Secondary amyloidosis AA with P component

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Abstract

The authors report a case of a 69 years old patient with a history of chronic obstructive lung disease and tuberculosis. In February 1994 he was admitted with refractory congestive heart failure and chronic respiratory failure. One month after discharge, the patient was readmitted with anasarca secondary to nephrotic syndrome. Renal biopsy revealed amyloidosis AA with P component. Heredofamilial amyloidosis and other causes of secondary amyloidosis were excluded. The final diagnosis was amyloidosis secondary chronic respiratory infections and tuberculosis. Eight weeks after admission acute renal failure emerged and haemodialysis was started. The patient died 6 weeks later. At necropsy, amyloidosis was confirmed with the involvement of the kidney and vessels of the myocardium, lung, adrenal gland and skin. The immunocytochemical test revealed secondary amyloidosis.

Key words: secondary amyloidosis AA with P component, nephrotic syndrome, congestive heart failure.

Introduction

Reactive secondary or systemic amyloidosis (RSA) is often associated with chronic infections, such as tuberculosis and bronchiectasis. It is the result of the deposition of an acute-phase lipoprotein, known as serum amyloid A (SAA) in multiple organs and systems in the form of nodules or fibrils.[1] The P-component (pentagonal unit) is a circulating non-fibrillar glycoprotein that is associated with fibrillar deposits, an analog and derivative of the serum component (SAP), which is a normal circulating protein of the pentraxin family.[1,2] The clinical manifestations are the result of the deposition of this material in various organs and systems.[1]

Secondary amyloidosis can manifest, in 60% of cases, as nephrotic syndrome, with renal failure being the leading cause of death;[3] it may also result in arrhythmia with sudden death; sudden, untreatable cardiac insufficiency; and respiratory failure associated with associated infectious complications. The therapeutic options are limited, consisting, in cases of secondary amyloidosis, of treatment of the underlying infection. The systemic forms have progressive evolution, and the prognosis is reserved (mean survival of one to four years). [3,4]

The clinical case described below was considered a type of congestive cardiac insufficiency, refractory to medical therapy, which led to successive hospitalizations and was associated with a severe nephrotic syndrome and massive proteinuria that progressed rapidly to oligoanuric renal failure, prompting the start of an urgent haemodialysis plan. Renal biopsy showed type AA amyloidosis with P-component (immunocytochemistry). The patient died after six weeks of haemodialysis, and the autopsy confirmed systemic type AA amyloidosis, with involvement of the kidney, heart, adrenal gland and skin, and also transmural myocardial infarction of the left ventricle, a focus of recent softening on the right cerebral hemisphere, bronchiectasis and bilateral bronchopneumonia.

Clinical case

Male, aged 69, a bricklayer, with a history of chronic alcohol abuse, chronic bronchitis due to smoking, recurrent respiratory infections and pulmonary tuberculosis, with first admission in February 1994 due to congestive heart failure (with clinical symptoms characterized by dyspnea, stasis rales in both hemithorax, jugular engorgement, painful hepatomegaly and edema of the lower limbs) and acute chronic respiratory failure. The patient received medical therapy with diuretics, aminophylline, salbutamol,

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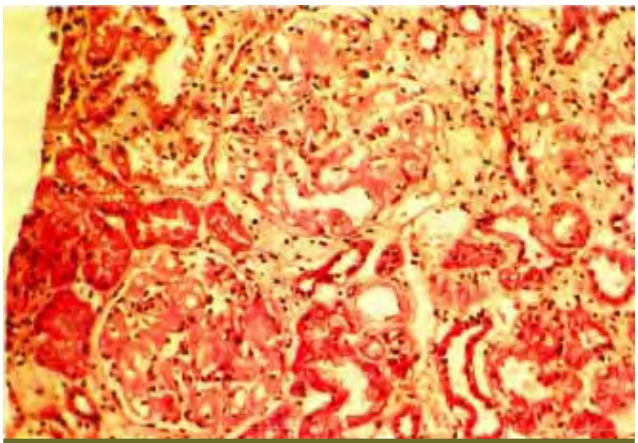
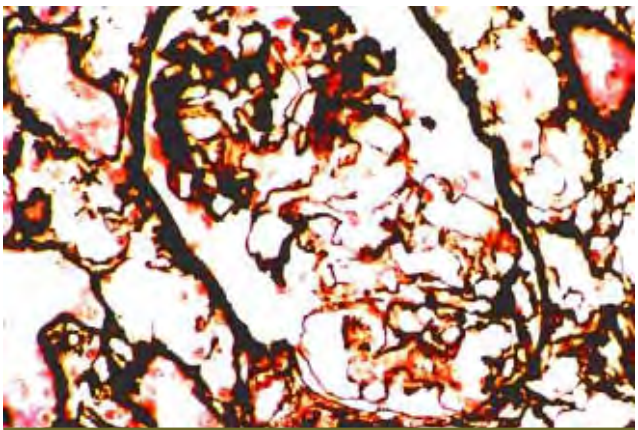


Renal biopsy: hematoxylin and eosin stain.

FIG. 1

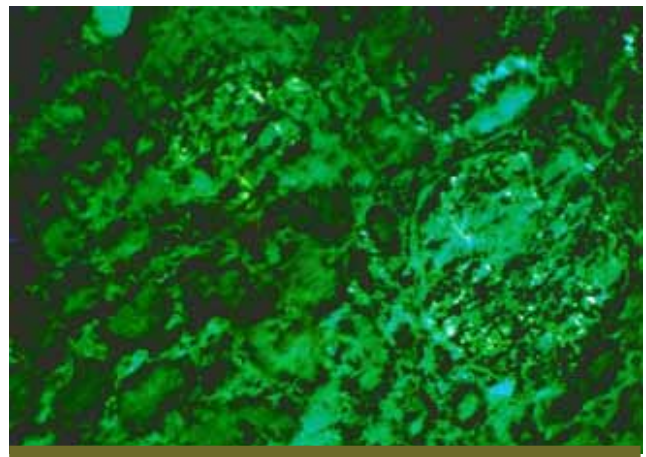


Renal biopsy: Congo red positive amyloid deposits

FIG. 2

ipratropium bromide and captopril, and was discharged, but readmitted one month later due to anasarca.

The clinical symptoms and laboratory results (Table 1) were demonstrative of nephrotic syndrome with massive proteinuria (5 - 13g/24h), marked hypoalbuminaemia (1.1 - 1.4 g/dL) and dyslipidaemia (cholesterol = 426 mg/dl and triglycerides = 347 mg/dl). A comprehensive investigation was carried out to clarify the aetiology, including the immunological study (ANAS: anti-DNA_{ss}; anti-DNA_{ds}; anti-RNP; anti-centromere antibodies; anti-scl70; anti-SSA; anti-SSB; ANCA; anti-SM; C3; C4; CH50; circulating immune complexes) which was negative. The test for Bence Jones proteinuria, serum and urine protein electrophoresis, and immunoelectrophoresis, ruled out the existence of associated monoclonal gammopathy. Due to an associated hypercoagulable condition, tests for protein C, protein S and antithrombin III were requested, the results of which were 51%, 60%, 50%, respectively. The ECG was normal.



Renal biopsy: birefringence of amyloid under polarized light.

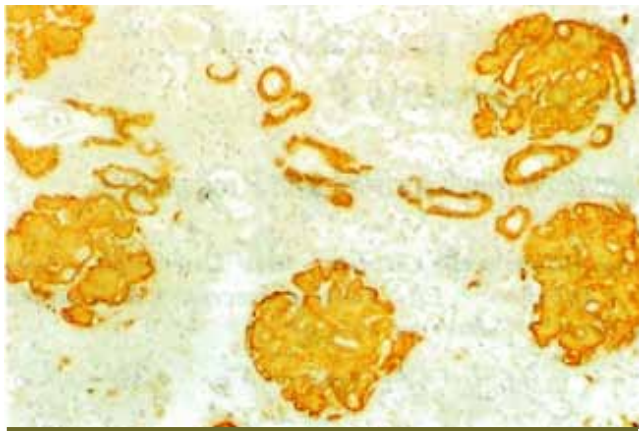
FIG. 3

Abdominal ultrasound showed enlarged kidneys (right kidney 12x5, 2x4.6 cm; left kidney. 12.4x6, 2x5.5 cm) with regular contours and increased diffuse echogenicity of the renal parenchyma, with a well-maintained parenchymal index; all these changes were confirmed by abdominal CT. Moderate ascites was also associated.

Renal biopsy revealed: deposits of amyloid substance in the glomerulus, invading the mesangium, but leaving most of the lumens free; amyloid deposits in the intertubular capillaries. The Congo red stain was positive in the glomeruli and some intertubular capillaries, and immunofluorescence identified deposits of type AA amyloid with P-component (*Figs. 1, 2 and 3*). [1,5,6,7]

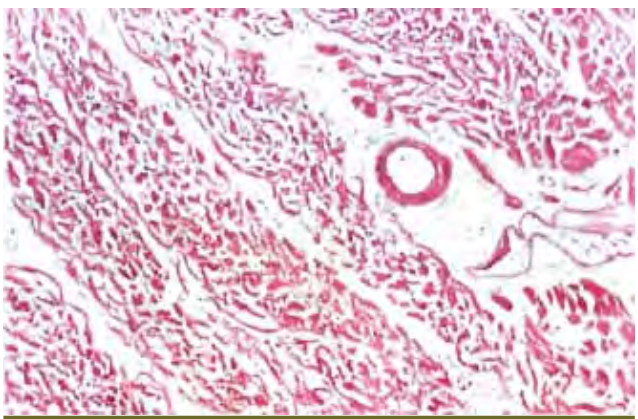
The respiratory function tests showed mixed ventilatory changes in which the obstructive component was the most accentuated, responding poorly to bronchodilators.

CT of the chest confirmed the changes shown in the chest X-ray: heterogeneous infiltration of the upper right lobe, predominantly posterior, bronchiectasis, and thickening of the bilateral posterior basal costal pleura, ruling out existence of mediastinal adenomegaly.



Amyloid deposits in the kidney.

FIG. 4



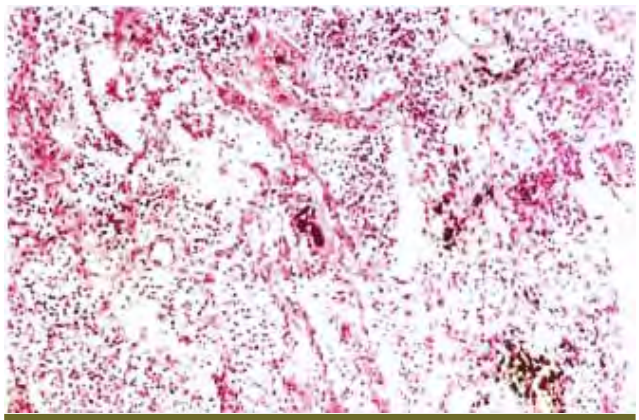
Amyloid deposits in the vessels of the myocardium.

FIG. 5

Upper endoscopy and colonoscopy were also performed to rule out a possible neoplasm of the digestive tract, which revealed no changes.

The patient received medical therapy with spironolactone (100 mg/day), furosemide (40 - 160 mg/day), desalted human albumin (q.b.), salbutamol, aminophylline-retard preparation, fraxiparine 7500 U/SC, due to progressive deterioration of the renal function, which led to the start of early haemodialysis with ultrafiltration. The patient also received antibiotics (amoxicillin/erythromycin) for intercurrent bronchopneumonia and erysipelas.

After six weeks of haemodialysis, the patient died, and autopsy was performed for the collection of multiple organ fragments. Histology showed amyloidosis



Multiple foci of bronchopneumonia; anthracosis of the lung.

FIG. 6

deposits in the kidney and vessels of the myocardium, adrenal glands, skin and lungs, associated with pulmonary anthracosis, pleural fibrosis, bronchiectasis and bronchopneumonia characterized by multiple foci (*Figs. 4, 5 and 6*).

Discussion

In a patient who had multiple hospital admissions due to congestive heart failure, refractory to medical therapy, with which a nephrotic syndrome is associated, it is imperative to consider a systemic disease with involvement of these corresponding organs.[8] Thus, systemic diseases like diabetes, systemic lupus erythematosus, lymphomas, neoplasm of the digestive tract and side effects of the drugs were ruled out.[3,4] In the present case, we encountered the following problems:

1 - Congestive heart failure, refractory to standard medical therapy, which was attributed to the underlying cardiomyopathy and ischemic heart disease, confirmed subsequently by pathological anatomical examination.

2 - Clinical symptoms suggestive of anasarca and laboratory results suggestive of nephrotic syndrome, ruling out systemic diseases and all other causes mentioned above.

3 - Progressive development of oligoanuric renal failure requiring haemodialysis.

Hereditary causes [9,10,11,12] were ruled out as the secondary aetiology; only previous pulmonary tuberculosis, the radiological evidence of bronchiectasis and recurrent respiratory infections with chronic respiratory failure were observed. Following the

TABLE I

Laboratorial results

	26Jan94	22Feb94	12April94	17April94	23April94	10May94
RBC (cells/mm3)	4,250,000	4,050,000	4,280,000	3,450,000	3,490,000	3,220,000
Hemoglobin (g/dL)	11.8	11.2	12.4	10.2	9.4	9.3
WBC (cells /mm3)	9,400	6,600	30,000	23,900	15,100	16,400
Neutrophils (%)	68	51	94	86	86	93
Lymphocytes (%)	25	36	3	1	14	5
Platelets (cells/mm3)	400,000	425,000	544,000	419,000	210,000	213,000
Sedimentation rate (mm)	110	50	100	100	130	48
Glucose (mg/dL)	110	59	104	74	86	104
Urea (mg/dL)	20	15	83	164	128	78
Uric acid (mg/dL)	4.9	6.0		10.7	8.0	4.5
Creatinine (mg/dL)	0.5	0.5	1.7	4.7	4.17	3.2
Creatinine clearance (ml/min.)				1.4	2.0	
Total protein (g/dL)	4.3	3.8	3.5	4.1		4.4
Albumin (g/dL)	1.1	1.4	1.3	2.8		2.9
a1 (%)	3.9	2.7	3.1			
a2 (%)	44.3	34.5	36.8			
b (%)	8.5	6.0	5.6			
g (%)	19.5	13.2	15.5			
Proteinuria 24h (g)	5.3	13.0				
Calcium (mg/dL)	7.9	7.3	6.8	7.5	8.2	8.2
Phosphorus (mg/dL)	1.6	2.5	4.6	4.7	3.6	3.0
Sodium (mEq/L)	138	132	130	133	145	138
Potassium (mEq/L)	4.7	4.9	2.3	2.7	3.7	3.0
Chlorine (mEq/L)	103	101	76	85	108	102
Magnesium (mg/dL)	3.4	1.4	1.3	1.9	1.6	2.4
T.B. (mg/dL) (total bilirubin)	0.16	0.19	0.66			0.38
D.B. (mg/dL) (conjugated bilirubin)	0.01					0.05
GOT (U/L)	23	10	11			9
GTP (U/L)	5	2	3			5
g - GT (U/L)	18	23	20			10
Alkaline P. (U/L)	101	70	75			91
CPK (U/L)	215	119	62			17
LDH (mg/dl)	468	342	346			444
PT (%)	>120	118	116		84	
PTT (sec.)	31.5	36.4	33.9		69.0	
Fibrinogen (g/L)	0.8	11.4	10.4		4.13	
Cholesterol (mg/dL)	426	258	265			
Triglycerides (mg/dL)	347	285	202			
LDH (mg/dL)	47	22	36			

investigation, renal biopsy was performed to clarify the aetiology, which showed amyloid deposits in the glomeruli and intertubular capillaries, and an immunofluorescence which characterized the condition as type AA amyloid with P-component.

This case is demonstrative of secondary amyloidosis with systemic involvement, with all possible treatment options performed, including antibiotics for the treatment of intercurrent infections and a chronic haemodialysis plan due to severe oligoanuric renal failure.

Other therapeutic options were ruled out that have no indication for this type of amyloidosis, including alkylating agents and colchicine, as well as kidney transplant.

The prognosis is always reserved (survival of one to four years), and our patient died four months after the development of anasarca.

The autopsy identified the following causes of death, in addition to multisystemic amyloidosis: acute myocardial infarction of the left ventricular wall, stroke of the right cerebral hemisphere, bronchiectasis, and bilateral bronchopneumonia. ■

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