CLINICAL AND HISTOLOGICAL REGRESSION OF SECONDARY AMYLOIDOSIS ASSOCIATED WITH SCHISTOSOMA MANSONI INFECTION

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SUMMARY:

A child with the nephrotic syndrome due to histologically documented renal amyloidosis and who also had amyloid deposits in the liver was found to have schistosoma mansoni infection. Treatment of the schistosoma infection was followed after 3 months, by complete disappearance of the hepatic amyloid deposits. Proteinuria and other features of the nephrotic syndrome disappeared and there was considerable diminution in the renal amyloid desposits. It is suggested that the association of amyloid with bilharzia is propably more common than is currently recognised and that treatment of the bilharzia infection may be followed by considerable regression of the secondary amyloidosis.

INTRODUCTION:

Secondary amyloidosis has long been recognised as a complication of some chronic inflammatory conditions like tuberculosis and rheumatoid arthritis.2 It has rarely been described in association with Mansoni schistosomiasis.3 We describe here a patient in whom other conditions known to be associated with amyloidosis have been ex cluded and who showed regression of the amyloidosis after specific antibilharzial treatment.

CASE HISTORY:

J.J. a 10 year old male child from the South of the Sudan was admitted to hospital on 10.5. 1974 because of progressive abdominal distension and gross swelling of the lower limbs for 5 month before Admission.

Examination showed gross generalised oedema, ascites, oedema of the abdominal wall, bilateral hydrocoele and scrotal oedema, and gross oedema of

the lower limbs. Blood pressure was 120/80. The cardiovascular and respiratory systems were normal The liver was enlarged to 7 cms. below the right costal margin spleen was enlarged to about 6 cms below the left costal margin. Hb, PCV, plasma proteins, cholestrol, blood urea, and 24hours urinary protein are shown in the table. ESR was 10mm/hour (Westergren) and he had a normal differential white cell count with no increased eosinophils. Electrolytes were: Sodium 134m Eq/L and Potassium 4.3 Eq/L. Repeated stools examination for parasites was negative. He was treated with a high protein diet and frusemide 20 mg daily for his nephrotic syndrome. A barrium swallow was later performed and it did not show oesophageal varies.

On 6.6.1974 a needle biopsy of the liver was performed (fig.1) and the following histopathological report was received "Adequate liver biopsyshowing preservation of the architecture. The portal tracts show a brisk lymphocytic infilteration but no significant fibrosis. The Kupffer cells contain brown pigment (bilharzial). There are several granulomata containing bilharzial eggs. Some

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of the hepatocytes are replaced by pink homogenous material which is Congo red positive.

Diagnosis: Bilharziasis and amyloidosis." In view of this the following investigations were carried out to exclude conditions known to be associated with amyloidosis :—

Chest X-Ray was normal, Mantoux test was negative, Kahn and W.R. tests were negative, skeletal survey was normal, L.E. cells and rheumatioid factor were negative and Hb. electrophoresis showed Hb.AA. A percutaneous renal biopsy was performed on 21.7.1974, and it showed excessive amyloid deposition in all the glomerular tufts and vessels (fig. 3). On 29.7.1974 he was given antibilharzial treatment in the form of a single injection of Hycanthone (eterenol).

Subsequently his heaptomegaly and splenomegaly underwent gradual regression. No frusemide was given from 15.8.1974 and no oedema reappeared. Clinical examination on 29.10.1974 showed a healthy looking boy with no evidence of oedema. The liver could just be felt on deep inspiration and the spleen was not palpable.

In view of this unexpected considerable improvement a respeat liver (fig.2) and renal biopsy (fig. 4) were performed to see if there is parallel diminution in the amyloidosis and comparison with the previous biopsies was made. The following histopathological reports were received :—

Liver biopsy :- 29.10.1974.

1. Architecture is preserved in both.

2. Less inflammatory infilterate and more fibrous tissue in post-treatment specimen.
3. Focal inflammatory infilterate within lobules in post treatment biopsy in which no bilharzia granuloma was seen.
4. The two biopsies are stained in parallel with a positive control for amyloid. Amyloid disappeared in post treatment biopsy.

Renal biopsy :- 2.11.1974.

1. The pre-treatment biopsy (21.7.1974) contains eight complete glomeruli all of which show extereme amyloid deposition affecting the whole glomerular tufts.
2. The post-treatment biopsy contains twelve complete glomeruli some of which show patchy amyloid desposits affecting only part of the glomerular tufts. Some glomeruli are almost completely free with only the afferent arteriole involved. None of the glomeruli show complete amyloid deposition in the pre-treatment specimen.
3. All vessels in the pre-treatment biopsy are involved. In the post treatment biopsy some of the vessels are normal.

CONCLUSION:

(1) complete regression of hepatic deposits.

(2) considerable regression of the renal amyloid deposits.

DISCUSSION:

This patient presents two important points. First the association of amyloidosis with bilharzia and secondly the clinical and histological evidence of regression of hepatic and renal amyloid deposits following specific therapy.

The clinical and histological improvement which followed specific anti-bilharzial treatment, as well as the absence of conditions known to be causally related to amyloid may be taken as evidence of the aetiological role of bilharzia in the genesis of amyloid. Similar association has rarely been described.3,4

On theoretieal grounds, the association of amyloidosis with Bilharzial infection is feasible. Present knowledge about the nature of secondary amyloidosis indicates that the major component of the deposit is a protein different from all immunoglobulins 5-8. An antigenically frelated but larger protein was found in the sera of normal subjects but in increased amounts in patients with amyloidosis and other chronic inflammatory conditions.5 It is postulated 5 that this may represnt the precursor or the transport protein for the amyloid subunit. Some studies9 have demonstrated in addition some light chain related proteins. Bilharzia is a chronic inflammatory condition and when there is

hepatic involvement by bilharzial granulomata there is increased production of immunoglobulins. 9,10 Thus showing similarities to conditions known to give rise to secondary amyloidosis. The fact that there has been so few reports may partly be due to the ease with which amyploid may be missed if specific stains are not employed.11

Moreover the association of the nephrotic syndrome with schistosoma mansoni infection has been reported from South America12, renal histology showed membrano-proliferative changes, glomerular sclerotic focal lesions and membranous lesions in that order of frequency. It is not metioned whether amyloid was specifically looked for.

Triger and Jockes11 describe a patient with memberanous glomerulonephritis who when he died 3 years later was found at autopsy to have amyloidosis and on reviewing the original biopsy using specific stains for amyloid showed that was the original diagnosis. They also point out that with silver stains some amyloidosis showed the typical epithelial speclar depositions characteristic of membranous glomerulonephritis thought to be due the deposition of antigen antibody complexes. Accordingly it would seem reasonable to assume that in at least some of the nephrotic patients with bilharziasis, currently considered to be due to immological mechnisms, 12,13amyloidosis amy be the cause. It would seem desirable to use specific amyloid stains in biopsies from all such patients.

The prognosis of renal involvement in secondary amyloidosis was generally considered to be poor, death resulting from progressive renal failure.15 Reports of clinical remission in histologically documented cases are infrequent. 16,17 Waldenstrom 17 demonstrated in serial biopsies the disappearance of hepatic amyloid in three patients treated for chronic tuberculous osteomyetitis. Lowenstein and Gallo17 have reported two cases of secondary renal amyloidosis which showed clinical remission with disappearance of proteinuria but the amyloid deposits were still present 27 and 6 months respectively after the disappearance of proteinuria. Triger and Jockes11 had 5 patients with secondary renal amyloidosis and nephrotic syndrome who showed considerable fall in their proteinuria and histological evidence of regression of renal amyloid deposits with adequate treatment of the causative pathology. These patients had adequate renal function before treatment. It is thus possible that adequate treatment of the underlying cause may result in regression of renal amyloidosis, probably before significant renal functional impairment has occurred. This case we present with considerable evidence of histological amyloid regression three months after treatment of bilharzia probably lends further support to this propostion.

TABLE 1:

LABORATORY INVESTIGATIONS

Date	Hb g/100 ml	PCV %	Total Plasma protein g/100 ml	Alb./glob. g/100ml	S. cholestrol mg/100ml	B.Urea mg/100 ml	24 hours Urine protein g/24 hr.
10.5	9.5	31	5.3	2.7/2.6	290	32	6.3
15.8	—	—	6.2	3.5/2.7	—	26	3.5
29.10	10.1	33	7.2	4.0/3.2	195	24	0.15

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ILLUSTRATIONS

Figure 1. Pretreatment liver biopsy showing areas of amyloid deposits (Congo Red x 120).

Figure 2. Post-treatment liver biopsy showing focal cellular infiltrate and absence of amyloid (Congo Red x 120).

Figure 3. Pretreatment renal biopsy showing extensive amyloid deposits in all glomeruli (Congo Red x 120).

Figure 4. Post-treatment renal biopsy showing diminution of amyloid deposits in glomeruli (Congo Red x 120).