.

15. Reynolds TL, Khan MA, Van der Linden S, Cleveland RP. Differences in HLA-B27 positive and negative patients with ankylosing spondylitis: study- of clinical disease activityaild concentration of serum IgA, C reactive protein, and, haptoglobin. Ann Rheum Dis 1991;50:154-7.

16. Kobak S, Oksel F, Kabasakal Y, Doganavsargil E. Ankylosing spondylitis-related secondary amyloidosis responded well to etanercept: a report of three patients. Clin Rheumatol 2007;26:2191–4.