Case Report

AMYLOID GOITER IN A PATIENT WITH CYSTIC FIBROSIS

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ABSTRACT

Objective: Amyloidosis (AA) is a disorder characterized by the local or systemic deposition of amorphous fibrous material. The most commonly affected organs are the kidneys, liver, and spleen, with the thyroid gland rarely affected.

Methods: We present the case of a 28-year-old female with cystic fibrosis (CF), renal AA, and a fast-growing goiter.

Results: Fine-needle aspiration puncture material was negative for Congo red staining. A total thyroidectomy was performed given the high degree of suspicion for amyloid goiter, a diagnosis that was later confirmed after analysis of the surgical specimen.

Conclusion: Subclinical infiltration of the thyroid gland may occur in up to 80% of patients with AA produced by inflammatory or chronic infectious diseases, though symptomatic infiltration of the thyroid gland is unusual. Given the increased survival of patients with CF, this complication may become more frequent. Clinicians should therefore be alert for its possible appearance. **(AACE Clinical Case Rep. 2015;1:e36-e39)**

Abbreviations:
AA = amyloidosis; **CF** = cystic fibrosis; **FNAP** = fine-needle aspiration puncture; **SAA** = serum amyloid A; **TSH** = thyroid-stimulating hormone

INTRODUCTION

Amyloidosis (AA) is characterized by the local or systemic deposition of amorphous fibrous material (1). One of its variants, inflammation-associated systemic AA, can accompany various chronic inflammatory disorders including cystic fibrosis (CF) (1,2). AA occurs when there is an imbalance between the production and degradation of serum amyloid A (SAA) protein. Secondary AA is a rare complication in CF, with only a few reported cases (3). The organs most commonly affected are the kidneys, liver, and spleen (4), with fewer described cases affecting the thyroid gland (1,5,6). We present a case of euthyroid amyloid goiter in a patient with CF.

CASE REPORT

The patient was a 28-year-old female with CF diagnosed at birth due to the presence of meconium ileus, rectal prolapse, and respiratory disease. She was homozygous for the mutation f508del/f508del. She had *Pseudomona aeruginosa* colonization since 1996 and *Serratia marcescens* colonization since 2010. During the year prior to the diagnosis of amyloid goiter, she experienced 2 exacerbations (1 mild-moderate and the other severe, with the latter requiring intravenous antibiotics). Her forced expiratory volume in 1 second (FEV1%) was 37.7% in a stable status, and her Bhalla score was 9 (7). Associated complications included diabetes mellitus treated with insulin (with good metabolic control, glycated hemoglobin of 6.3%); mild malnutrition (body mass index [BMI] 18.02 kg/m^2 with a lean

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mass index of 14.47 kg/m^2) treated with oral supplements, osteoporosis (T score –2.6 SD, Z score –2.3 SD) treated with alendronate, calcium, and vitamin D; and cholelithiasis. She underwent surgery in December 2002 for intestinal volvulus with resection of the terminal ileum and right colon but later developed a subocclusive crisis, possibly related to the use of postsurgical bands. In August 2010, she was diagnosed with primary hepatitis C infection (previous markers were negative) and, at the same time, she was found to be positive for microalbuminuria that confirmed within a few weeks (proteinuria >3 g in a 24-hour urine collection with normal renal function). Given these findings, she underwent a kidney biopsy, leading to the diagnosis of secondary AA in October 2010.

At a regular check-up 5 months later, the patient reported a previously absent fast-growing goiter, with no associated symptoms of thyroid dysfunction or laboratory changes in the thyroid profile (thyroid-stimulating hormone [TSH], free thyroxine [T4], free triiodothyronine [T3], antibodies negative). Given the suspicion of amyloid goiter, she had a thyroid ultrasound exam and fine-needle aspiration puncture (FNAP) with Congo red staining that was described as follows: "blood with scant amount of thyroid normal cells. Some of them, tightly packed, with abundant cytoplasm, common in benign colloid goiter. No evidence of amyloid." Although the FNAP was negative for amyloid goiter, because of its rapid growth and local oppressive disturbance, she was referred to the endocrine surgeon for total thyroidectomy. Analysis of the surgical specimen confirmed amyloid goiter with the following microscopic findings: "Diffuse amyloid deposits. Extracellular accumulation of acellular homogeneous eosinophilic material with smudgy appearance. Angiocentric deposits and amyloid in walls of blood vessels. Atrophy of follicular component of thyroid." The histochemical features included salmon-colored Congo red deposits with apple-green birefringence under polarized light. The histochemical findings of the resected thyroid are shown in Figures 1 through 4.

DISCUSSION

The survival of patients with CF has increased greatly in recent years. However, this increased survival can affect the incidence of AA (8), previously a little-known entity in CF patients. A retrospective autopsy study of 33 CF patients aged over 15 years at the time of death demonstrated the presence of AA in 33% of cases, mainly involving the spleen, liver, and kidney (9). The frequency of exacerbations and the associated inflammatory status may be related with an increased risk of developing AA. It has been suggested that the disease may be related with an increase in SAA levels, especially in patients colonized by *Pseudomonas aeruginosa*. The concentration of SAA could be influenced by antibiotic exposure, decreasing during treatment and later increasing (10).

Subclinical infiltration of the thyroid gland may present in up to 80% of patients with AA caused by inflammatory or chronic infectious diseases (5,11), though symptomatic infiltration of the thyroid gland is unusual (3,5,12,13). Most cases have normal thyroid function, though some patients with hyper- (1,14) and hypofunction (6,14) have been reported. Amyloid goiter is characterized by gradual, painless, diffuse, firm growth. It can occasionally grown enough to compress the trachea. The most symptomatic patients experience rapid growth of a cervical mass.

The diagnosis of amyloid goiter requires pathological confirmation. Obtaining adequate samples by FNAP is difficult (15), and a negative result should not rule out its

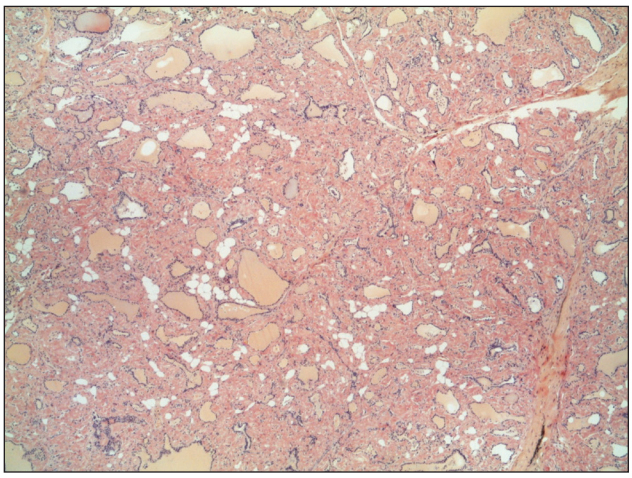

Fig. 1. Congo red staining (×4). The slide shows evidence of diffuse amyloid deposits, extracellular accumulation of acellular homogeneous eosinophilic material with a smudgy appearance, angiocentric deposits and amyloid in blood vessels walls, and atrophy of follicular component of thyroid.

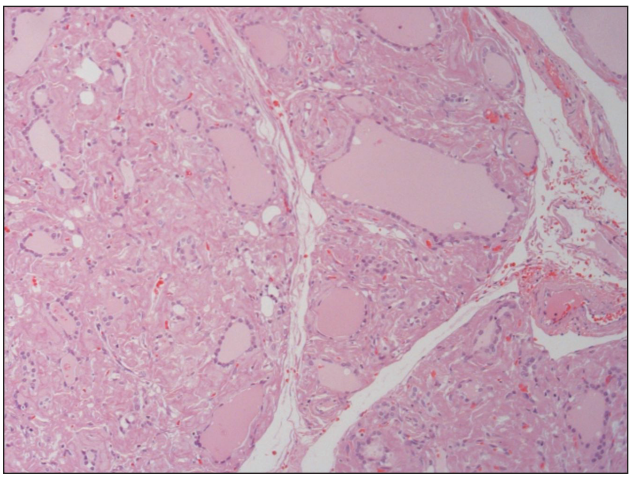

Fig. 2. Hematoxylin & eosin and Congo red staining (×4). The slide shows diffuse amyloid deposition surrounding thyroid follicles with fatty infiltration.

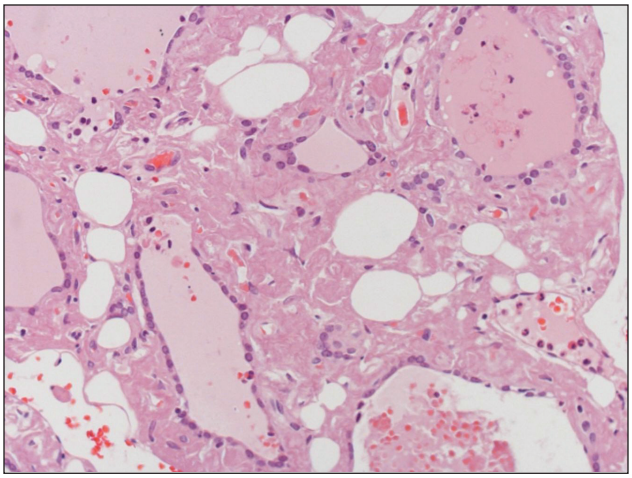

Fig. 3. Hematoxylin & eosin and Congo red staining (×20). Salmon-colored amorphous material within interfollicular sites provide more evidence of amyloid deposition.

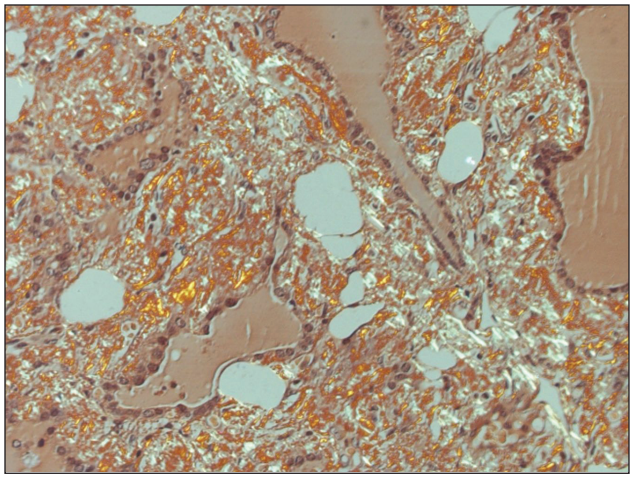

Fig. 4. Apple-green birefringence (×20).

diagnosis. In the case of the patient reported here, FNAP with Congo red staining gave a false-negative result, and the diagnosis was later confirmed in the surgical specimen. Certain thyroid tumors, like medullary carcinoma, can also present deposits of amyloid material. Staining of deposits of amyloid material with Congo red produces a diagnostically useful green birefringence under a polarized light microscope. The precise type of fibrous material deposited can also be determined by immunohistochemical techniques.

The treatment of AA is based on targeting the affected organ. However, in the case of amyloid goiter, there is limited information about the effects of treatments. Siddiqui et al reported a significant reduction in goiter size and improvement in renal function with dexamethasone and autologous peripheral blood stem cells, but this case concerned a patient with primary AA kappa light chain deposition (16), not secondary AA as in the present case In the event of thyroid hypofunction, replacement therapy should be administered. Given the complicated situation regarding lung function in CF patients, thyroidectomy is usually necessary to release the airway from compression by the goiter (5).

The coexistence of CF and AA is associated with a reduced short-term survival (3). Nonetheless, the patient described here has remained stable after almost 3 years of follow-up since the diagnosis of AA, with good control of her kidney disease (proteinuria <1 g in 24-hour urine on an angiotensin II receptor antagonist), lung function without changes (FEV1%, 37.2%), and normal nutritional status (BMI 18.8 kg/m^2).

CONCLUSION

We have found very few reports of CF patients with symptomatic amyloid goiter (1,5,6). However, given the increased survival of CF patients, this complication may become more frequent. Clinicians should therefore be alert for its possible appearance.

DISCLOSURE

The authors have no multiplicity of interest to disclose.

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