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Case Report

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The Possible Association of Chronic Hepatitis B with Renal AA Amyloidosis

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Abstract

Renal amyloid A (AA) amyloidosis is one of the systemic etiologies of nephrotic syndrome (NS) in adults. Chronic inflammatory conditions including rheumatoid arthritis, familial periodic fever syndromes, spondyloarthropathies, and chronic bacterial infections such as tuberculosis and chronic osteomyelitis are the common causes of secondary AA amyloidosis. In this case report, we reported a patient presented with nephrotic syndrome and secondary AA amyloidosis due to chronic hepatitis B infection in the absence of any glomerulonephritis.

Keywords: Amyloidosis, hepatitis B infection, nephrotic syndrome

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INTRODUCTION

Amyloidosis is a group of chronic diseases characterized by extracellular deposition of beta-sheet fibrils. The systemic accumulation of amyloid proteins causes progressive organ dysfunction and ultimately death in patients (1). Amyloid A (AA) amyloidosis is the most common form of systemic amyloidosis worldwide. AA amyloidosis is associated with increased hepatocyte production of the acute phase reactant serum amyloid A (SAA) that may be related with the release of cytokines especially interleukin-1 from activated macrophages. Amyloid fibrils have a distinct appearance on microscopy that can be detected in biopsy specimens and by their ability to bind Congo red (leading to apple-green birefringence under polarized light) (1, 2). AA amyloidosis may complicate a number of chronic inflammatory diseases, including rheumatoid arthritis (RA), familial Mediterranean fever (FMF), ankylosing spondylitis, inflammatory bowel disease, and certain neoplasms and chronic infections such as tuberculosis and osteomyelitis (2). Renal involvement of AA amyloidosis is one of the systemic reasons for nephrotic syndrome, and it often leads to end-stage renal disease (3).

However, AA amyloidosis is uncommon in chronic viral infections including hepatitis B. Herein, we reported a patient with nephrotic syndrome and renal AA amyloidosis secondary to chronic hepatitis B infection.

CASE PRESENTATION

A 62-year-old man was admitted to family medicine unit for polyuria and frequent urination in February 2017. During the last week before his admission, he had the complaints of anorexia, nausea, intermittent vomiting, polyuria, pollakiuria, and nocturia. His laboratory results revealed BUN: 50 mg/dL, creatinine: 7.0 mg/dL, sodium: 135 mEq/L, potassium: 5.49 mmol/L calcium: 8.42 mmol/L, phosphorus: 5.84 mmol/L, albumin: 2.14 g/dL in family medicine unit. His renal function tests were within normal range in August 2016 with results as BUN: 20 mg/dL creatinine: 0.8 mg/dL. He was referred to our nephrology department for impaired kidney function tests. He reported that he had used diclofenac sodium once daily

for knee pain in last week. Twenty years ago, he had a history of brucellosis that had been successfully treated. Four years ago, he was diagnosed with chronic hepatitis B infection. His medication for chronic hepatitis B infection includes only tenofovir disoproxil 245 mg daily. He had a history of smoking 10 cigarettes per day for 30 years. He had no history of any operation. The main physical examination findings were: normal blood pressure with 120/80 mmHg, normal cardiovascular examination with heart rate 80 per minute, normal respiratory system examination, no edema, no joint swelling and hyperemia. The patient was hospitalized to investigate the reason of kidney failure. Results of the laboratory findings in nephrology clinic were as follows: WBC: 11.75×10^3/μL (4.8-10.7 10^3/μL), hemoglobin: 15.2 g/dL (14-18 g/dL), platelets: 432×10^3/μL (130-400 10^3/μL), glucose: 86 mg/dL, BUN: 56 mg/dL, creatinine: 7.3 mg/dL, Na: 135 mmol/L, K: 6.4 mmol/L, Ca: 8.4 mmol/L, phosphorus: 5.8 mmol/L, uric acid: 4.6 mg/dL, total cholesterol: 260 mg/dL, LDL: 185 mg/dL, GGT: 98 U/L, ALP: 114 U/L, AST: 18 U/L, ALT: 16 U/L, total protein: 5.8 g/dL, albumin: 2.1 g/dL, LDH: 422 U/L, CPK: 71 U/L, and serum iPTH levels: 58 pg/mL (15-65). The serum CRP level was 39.7 mg/dL (0-6). The urine dipstick test revealed four positive protein. Urine microscopy was negative for casts with normal findings; 24-hour urine protein level was 21 g. ANA, anti-ds DNA, anti-GBM, and ANCA profiles were all negative. Serum complement 3c and complement 4 levels were within normal range. The HBV DNA level reported as low positive (<20 IU/mL). Abdomen ultrasonography revealed the normal-sized kidneys and normal parenchymal thickness with grade 2 increased renal cortical echogenicity; other findings were normal. The patient was consulted with gastroenterology department for chronic hepatitis B. Tenofovir was stopped, and entecavir was started according to the gastroenterology recommendation. Kidney biopsy was performed, and pathological examination of biopsy showed Congo red staining was positive AA type amyloidosis (Figure 1). Genetic test was performed for familial Mediterranean fever, and it was reported as negative in terms of common MEFV gene mutations. Serum immunoelectrophoresis revealed polyclonal gammopathy. Chest X-ray of the patient revealed no pathologic appearance. Computed tomography was performed for bronchiectasis presence, and it revealed no pathologic findings except for chronic fibrotic changes. He had no history of abdominal pain and bloody mucous diarrhea or night diarrhea in terms of inflammatory bowel disease presence. During follow-up, on the third day metabolic acidosis and uremic symptoms were occurred, oliguria was developed, and creatinine clearance was decreased to 10 mL/min. He was admitted to veno-venous hemodialysis intervention via double-lumen dialysis catheter in jugular vein. Since kidney function deterioration did not improve during follow-up, three times weekly routine hemodialysis programme has been initiated to the patient permanently. Written informed consent was obtained from the patient who participated in this study.

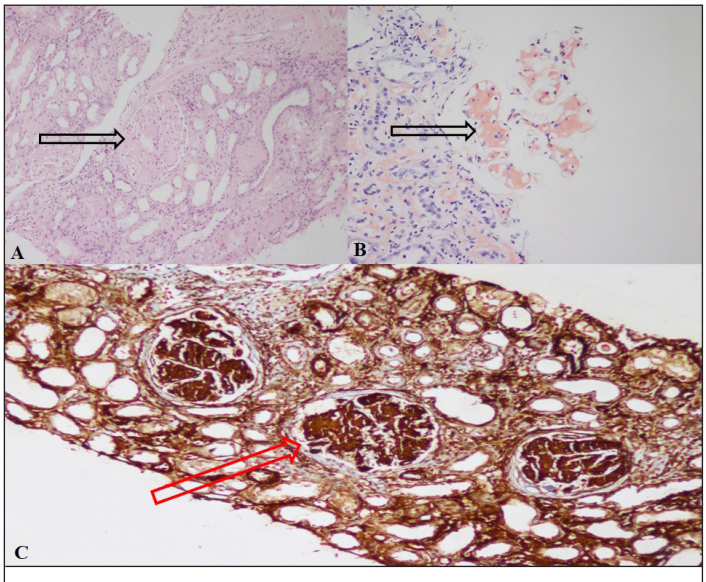

Figure 1. a-c. Pathological examination of the kidney biopsy demonstrates AA amyloidosis in the light microscopy. a) Black arrow shows accumulation of amorphous eosinophilic cast material in a glomerulus (hematoxylin & eosin X 400), b) Black arrow shows Congo red staining amyloid deposits in a glomerulus (hematoxylin & eosin X 400), c) Red arrow shows that immunohistochemical amyloid A staining is positive in the renal biopsy specimen (amyloid A X 100).

DISCUSSION

Diagnosis of amyloidosis is generally confirmed by tissue biopsy that shows the presence of amyloid deposition. Biopsy of the subcutaneous fat, rectal tissue, bone marrow, or a clinically involved organ may be used to document the amyloid accumulation. If amyloid is detected by biopsy, further immunofluorescence or immunochemical staining are needed for serum amyloid A protein or for kappa and lambda light chains presence (1-4). In addition, laboratory testing has little role in confirming the presence of AA amyloidosis. However, tests for monoclonal immunoglobulins in serum, such as immunofixation and measurement of free immunoglobulin light chains, are essential in excluding AL amyloidosis (5, 6).

Common causes of AA amyloidosis include chronic inflammatory conditions such as rheumatoid arthritis, anklyosing spondylitis, and periodic fever syndromes such as FMF, tumor necrosis factor receptor associated periodic syndrome (2, 3, 7). Moreover, chronic bacterial infectious diseases including tuberculosis and osteomyelitis are important causes of AA amyloidosis (8, 9). The relationship with viral infections and AA amyloidosis has not been well established yet. Little is known about the relationship between viral infections and amyloidosis. In the current literature, there are some cases such as a case of Still's disease complicated with AA amyloidosis and hepatitis B and a case of common variable immunodeficiency with hepatitis C and systemic amyloidosis (10, 11). More recently, Saha et al. (12) first reported a 13-year-old boy with nephrotic syndrome due to AA amyloidosis associated with chronic hepatitis B infection. According to the best of our knowledge, this case report also emphasizes the uncommon association of renal AA amyloidosis and chronic hepatitis B infection for the second time in the absence of any other inflammatory condition.

The long-term prognosis of untreated AA amyloidosis is usually poor. Prognosis is related to the degree of renal involvement, and the diagnosis is often not clarified until major organ infiltration has developed. Moreover, kidney involvement and dysfunction was the leading cause of death in approximately 70% of cases. The aim of the treatment is to eliminate the supply of precursor protein by suppressing the acute-phase response (2, 3). Anti-inflammatory agents such as colchicine, chlorambucil, and tocilizumab are beneficial in chronic rheumatologic disorders like RA and FMF, respectively. ACE inhibitors/ARB are also useful in decreasing proteinuria in renal amyloidosis. Recently, newer drugs such as eprodisate have demonstrated promising results in halting the progression of AA amyloidosis (13-16). However, there is no widely accepted treatment option to reverse the clinical involvements of AA amyloidosis.

CONCLUSION

We report a case of 62-year-old man who developed nephrotic syndrome due to renal AA amyloidosis. Work-up of the AA amyloidosis revealed chronic hepatitis B infection. Physicians should be alert in terms of AA amyloidosis in patient with hepatitis B infection if nephrotic syndrome is clinically evident.

Informed Consent: Written informed consent was obtained from the patient who participated in this study.

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