CASE REPORTS

PULMONARY TUBERCULOSIS AND RENAL AMYLOIDOSIS – A CASE REPORT

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INTRODUCTION

Secondary (AA) amyloidosis is a disorder characterized by the extracellular tissue deposition of fibrils composed of fragments of serum amyloid A protein (SAA), an acute phase reactant. AA amyloidosis can complicate a number of chronic inflammatory conditions, including rheumatoid arthritis (RA), juvenile RA, and ankylosing spondylitis[1,2]. Tuberculosis, a very common chronic infection in developing countries, is not a very common cause of secondary amyloidosis[3]. AA amyloidosis is associated with increased hepatocyte production of the acute phase reactant serum amyloid A (SAA); in chronic inflammatory disorders, this process may be stimulated by the release of cytokines (perhaps interleukin-1) from activated macrophages[1]. Cleavage in circulating monocytes /macrophages results in the generation of smaller fragments, called AA protein that can then deposit in the tissues. We are reporting a case of pulmonary tuberculosis, which remained untreated for a considerable period and presented with nephrotic syndrome due to renal amyloidosis.

CASE REPORT

A young man of 35 years, resident of rural area of Baluchistan, presented with about two years history of cough productive of mucoid sputum and generalized ill health. Six months previously he noticed generalized swelling of body, especially noticeable at face, ankles and feet. He was found to have significant proteinuria at a local hospital and treated for some time, probably with corticosteroids and diuretics for a month or so. Generalized swelling improved but the treatment stopped by the patient himself. The chest radiograph was probably not carried out at that time and he was never treated for pulmonary tuberculosis. His cough had worsened in the previous few weeks, associated with moderate fever, breathlessness on mild exertion and generalized weakness. Generalized swelling of the body had again recurred and gradually increased with slight abdominal distension also. On examination, he was a sick looking, thinly built man, with a pulse rate of 106 beats per minute, temperature 38.4 degrees centigrade and blood pressure 110/70 mm Hg. He was pale but not jaundiced. He had facial puffiness and significant generalized oedema. There was no lymhadenopathy. Examination of respiratory system revealed a central trachea and signs of pleural effusion on right side. Abdomen was full, soft and non-tender. There was no visceromegaly but shifting dullness at flanks was present. Rest of the clinical examination was unremarkable. His Hb% was 10.9 g/dl, total leucocyte count 10.4 x 10^9 /l and ESR 100 mm fall at the end of first hour. Urine examination by dipstix revealed proteinuria (+ ++). Twenty four hour urinary protein was 5.825 g. Serum albumin was 26 g/l and serum total protein was 56g/l. Serum urea was 10.2 mmol/l, creatinine 167 micromol/l, sodium 134 mmol/l and potassium 2.8 mmol/l. Chest radiograph showed nodulostriate opacities, fibrosis and destructive changes in both lung fields and mild right sided pleural effusion. Ultrasonographic (USG) examination of the abdomen revealed enlarged and oedematous kidneys measuring 13.4 and 13.7 cm length on right and left sides respectively. Cortical parenchymal echogenecity was increased (grade-II). There was moderate ascites and mild right sided pleural effusion. Liver, spleen, portal vein and pancreas appeared normal on USG examination of abdomen. Echocardiography revealed a normal study. Serum was negative for HBsAg but positive for anti HCV antibodies. Renal biopsy was performed and histopathological examination

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showed mesangial deposition of hyaline, pink acellular material, with mild patchy tubular atrophy and interstitial inflammation. There was no vasculopathy. Immunohistochemical staining confirmed the presence of amyloid-A. Conclusion was Secondary Renal Amyloidosis (Amyloid A - positive). PCR for HCV RNA was negative. Mantoux test with 5 tuberculin units was positive with an induration of 14 mm. Sputum smear was positive for acid fast bacilli (AFB) on ZN staining. Pleural fluid examination revealed a transudate, with a protein content of 2.2 g/l and cell count of 70/microlitre. Leishman's stain showed mostly lymphocytes and occasional neutrophils. No AFB seen on ZN staining and no micro-organism was seen on Grams staining. Cytology of fluid did not show any malignant cells. Serum was negative for RA factor and antinuclear antibody. A final diagnosis of pulmonary tuberculosis leading to Renal Amyloidosis type AA and nephrotic syndrome was made. Keeping in mind the possibility of regression of renal amyloidosis with treatment of the primary cause, anti-tuberculosis drug therapy was started with a usual four drug regimen in a modified doses due to renal impairment. Isoniazid and rifampicin were given in full adult doses according to weight but pyrazinamide and ethambutol were given in doses of 25 mg/kg and 15 mg/kg respectively three times a week. Diuretics were given to reduce oedema. He showed some improvement in the next 3 to 4 weeks, with improvement of fever, cough and oedema, without any further deterioration of renal functions. He then moved to his native town with a full summary of the case and lost to follow up.

DISCUSSION

The association of tuberculosis with amyloidosis has been reported in adults[2] as well as in children[3]. Secondary (AA) amyloidosis is a serious disease. If untreated, it is associated with a significant mortality due to end-stage renal disease, infection, heart failure, bowel perforation or gastrointestinal bleeding[4].

Successful treatment of the underlying inflammatory process can lead to stabilization or improvement in renal function, reduction in protein excretion, and partial resolution of amyloid deposits[2,5,6]. The cases have been reported in the literature in which there was remission of nephrotic syndrome following treatment of tuberculosis[3,7]. We lost our patient's follow up, so unable to monitor the course of his illness.

Clinically evident renal involvement mainly occurs in AL or AA amyloidosis[8]. Patients with renal amyloidosis who progress to end-stage renal disease can be treated with either dialysis or renal transplantation. Hemodialysis and continuous ambulatory peritoneal dialysis (CAPD) appear to be equally effective, with the limiting factors being the degree of extrarenal amyloid deposition, hypotension with hemodialysis, and peritonitis with CAPD[9].

The prognosis among those who require dialysis is not good, although some studies suggest increased survival among patients with AA amyloidosis. In a retrospective study of 19 patients with AL amyloidosis and 20 with AA amyloidosis, which required dialysis and were followed up after approximately 35 months, 15 (79 %) with AL and 3 patients (15 %) with AA amyloidosis died[10].

The largest study of renal transplantation compared the results in 45 patients with amyloidosis to that in a matched control group with other disorders[11]. The patient survival was lower in the amyloid group due predominantly to infectious and cardiovascular complications.

The interval between the onset of pulmonary tuberculosis and the first evidence of renal amyloidosis is variable in different studies. In a recent study by Ramakant Dixit and colleagues[12], this interval was 2 months to 7 years (mean 2.25 years). They found that 15.1% patients developed amyloidosis in less than three months period after the diagnosis of pulmonary tuberculosis. An early onset amyloidosis after the diagnosis of active tuberculosis has also been reported by some other researchers[13]. We could not assess the time of onset of either pulmonary tuberculosis or renal amyloidosis in our patient as both conditions were fairly advanced on

presentation. Due to variable preclinical stage, the true interval between the preceding disease and the onset of amyloidosis is not known exactly, so it is reasonable to suspect renal amyloidosis in any patient with a known history of pulmonary tuberculosis presenting with pedal edema and proteinuria.[12]

REFERENCES

1. Rocken C, Shakespeare, A. Pathology, diagnosis and pathogenesis of AA amyloidosis. Virchows Arch 2002; 440:111.
2. Lachmann HJ, Goodman HJ, Gilbertson JA. Natural history and outcome in systemic AA amyloidosis. N Engl J Med 2007; 356:2361.
3. Krishnamurthy S, Samanta D, Yadav S. Renal amyloidosis secondary to childhood tuberculosis: A report of two cases. J Postgrad Med 2009; 55:121-3.
4. Tanaka F, Migita, K, Honda S. Clinical outcome and survival of secondary (AA) amyloidosis. Clin Exp Rheumatol 2003; 21:343.
5. Gillmore JD, Lovat LB, Persey MR. Amyloid load and clinical outcome in AA amyloidosis in relation to circulating concentration of serum amyloid A protein. Lancet 2001; 358:24.
6. Gillmore JD, Hawkins PN. Drug Insight: emerging therapies for amyloidosis. Nat Clin Pract Nephrol 2006; 2:263.
7. Costellano I, Gomez-Martino JR, Hernandez MT. Remission of nephrotic syndrome caused by renal amyloidosis secondary to pulmonary tuberculosis after tuberculostatic treatment. Nefrologia 2001; 21:88-91.
8. Dember LM. Amyloidosis-associated kidney disease. J Am Soc Nephrol 2006; 17:3458.
9. Moroni G, Banfi G, Montoli A. Chronic dialysis in patients with systemic amyloidosis: The experience in northern Italy. Clin Nephrol 1992; 38:81.
10. Bollee G, Guery, B, Joly D. Presentation and outcome of patients with systemic amyloidosis undergoing dialysis. Clin J Am Soc Nephrol 2008; 3:375.
11. Pasternack A, Ahonen J, Kuhlback B. Renal transplantation in 45 patients with amyloidosis. Transplantation 1986; 42:598.
12. Dixit R, Gupta R, Dave L. Clinical profile of patients having pulmonary tuberculosis and renal amyloidosis. Lung India. 2009 Apr-Jun; 26(2): 41–45.
13. Malhotra P, Agarwal R, Awasthi A. How long does it take for tuberculosis to cause secondary amyloidosis? Eur J Intern Med. 2006; 16:437–9.