CASE REPORT

Renal Amyloidosis in Juvenile Rheumatoid Arthritis

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ABSTRACT

We report a case of a rare disorder of renal amyloidosis occurring as a complication of juvenile rheumatoid arthritis in a 16-year-old adolescent male. He presented with generalized edema and hypertension. The laboratory work-up showed nephrotic-range proteinuria and hypoalbuminemia and normal renal function despite bilateral shrunken kidneys revealed by the abdominal ultrasound. His renal biopsy showed deposition of amyloid fibrils in the form of homogenous eosinophilic material within the glomeruli demonstrating the pathognomonic apple-green birefringence by polarized light microscopy.

Key words: *Amyloidosis. Kidneys. Juvenile rheumatoid arthritis.*

INTRODUCTION

Amyloidosis is a disorder of protein folding in which normally soluble proteins undergo a conformational change and are deposited in the extra-cellular space in an abnormal fibrillar form causing progressive disruption of the structure and function of tissues and organs – systemic amyloidosis.[1] Renal dysfunction is a common manifestation of systemic amyloidosis which occurs in the course of a chronic inflammatory disease of either infectious or non-infectious etiology, the most common instigators being pulmonary tuberculosis and bronchiectasis, while Juvenile Rheumatoid Arthritis (JRA) is considered as a rare cause of amyloidosis in Pakistan.

The age of onset of amyloidosis is related to onset, severity and duration of the underlying inflammatory disease. Thus, in the course of JRA, amyloidosis occurs in teenagers, mostly presenting as nephrotic – nephritic syndrome with renal insufficiency being a late manifestation in addition to major physical findings associated with the primary inflammatory condition, notably deforming arthritis. The diagnosis is confirmed by renal biopsy along with presence of proteinuria, hypoalbuminemia, normal or deranged renal function and normal or reduced renal size on abdominal ultrasound.

At present, the major therapeutic strategy is intensive treatment of the primary inflammatory disease in order to decrease the levels of the amyloid precursor protein, Serum Amyloid A (SAA), and thus halt the disease progression inducing a slow progressive recovery of renal function.

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The rarity of this condition prompted the authors to report the case of renal amyloidosis presenting with nephrotic syndrome occurring as a complication of JRA.

CASE REPORT

A 16-year-old boy presented through outpatient clinic with complaints of generalized body swelling for the last 4 months. The history dated back to 5 years of age when he developed arthritis involving large and small joints of the body for which he did not seek any medical advice resulting in severe joint deformities and inability to walk later on.

Physical examination revealed anasarca with stable vitals except a blood pressure of 130/100 mmHg (> 95th percentile). There were obvious joint deformities in the form of severe extension contractures of both the knees while the remaining general and physical examination were unremarkable including ophthalmological assessment.

The biochemical work-up showed normal renal function tests, hypoalbuminemia (serum albumin = 2.2 g/dl) and nephrotic range proteinuria (spot urine protein: creatinine ratio = 11.3). The immunological markers of the disease were negative including the R.A. factor. The initial evaluation also included abdominal ultrasound showing bilateral shrunken kidneys (right being 7.0 cm and left being 7.5 cm in length), while the skeletal survey of all the joints of the body was suggestive of radiographic evidence of JRA. The Tc_{99m} DTPA renal scan showed bilateral reduced functioning kidneys and the renal biopsy performed confirmed the diagnosis of amyloidosis by Hematoxylin and Eosin as well as Congo red staining methods. The polarized light microscopy showed green birefringence (Figure 1).

Antihypertensive agents were initiated in the form of ACE inhibitors (enalapril) and calcium channel blockers (amlodipine), which maintained the blood pressure within normal limits. The course of the disease was

discussed with the parents regarding progressive renal impairment if specific therapy (methotrexate) was not given but they lost follow-up.

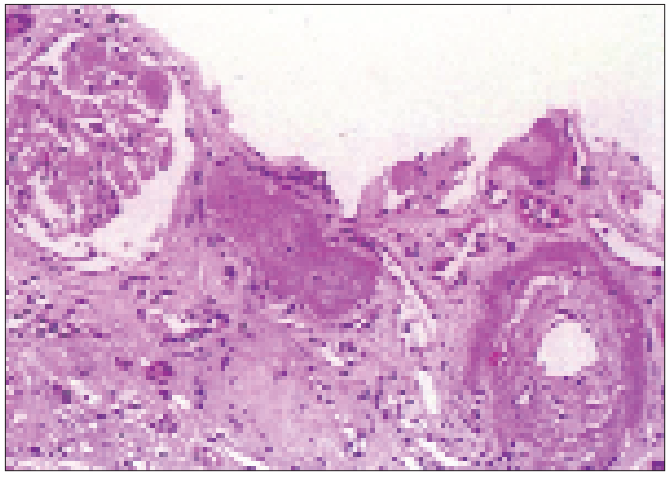

Figure 1: Hematoxylin, Eosin and Congo red staining.

DISCUSSION

Juvenile rheumatoid arthritis is a systemic inflammatory disease which is rarely accompanied by renal amyloidosis, an important complication that influences the prognosis of the disease. It has been reported uncommonly as the incidence in JRA has been estimated to be 5-30%.[2] The prognosis of renal disease in such patients is determined during the first 10-15 years by the course of the inflammatory joint disease. Patients not evincing the clinical renal manifestations during this period of time after onset of rheumatoid arthritis are not particularly prone to more serious kidney disease later on.[3] Secondary amyloidosis has resulted in a poor prognosis and is a significant cause of death related to renal complications. Therefore, radical and effective treatment is essential for children to control the disease activity and to prevent the progression to renal failure.

The inflammatory rheumatic conditions are frequently complicated by subclinical or overt abnormalities commonly vascular, glomerular and tubulointerstitial changes.[4-6] The long-term clinical outcome of isolated hematuria and isolated renal failure in patients with rheumatoid arthritis is more favourable with regard to proteinuria alone or combined with hematuria and / or renal failure, which is related to a poorer prognosis. The fate of amyloid nephropathy in rheumatoid patients depends on the duration of the proteinuric phase – the prognosis is worst the longer the duration.[7] Other prognostic factors include hypoalbuminemia and rising creatinine levels which have been found to be associated with a high mortality.[8]

Several studies have reported that chemotherapy using alkylating agents (cyclophosphamide, chlorambucil and azathioprine) can induce remission in nephrotic syndrome.[9] Those patients with good results were treated adequately and for long periods. These facts indicate that it may take a few years to degrade amyloid depositions from injured glomeruli accompanied by arthritis, because production of the precursors of amyloid proteins can be suppressed by decreasing rheumatoid activity under effective treatment. In fact, it was shown that amyloid deposits in renal tissue disappeared in repeated renal biopsies after therapy. Low-dose methotrexate has been used in JRA and the efficacy and safety of the agent are widely recognized.[2] Dember *et al.* found that eprodisate is a promising new drug which delays progression of amyloid A – associated renal disease by interfering with interactions between amyloidogenic proteins and glycosamino-glycans, thus inhibiting polymerization and deposition of amyloid fibrils in tissues.[10] As tumour necrosis factor – alpha (TNF-alpha) is thought to be involved in amyloid deposition, the efficacy of anti-TNF-alpha therapy (etanercept) in the treatment of renal amyloidosis complicating rheumatoid arthritis has been demonstrated.[11]

Rheumatoid arthritis ranks first among causes of secondary amyloid A amyloidosis. As renal involvement due to long-standing inflammatory joint disease can lead slowly to end-stage renal failure, it is essential that the joint disease be treated intensively with modern therapies including Disease Modifying Anti-Rheumatic Drugs (DMARDs) and/or biological agents like anti-TNF-alpha inhibitors.

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