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From the lungs to the kidneys; a case of renal AA amyloidosis in a patient with pulmonary TB

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ABSTRACT

AA amyloidosis is a complication related to several chronic inflammatory conditions like cancer, autoimmune diseases and infections, among others. The disease implicates amyloid fibrils deposit in tissues leading to organ failure. Renal involvement has been closely associated with amyloidosis and sometimes with tuberculosis too. Therefore, it is important to achieve a renal biopsy that allows elucidating the etiology of the clinical picture in order to provide the correct treatment to the patients. In this paper, we present a case of renal amyloidosis secondary to pulmonary tuberculosis which debuted as nephrotic syndrome.

Brief Report

Implication for health policy/practice/research/medical education:
Renal AA amyloidosis is an uncommon disease and histopathological recognition is essential in early and ideal treatment, because nephrotic syndrome in patient treatment for tuberculosis can confuse etiology the kidney injury.

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Introduction

Amyloidosis comprises a group of various extracellular protein deposition diseases of amyloid fibrils involving any type of organ or tissue leading to organic dysfunction (1). Amyloid protein can develop in the presence of an abnormal protein (eg, hereditary amyloidosis and acquired immunoglobulin light chain AL amyloidosis), in association with overproduction of a typical protein (eg, systemic AA amyloidosis) and of unknown etiopathogenesis (2). Amyloid fibril formation is due to a nucleation-dependent polymerization defect as proven in vitro in various types of human amyloid proteins. An 18-year-old man with a history of pulmonary tuberculosis was referred to our center because of six days of lower limbs and eyelids edema, which subsequently generalized and was accompanied by abdominal distension. He had been followed in the outpatient National TB programme receiving rifampin, isoniazid, pyrazinamide and ethambutol for the last 29 days. The patient attended a medical appointment previously and was discharged home with furosemide, spironolactone and enalapril. Three days later, he returned, reporting worsening of symptoms, including swelling of the whole body.

On physical examination, the patient was afebrile without distress. Vital signs were notable for heart rate of 96 beats per minute, respiratory rate of 22 breaths per minute and oxygen saturation of 94% requiring supplemental oxygen by nasal cannula. The blood pressure was 103/65 mm Hg and his temperature was 36°C. His respirations were unlabored but crackles in the lower left

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lung field and diminished breath sounds bilaterally were noted on auscultation. There was abdominal wall edema as well as grade 2 edema in the lower limbs. Neurologic exam was unremarkable.

Laboratory studies were obtained (Table 1). Chest X-ray revealed bilateral apical pleural thickening with hyperaeration of pulmonary bases and bilateral parenchymal fibrous tracts with some mixed infiltrates (Figure 1). A computed tomography (CT) of the chest revealed mediastinal nodes and distortion of the pulmonary architecture, upper lobes volume loss and fibroatelectasis tracts with cavitated lesions. Apical pleural thickening, centrilobular nodules, tree-in-bud pattern and bilateral pleural effusion was also observed (Figure 2).

Screening for infectious hepatitis and HIV were negative. Antinuclear antibodies, anti-dsDNA, ANCA, extractable nuclear antigens, Ro and La were also negative. Complement components C3 and C4 were within normal limits.

The patient received treatment with high dose diuretics, statin, enalapril, thromboprophylaxis with low molecular weight heparin and directly observed therapy for TB was continued. Since the abdominal ultrasound showed ascites and enlarged kidneys, therefore a renal biopsy was conducted (Figure 3).

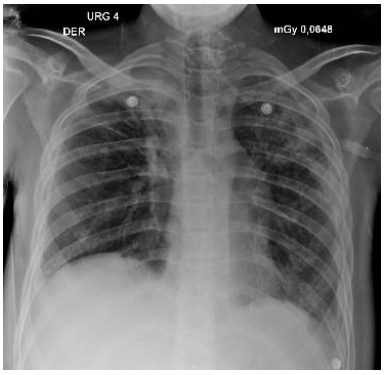

Figure 1. Chest X-ray.

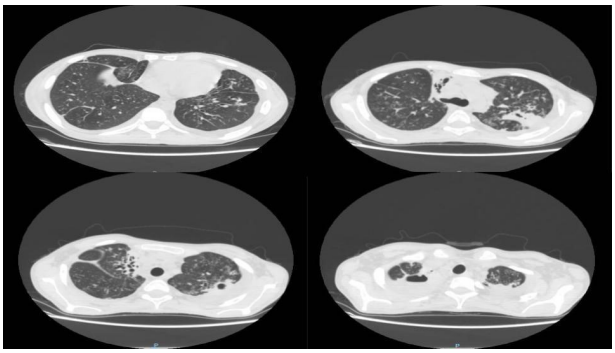

Figure 2. CT of the chest.

AA Amyloidosis

Systemic AA amyloidosis is secondary to chronic inflammatory diseases (eg, tuberculosis, rheumatoid arthritis, inflammatory bowel disease). Amyloid precursor is serum amyloid A (SAA), a soluble apolipoprotein mainly encoded by the SAA1 gene (1). Although its pathophysiology is unknown, it is believed that an elevation of proinflammatory cytokines, particularly tumor necrosis factor alpha (TNF-α), interleukin-1 beta (IL-1β) and IL-6, stimulates hepatocytes to secrete large amounts of SAA which latterly deposit in various tissues (2). Incidence of AA amyloidosis is estimated of 1 to 2 cases per million person-years, less than primary amyloidosis, amyloid light-chain (AL) or wild-type transthyretin amyloidosis. This is due to a less rate of chronic infections nowadays and improved treatments for rheumatologic diseases (3).

The kidney is one of the most frequent sites of amyloid depositions. Nephrotic syndrome represents the main clinical manifestation and accounts 50% of the patients with renal involvement (4). When gastrointestinal tract is affected, cirrhosis, malabsorption and GI bleeding can occur (4). Other manifestations include atraumatic organ rupture and acute obstruction (5,6).

Laser microdissection and proteomic analysis using mass spectrometry represents the gold standard to recognize the amyloid fibril nature but because this test is only available in limited sites, biopsy is used to look for amyloid proteins in tissues, although a negative result does not rule out amyloidosis (3). Congo red stain preparations under polarized light shows apple-green birefringence and is indicative of the presence of amyloid

Table 1. Laboratory results

Leukocytes	8.880 cell/mL	**Alanine aminotransferase**	16.59 U/L
Granulocytes	4.617 cell/mL	**Aspartate aminotransferase**	21.07 U/L
Hemoglobin	12 g/dL	**Total bilirubin**	0.50 mg/dL
Hematocrit	38.5 %	**Direct bilirubin**	0.35 mg/dL
Platelets	553.000/mL	**Serum creatinine**	0.36 mg/dL
Albumin	0.76 g/L	**Blood urea nitrogen**	6.51 mg/dL
Glucose	86 mg/dL	**24-hour urine protein test**	13.5 g

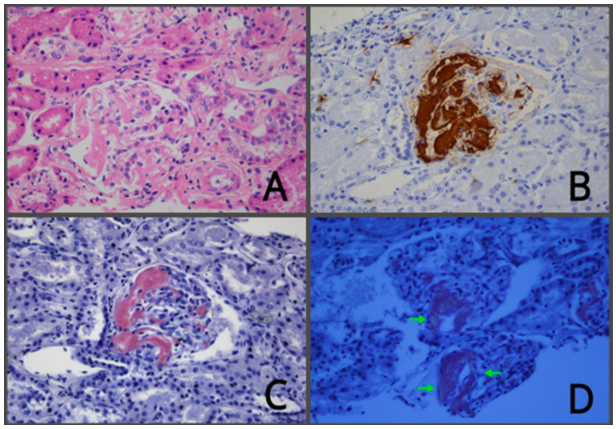

Figure 3. Renal biopsy showing amyloid deposition as amorphous material in hematoxylin eosin staining (panel A), [Congo red stain (panel C) with apple-green appearance when exposed to polarized light (panel D) confirms the presence of amyloid. An additional immunohistochemical study (panel B) confirms the presence of A amyloid protein.

fibrils. Furthermore, biopsy allows to evaluate extent and severity of the damage, without increased incidence of bleeding (7). Confirmation of the type of amyloid fiber by immunohistochemical staining remains the most available method and with a high diagnostic value for systemic AA amyloidosis, allowing the initiation of adequate treatment. Total body serum amyloid P component scintigraphy is a noninvasive procedure to obtain information on the distribution and magnitude of amyloid deposits (8).

The therapeutic key objective of systemic AA amyloidosis is to reduce the secretion of SAA from the liver by modulating autoimmune and inflammatory diseases with anti-inflammatory drugs (eg, corticosteroids, monoclonal antibodies or specific inhibition of interleukins) (9,10). In patients with renal amyloidosis, removing the Ig component improves renal function (11). Concentrations of SAA less than 4 mg/L are related with best results (9). Serum creatinine, urine protein/creatinine ratio and serum albumin are useful markers of organ function for response to treatment in patients with nephrotic syndrome (11). In gastrointestinal forms, somatostatin analogs as octreotide can be used (12).

Discussion

Even though our patient was on antibiotic treatment for tuberculosis he had an active inflammatory process but this infection in his lungs did not explain the kidney injury. Considering the patient's edematous syndrome, it was decided to request certain blood and urine parameters, which led us to nephrotic syndrome however it was the enlarged kidneys seen in ultrasonography which allowed us to consider amyloidosis as the causal event of his symptoms thereby it was decided to perform a renal biopsy in order to find amyloid deposits.

Conclusion

We have illustrated a case of renal AA amyloidosis in a patient with pulmonary TB. As mentioned in literature, the kidney is one of the most frequent sites of amyloid depositions and histopathologic diagnosis is essential to define therapeutic strategies. As in this case, a renal biopsy allowed us elucidating the etiology of the nephrotic syndrome, therefore we continued antituberculous medicine as the core treatment along with diuretics and antiproteinuric drugs. Several days later the patient made a full recovery and returned to his baseline renal status.

Authors' contribution

YM wrote initial draft, treated the patient and revisited the case. CC and PR; were part of the physician staff also and reviewed the final manuscript. ET an ND; both involved in writing, discussion and review section. All authors read and signed the final paper.

Conflicts of interest

The authors declare no conflicts of interest.

Ethical considerations

The patient gave his written informed consent for the use of the photographs of the samples taken from him. Information was obtained to contact the patient for follow-up.

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