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# A Case Report of the Association Renal AA Amyloidosis and Thyroid Papillary Carcinoma

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## Abstract

AA amyloidosis is often secondary to chronic inflammatory diseases but can rarely occur in patients with malignant neoplasms. A 33 years old woman with papillary carcinoma of thyroid was hospitalized in our department of Nephrology for nephrotic syndrome. Renal histology finds AA amyloidosis. To our knowledge, this is the first report of a patient with papillary carcinoma of thyroid and secondary (AA) amyloidosis with amyloid deposition in the kidneys causing nephrotic syndrome.

## Keywords

Papillary Carcinoma or Thyroid, AA Amyloidosis, Nephrotic Syndrome

## 1. Introduction

Amyloidosis represents a heterogeneous group of diseases related to the extracellular deposition of highly organized polymerized proteins which are capable of adopting an abnormal fibrillar conformation insoluble in tissues [1].

Amyloidosis is classified according to the protein responsible for the anomaly. There are more than 18 proteins capable of forming amyloid deposits.

In the course of AA amyloidosis, amyloid substance deposition is derived from the Serum Amyloid A (SAA) protein, one of the major proteins of inflammatory reactions [2].

The main causes of AA amyloidosis are chronic inflammatory diseases (rheumatoid arthritis ankylosing spondylitis, autoimmune diseases), infectious diseases (tuberculosis and bronchiectasis) or familial Mediterranean fever (FMF) or rarely tumors.

All of these conditions are associated with elevated circulating levels of serum amyloid A (SAA) [1].

We report a case of the association of thyroid papillary carcinoma with renal AA amyloidosis.

## 2. Case Report

A 33 year-old female was referred to our hospital for generalized oedema.

She had no history of fever, recurrent infections or chronic inflammatory disease. She had no family history or any clinical presentation compatible with FMF or familial amyloidosis.

In June 2013 she underwent total thyroidectomy for a suspicious thyroid nodule, of which the histopathology results were in favour of a papillary carcinoma of the thyroid with vesicular differentiation without capsular invasion.

There was no adjuvant treatment necessary postoperatively.

Six months later, in December 2013, the patient was admitted to our nephrology department.

Her physical examination was notable for generalized oedema with facial puffiness and hypotension at 90/50 mmHg.

Laboratory exams were in favor of a nephrotic syndrome with hypoprotidemia at 33 g/l, hypo albuminemia at 13 g/l, massive proteinuria at 11 g daily.

There was no microscopic hematuria and renal function was within normal range with serum creatinine at 0.5 mg/dL.

Other tests showed an inflammatory syndrome with an elevation of CRP at 55 mg/l, hyperferritinemia at 513 mg/L and anemia at 102 g/l with normal reticulocyte count, normal white blood cell count ($9 \times 10^3/\mu L$), and normal platelet count ($250\ 10^3/\mu L$).

The viral serologies of hepatitis B, C were negative as well as HIV and TPHA-VDRL serology.

Antinuclear factor and antineutrophil cytoplasmic autoantibody was negative, and normal antiproteinase 3 and antimyeloperoxidase concentrations.

The thyroid panel found severely low levels of TSH in relation to urinary loss of thyroid hormone binding proteins.

The cervical ultrasound found an empty thyroid lodge without any tumor residues.

A body CT scan did not find any other malignancies.

The bone scintigraphy was normal.

Abdominal ultrasound showed normal bipolar diameter of both kidneys (left, 12 cm; right, 11 cm.

The biopsy containing 19 glomeruli without cell proliferation.

Renal histology found massive amyloid deposits in the glomerulus without vascular deposits.

Congo red coloration was positive and the presence of AA amyloid was confirmed by means of the standard immunohistochemical technique using mo-

noclonal AA antiserum (Figure 1).

The diagnosis of a secondary AA-type amyloidosis caused by papillary carcinoma of thyroid was concluded.

Three years after the disease progression was notable for a deterioration of renal function with estimate glomerular filtration rate 20 ml/min.

## 3. Discussion

We present a patient with papillary carcinoma papillary of thyroid surgically treated. Six month later, she presented with nephrotic syndrome caused by secondary (AA) renal.

Renal involvement is common in AA systemic amyloidosis, and is the primary clinical manifestation and the leading cause of morbidity and mortality [3] [4].

AA amyloidosis is well known to develop in the setting of persistently high levels of SAA, which is produced by the liver in response to proinflammatory cytokines such as IL-1$\beta$, IL-6, and TNF-$\alpha$. Chronic inflammatory diseases such as tuberculosis, sarcoidosis, Crohn's disease, ulcerative colitis, aortitis syndrome, polyangitis, Behcet's disease, and FMF are reported causes of secondary amyloidosis.

However, AA amyloidosis can rarely occur in patients with malignant neoplasms essentially in patients with renal cell carcinoma [5] [6].

Others publications reported association of amyloidosis with adrenal carcinoma, hepatic tumor, pleomorphic sarcoma of the spleen and Hodgkin lymphoma and gastro intestinal tumor [7] [8] [9].

Hemminki *et al.* reported an increase in the incidence of NHL in elderly patients with AA amyloidosis [10].

There are several possible mechanisms by which high levels of SAA in patients with malignant neoplasms can lead to amyloidosis.

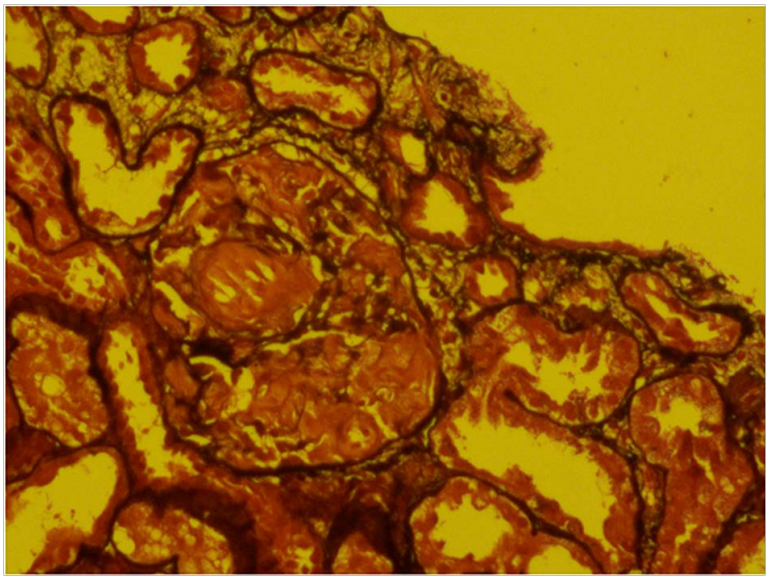

Figure 1. Amyloid deposit in glomerulus (reticuline ×20).

One of the hypotheses is the secretion of SAA by the tumor cells [11], as was demonstrated by Urieli-Shoval et al in patients with ovarian carcinoma who had high SAA serum levels. This suggested the role of SAA in ovarian tumogenesis [12]. The second hypothesis is that malignant cells can also secrete pro-inflammatory cytokines which stimulate the liver in producing SAA. Furthermore pro-inflammatory cytokines can also be produced by anti-tumor lymphocytes or macrophages [13] [14].

Any combination of these three mechanisms is possible.

In our case, the renal amyloidosis which presented as a nephrotic syndrome did not regress despite the elimination of the causative agent which was thyroid papillary carcinoma.

It is important to note that early recognition of these entities can lead to better management of secondary amyloidal disease. This is to avoid a generalization of the disease.

This is the first case report, to our knowledge, of the association of thyroid papillary carcinoma with systemic AA amyloidosis. Although such a case is very rare, it is of interest in the understanding of the pathophysiology of secondary AA Amyloidosis.

## 4. Conclusions

AA amyloidosis remains a complication of chronic inflammatory diseases. But its association with malignancy is not uncommon.

Studies are necessary to determine the mechanism for amyloidosis related cancers, highlighting the role of chronic stimulation by amyloidal proteins.

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