Case Report

Amyloid Goiter in a Patient with Rheumatoid Arthritis and End-Stage Renal Disease

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Abstract

The association between amyloidosis and collagen vascular diseases, such as rheumatoid arthritis (RA) is well-documented. Amyloid goiter is an extremely rare pathologic condition caused by a massive amyloid infiltration of the thyroid tissue. Our patient had been diagnosed with RA 20 years ago and was on hemodialysis for 7 years. He was assessed for decreased appetite, dysphagia, and nausea during the hemodialysis. On physical examination, the thyroid was diffusely enlarged with multiple nodules. He was biochemically euthyroid. Ultrasound of the thyroid gland showed multinodular goiter. A total thyroidectomy was performed. Histopathological examination showed dilated follicles surrounded by abundant homogeneous substance that stained positive with Congo red. The patient was reported as amyloid goiter. Complaints of the patient improved after the surgery. In the literature, amyloid goiter with RA in a hemodialysis patient is very rare. Amyloid goiter should be considered if there is a rapid thyromegaly causing pressure symptoms in the background of any disease with chronic inflammation.

Keywords: *Amyloid goiter, hemodialysis patient, rheumatoid arthritis*

Introduction

Amyloidosis is characterized by the accumulation of amorphous and, proteinaceous material in various organs and tissues of the body.[1] It is classified as primary or secondary. Major fibrillar protein amyloid L, which is derived from the immunoglobulin (Ig) light chain, accumulates in primary amyloidosis, whereas amyloid A accumulates in secondary amyloidosis, which is derived from serum amyloid A (SAA) protein. SAA protein is an acute-phase protein produced by an inflammatory process in the liver.[2] Amyloid goiter is defined as the accumulation of amyloid in the thyroid that leads to thyroid gland enlargement. In autopsy-based studies, intrathyroidal amyloid is present in approximately 80% of the patients with secondary amyloidosis and 50% of those with primary amyloidosis.[3]

Secondary amyloidosis accompanies malignancies or chronic inflammatory diseases (CIDs), such as tuberculosis (TB), rheumatoid arthritis (RA), ankylosing spondylitis (AS), cystic fibrosis (CF), bronchiectasis, and inflammatory bowel disease (IBD).[2]

The actual incidence of AA amyloidosis in RA is probably underestimated. Subclinical AA amyloidosis may be common in RA. In a cohort study that analyzed the prevalence of subclinical amyloid fat deposits in patients with RA, amyloid was found in 16.3% of the patients.[4] As intensively suppressing the production of SAA with anti-inflammatory drugs may prevent worsening organ dysfunction, it is important to make the diagnosis in the early phase.[5]

Amyloid accumulation in the thyroid gland is a common phenomenon, but diffuse clinically apparent enlargement of the thyroid as the first manifestation of systemic amyloidosis is very rare. Amyloid goiter secondary to RA is also uncommon in the literature.[6,7]

The presence of amyloid in association with thyroid gland enlargement is frequently seen in medullary carcinoma of the thyroid, being identified in 50–70% of the cases.[3]

Herein, we present a 55-year-old male, hemodialysis patient with amyloid goiter secondary to RA.

Case

A 55-year-old man with the end-stage renal disease was assessed for decreased appetite,

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dysphagia, and nausea during the hemodialysis. He was on a routine hemodialysis program for 4 h, three times a week, for 7 years. In his history, he had essential hypertension for 15 years. The etiology of end-stage renal disease may be hypertension or systemic amyloidosis in our patient, but kidney biopsy had never been performed. He had been diagnosed with RA 20 years ago and had been taking leflunomide 20 mg/day regularly. His other medication was darbepoetin alfa 40 mcg/week, acetylsalicylic acid 100 mg/day, calcium acetate 700 mg three times a day, and lansoprazole 30 mg/day. On physical examination, the thyroid was diffusely enlarged (Grade 4) with multiple nodules. He had signs of long-standing RA in the form of joint deformities and rheumatoid nodules.

Laboratory findings of the patient can be seen in Table 1. Abdominal ultrasonography (USG) was performed, and it revealed normal findings. In addition, the fecal occult blood test was negative, and the patient did not have weight loss, so intraabdominal malignancy was not considered.

On thyroid USG, the parenchyma was homogeneous. Both of the thyroid lobes were enlarged. A large number of heterogeneous, hypoechoic solid and mixed nodules with cystic and calcified degeneration were found on both the lobes and isthmus, the largest one being on the right lobe (50 × 28 × 24 mm). Aspiration biopsy of the largest nodule showed a benign characteristic. As the patient had a large number of nodules, total thyroidectomy was performed.

According to macroscopic pathological examination, the right lobe was 12 × 7.5 × 7 cm, left lobe was 9.6 × 6 × 5 cm, and whole surface was encapsulated. In the right lobe section, a partially cystic nodule 4 × 3 cm in size separated by marked and regular borders from surrounding tissue was detected. One cystic nodule 4 × 4 cm in size in the left lobe of the section was observed. The surrounding thyroid tissue was hardened and had a light brown and homogeneous appearance. Microscopic examination revealed colloid-containing, enlarged and elongated thyroid follicles. Extracellular, acellular and homogeneous eosinophilic amorphous proteinaceous material (amyloid) accumulation was observed diffusely between or around the follicles and around the blood vessels. Mature fat attracted attention among the follicles and amyloid [Figure 1]. In the sections stained with Crystal Violet, between thyroid follicles and blood vessels, diffusely metachromatic staining extracellular amyloid accumulations were observed [Figure 2].

Table 1: Laboratory findings of the patient

Test performed	Patient value	Reference range
Hemoglobin	11 g/dl	12-16
WBC count	9300/mm^3	4000-10000
C-reactive protein	25 mg/L	<0.5
Glucose	72 mg/dl	70-110
Creatinine	5.3 mg/dl	0.6-1.2
TSH	0.27 mIU/mL	0.27-4.2
FT4	1.06 ng/dl	0.82-1.77
FT3	2.08 pg/ml	2.5-3.9
Anti-thyroglobulin autoantibodies	Negative	Negative
Anti-thyroid peroxidase autoantibodies	Negative	Negative
Intact parathormone	527 pg/ml	12-65
Kt/V	1,67	
URR	72%	
Occult blood in the stool	Negative	Negative

WBC=White blood cell, TSH=Thyroid stimulating hormone, FT4=Free thyroxine, FT3=Free triiodothyronine, Kt/V=Dialysis adequacy , URR=Urea reduction rate

In the sections stained with Congo red, the accumulation of amyloid showed apple-green birefringence under polarized light. Immunohistochemical examination for CD3, CD20 and CD138 were performed to exclude plasma cell dyscrasias and hematolymphoid neoplasms that could be avoided even though no significant mass was observed in the case. Due to these examinations, a very small number of CD138-stained plasma cells were detected but CD3, CD20-stained lymphocytic cells were not detected.

Immunohistochemical examination with thyroglobulin, TTF-1, CEA, synaptophysin, chromogranin, and CD56 was performed to show that the follicles were lined with thyroid cells in order to differentiate medullary carcinoma. Cells that lined the follicles were stained with thyroglobulin and TTF-1 while staining with CEA, synaptophysin, chromogranin, and CD56 was not detected. There was no evidence of medullary carcinoma. In light of all these clinical, macroscopic, histopathologic, and histochemical and immunohistochemical findings, the case was reported as amyloid goiter.

Complaints of dysphagia, nausea, and decreased appetite of the patient improved after the surgery. The patient is at the postoperative 12th month of follow-up and on 100 mcg levothyroxine replacement therapy, leflunomide 20 mg/day, and undergoing regular hemodialysis in our center.

Discussion

Von Rokitansky first described the presence of minor amyloid deposits in the thyroid in 1855.[8] Eiselberg named the condition ‘’Amyloid goitre” in 1904.[3]

Amyloid goiter rarely presents as the first manifestation of systemic amyloidosis. It may present as diffuse enlargement of the thyroid gland within several weeks or months. This enlargement may be accompanied by stridor, hoarseness, dyspnea, and dysphagia. In a review of 30 investigated cases of amyloid goiter, 13 were FMF, 10 were secondary amyloidosis due to other inflammatory diseases and 7 were primary amyloidosis. In 21 cases, amyloid goiter was manifested as a non-tender rapidly enlarging neck mass; of

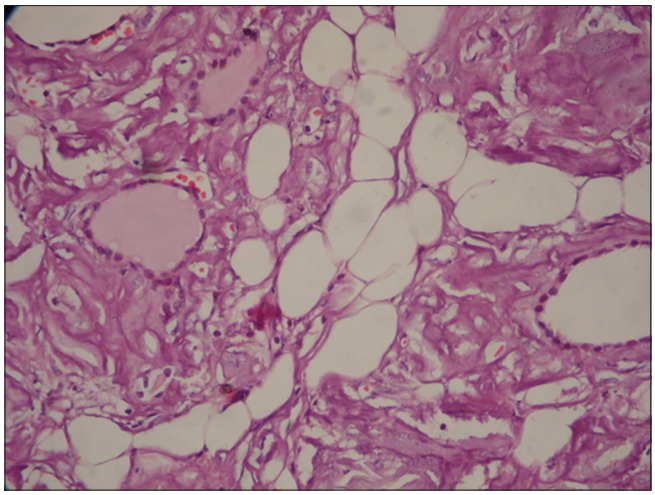

Figure 1: Accumulation of common extracellular and acellular homogeneous eosinophilic amorphous proteinaceous material (amyloid) between follicles in thyroid parenchyma with occasional mature fat deposits (arrows). Enlarged and elongated colloid-containing thyroid follicles with squamous metaplasia. (Hematoxylin Eosin 40X)

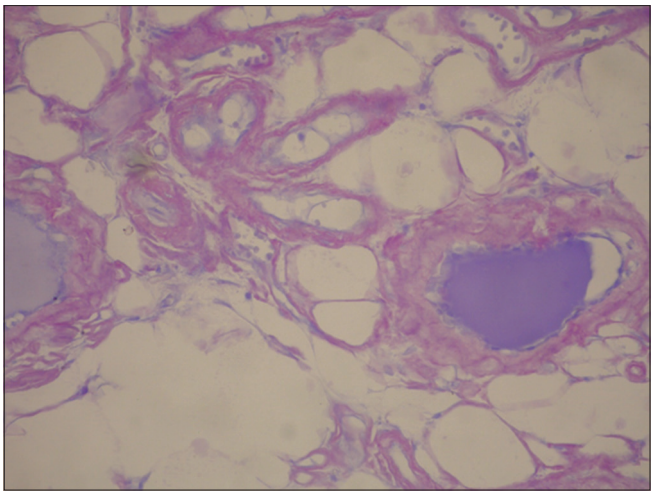

Figure 2: Thyroid follicles and blood vessels are surrounded by the accumulation of amyloid deposits, which are metachromatic-stained with Crystal Violet (arrows) (Crystal Violet 40X)

these 6 patients had upper airway obstructive symptoms. The remaining 9 cases were identified at autopsy. In the autopsy cases, in addition to the thyroid, the organs invariably involved in an amyloid deposition included the kidney, adrenal, liver, and spleen.[3] Our patient did not have a rapidly growing goiter, but had a complaint of dysphagia and nausea, which had recently increased.

Dialysis-related amyloidosis may occur in patients with end-stage renal disease. This condition results from retention of β2 microglobulin and its deposition as amyloid fibrils into osteoarticular tissue. The clinical manifestations usually develop after several years of dialysis dependence and include carpal tunnel syndrome, destructive arthropathy, and bone cysts and fractures. Thyroid involvement is not common in dialysis-related amyloidosis.[9] Mousa *et al.* reported a hemodialysis patient who had amyloid accumulation in the thyroid even in a toxic nodule. Musculoskeletal manifestations were absent, and the etiology of amyloidosis in their patient was uncertain. As the patient had a 5-year history of peritoneal dialysis and had peritonitis attacks, they commented that repeated peritonitis attacks may have to her developed secondary systemic amyloidosis.[10] Amyloid goiter in patients with chronic kidney failure has been reported in some other publications.[11,12]

Most patients with amyloid goiter are clinically euthyroid, but many different presentations have been reported. The thyroid gland can be soft, hard, diffuse or nodular in character according to the amount of amyloid deposited.[13]

Kimura *et al.* reported 10 thyroidal involvements out of 30 cases with systemic amyloidosis. Nine of these patients had some kind of thyroid dysfunction. Five patients had hypothyroidism, two had low T3 syndrome, one had the subacute thyroiditis-like syndrome and one had coexisting Graves' disease. Five out of the nine patients had positive thyroid autoantibodies.[14]

The life expectancy of patients with RA has been estimated to be 1.2 to 1.7 times worse than that of the general population.[15] Complications involving AA amyloidosis may further reduce the life expectancy of such patients. Subclinical amyloidosis is common in RA, and thyroid involvement may be the first sign of amyloidosis. For this reason, it is important to diagnose with biopsy or surgery if there is a goiter in rheumatic disease patients.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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