AMYLOID GOITER: A CASE REPORT AND REVIEW OF THE LITERATURE

Amra Jakubović-Čičkušić, Begzada Hasukić, Maja Sulejmanović, Alma Čičkušić, Šefik Hasukić

Departments of Nuclear Medicine and ENT, University Clinical Center Tuzla, Faculty of Medicine, University of Tuzla, Eye Clinic, University Clinical Center Tuzla, Clinic for Surgery, University Clinical Centre Tuzla, Faculty of Medicine, University of Tuzla, Tuzla, Bosnia and Herzegovina

Abstract

Amyloid goiter is a very rare manifestation of amyloidosis. Here, we describe the case of a 40-year-old male, who presented with upper airway obstructive symptoms including hoarseness and breathing difficulty, to highlight the clinical and pathological features of secondary amyloidosis of the thyroid gland and the difficulties in making a preoperative diagnosis. The patient had previously been wounded in the war in Bosnia, which resulted in the right kidney being surgically removed. Further, he had undergone two surgical interventions on both hips due to osteomyelitis and was on a chronic dialysis program due to a progressively poor left kidney function that had eventually resulted in complete loss of renal function. Thyroid function tests were normal, and the patient clinically was euthyroid; biochemical investigations were within normal limits. Results from sonography, computed tomography scan of the neck, scintigraphy and fine-needle aspiration cytology were nondiagnostic. Therefore, a thyroid biopsy was carried out, and amyloid deposits were found. After preoperative work-up, total thyroidectomy was performed with no complications. We conclude that amyloid goiter may have no major impact on thyroid function even when a substantial amount of amyloid has replaced the normal thyroid parenchyma, as was the case in our patient. Amyloid goiter should be suspected in all patients with a progressive, rapidly growing bilateral thyroid enlargement with concomitant inflammatory processes or in patients undergoing hemodialysis treatment.

Keywords: Amyloid goiter, secondary amyloidosis, thyroid enlargement, thyroidec tomy

INTRODUCTION

Amyloidosis is a group of β-pleated-sheet structure protein deposition disease. It can occur as systemic (generalized), localized, sporadic, hereditary or associated with chronic inflammation. Amyloidosis can cause a wide range of symptoms that mimic clinical feature of other diseases, depending on the localization of the accumulation of amyloid in tissues or organs. Amyloid goiter is a very rare manifestation of amyloidosis and is defined as the presence of amyloid within the thyroid gland in such quantities that produces a clinically apparent enlargement of the thyroid gland.[1] The diagnosis of this rare entity is usually made postoperatively. Although there is no effective medical therapy for amyloid goiter, there are current regimens to treat amyloid by chemotherapy.[2,3]

We present a case highlighting the clinical and pathological features of secondary amyloidosis of the thyroid gland and the difficulties in making a preoperative diagnosis.

How to cite this article: Jakubović-Čičkušić A, Hasukić B, Sulejmanović M, Čičkušić A, Hasukić Š. Amyloid goiter: A case report and review of the literature. Saudi J Med Med Sci 2020;8:151-5.
CASE REPORT

A 40-year-old male was admitted to our hospital with goiter and upper airway obstructive symptoms including hoarseness and breathing difficulty. On physical examination, the thyroid gland was diffusely enlarged, nontender with no apparent nodularity and firm in consistency [Figure 1]. There was no family history of amyloidosis or thyroid disease.

The patient’s medical history revealed that in 1993, his right kidney and spine had severely been injured in the Bosnian war, which resulted in the right kidney being surgically removed. Since then, because of spine injury, the patient was independently immobile and could not control urination and defecation. In addition, his past history revealed that he had undergone two surgical interventions in both hips, in 1998 and 2000, due to osteomyelitis. In 2002, the laboratory tests had shown elevated blood urea nitrogen and creatinine and also the presence of massive proteinuria. The function tests of the left kidney performed periodically had shown very poor function, which progressed over time to complete loss of renal function. Therefore, in 2005, the patient was started on a chronic dialysis program. Because of suspected amyloidosis as a cause of loss renal function, the patient underwent renal biopsy, which revealed renal amyloidosis. In 2007, the patient underwent left-sided nephrectomy.

The patient’s vital signs at admission, including heart rate, blood pressure and temperature, were normal. The result of cardiopulmonary examination was unremarkable. Clinical laboratory tests were unremarkable, except coagulation tests, which showed a deficit factor of prothrombin complex and the intrinsic coagulation pathway. Thyroid function tests were normal with free thyroxine level of 11.5 pmol/L (normal range: 10–25 pmol/L), free triiodothyronine level of 5.8 pmol/L (normal: 3.4–8.5 pmol/L) and thyroid-stimulating hormone level of 0.52 µIU/ml (normal: 0.3–4.0 µIU/ml). Antimicrosomal and antithyroglobulin antibodies were negative.

Preoperative neck sonography showed an enlarged thyroid with an ultrasound estimated gland volume of 115 ml, with multiple cystic nodules in both lobes (the biggest cysts had dimensions of 3.5 cm × 2.8 cm × 3.6 cm) and the presence of severe compression of surrounding neck structures. Thyroid scintigraphy showed a diffusely enlarged gland with markedly reduced and inhomogeneous distribution of the radionuclide [Figure 2].

Chest X-ray revealed a deviation of the trachea. Computed tomography scan of the neck showed a diffusely enlarged thyroid gland, which compressed and pushed the surrounding structures of the neck and descended caudally to the sternoclavicular joints. Because of suspected malignant thyroid tumor, the patient underwent fine-needle aspiration cytology (FNAC), which was nondiagnostic. As the cytological finding was nondiagnostic, the patient underwent thyroid biopsy, which showed amyloid deposits.

Given the overall clinical condition of the patient, this case was presented to the multidisciplinary committee for further therapeutic approach. After examining the medical records, the multidisciplinary committee decided that the treatment of choice in this case is total thyroidectomy because of obstructive symptoms caused by diffusely enlarged thyroid gland to alleviate pressure symptoms and exclude a malignancy. During surgery, a large multinodular goiter was identified that circumferentially encased the trachea [Figure 3].

Grossly, the surface of the received thyroid specimen, measuring 11 cm × 5 cm, was lobulated, muddy and the cut surface had a tan, lobulated appearance with some microcystic areas filled with homogeneous, brownish, glossy

![Figure 1: Diffusely enlarged thyroid gland](image1)

![Figure 2: Thyroid scintigraphy](image2)
content. The final diagnosis was based on postsurgical histology. Frozen section biopsy was performed, and microscopic analysis showed fat and fibrous tissue without neoplastic growth. No thyroid tissue was detected on frozen section cuts. Additional tissue sample was taken for definitive analysis. Microscopic examination by hematoxylin–eosin-stained sections taken from all received surgical specimens of the thyroid revealed mostly a fat tissue with rare, slightly dilated follicles filled with colloid and lined with thin, inactive epithelium [Figure 4].

Immunohistochemical analysis showed thyroid transcription factor 1 expression in the epithelium and thyroglobulin expression in colloid. In the thyroid interstitium, between the metaplastic fat tissue and in the wall of thin vessels, eosinophilic amorphous material was noted [Figure 5]. This material was brown-stained on Congo red and showed green polarization, which is consistent with amyloid substance [Figure 6]. Accordingly, a final diagnosis of amyloidosis glandulae thyroideae (amyloid goiter) was made. The patient had an uneventful postoperative period and left the hospital in a good general condition. The patient continued with the chronic dialysis program at the previously established schedule. After 2 years of follow-up, the patient was feeling well with no evidence of recurrence of the disease and using replacement therapy with 150 mcg levothyroxine.

DISCUSSION

Amyloid goiter is a very rare entity, occurring in only 0.04% of patients with systemic amyloidosis, and is predominantly reported as case reports. It may be associated with either primary or secondary amyloidosis. The majority of cases are associated with secondary amyloidosis, which is also called reactive amyloidosis because it is generally associated with chronic inflammatory diseases such as rheumatoid arthritis, Crohn's disease, osteomyelitis and...
tuberculosis.[7] Rarely, amyloid goiter may occur as the first sign of systemic amyloidosis.[8] In our case, we confirmed the view that chronic inflammation is one of the most common causes of secondary amyloidosis because our patient had osteomyelitis in both hips caused by a previous wound complication.

Amyloid accumulates extracellularly in the thyroid parenchyma and disrupts the normal follicular patterns. The exact mechanism of the disease is not yet defined clearly. Amyloid goiter occurs over a wide age range from adolescents (especially with juvenile rheumatoid arthritis or familial Mediterranean fever) to the elderly with hematolymphoid neoplasia. In 1982, Amado et al.[9] reported 80 cases in their review of the literature, most of which occurred in adults, although few cases were also reported in children.[10] The gender predilection of amyloid goiter is not known.[11] Amyloid deposition can also be seen in other conditions such as medullary thyroid carcinoma, multiple myeloma, solitary plasmacytoma, infections and familial Mediterranean fever. Medullary carcinoma of the thyroid is a very important diagnostic consideration, and calcitonin staining is helpful in establishing or excluding its presence. However, this test was not performed because it is not routinely done in Bosnia and Herzegovina.

In patients with amyloid goiter, thyroid function tests are often normal, and patients are clinically euthyroid.[12] Our patient also had normal thyroid function tests and clinically was euthyroid. Recently, Mohammed et al.[13] reported two cases of amyloid goiter. The first case had a primary localized amyloidosis in the thyroid and was hypothyroid, whereas the second case had systemic amyloidosis secondary to interstitial pulmonary fibrosis and was euthyroid, which was similar to the case being reported here.

In the literature, there are conflicting reports regarding the effectiveness of FNAC as a diagnostic method in the preoperative diagnosis of amyloid goiter. Cannizzaro et al.[14] performed FNAC in one nodule in a patient with primary amyloidosis, and it showed the presence of colloid and histiocytes. However, in our case, FNAC was nondiagnostic, and thus, the patient underwent thyroid biopsy, which showed amyloid deposits. The main reason FNAC is nondiagnostic is probably a heterogeneous involvement of thyroid with cystic changes. FNAC or tru-cut biopsy has been reported to likely cause excessive bleeding because of vascular fragility due to progressive capillary destruction by amyloid deposition.[15] Therefore, Siddiqi et al.[16] suggest that radiologic findings in cases of proven systemic amyloidosis may avoid the complications of biopsy.

Regardless of the applied diagnostic methods, amyloid goiter is rarely diagnosed before surgery because the clinically detectable thyroid enlargement caused by amyloid deposition is rarely considered even in cases of known amyloidosis, as was also the case in our patient.[12] Although a fine-needle aspiration may result in a definitive diagnosis, histologic examination of the resected tissue is usually necessary. In the present case, there were large foci of mature adipose tissue, but there was no foreign body-type reactions and squamous metaplasia. Histochemical stains aid in the confirmation of amyloid, as immunohistochemical techniques may help in differentiating amyloid A from other types of amyloid.

CONCLUSION

Based on the presented case, it may be concluded that amyloid goiter had no major impact on thyroid function even in cases where a greater amount of amyloid replaces the normal thyroid parenchyma. Amyloid goiter should be suspected in all patients with a progressive, rapidly growing bilateral thyroid enlargement with concomitant inflammatory processes or in patients undergoing hemodialysis treatment. Total thyroidectomy is the method of choice for both diagnosis and treatment of amyloid goiter. Histological evaluation of the resected thyroid gland is crucial in making a definitive diagnosis.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient has given his consent for his images and other clinical information to be reported in the Journal. The patient understands that his name and initials would not be published and due efforts will be made to conceal his identity, but anonymity cannot be guaranteed.

Peer review

This article was peer-reviewed by two independent and anonymous reviewers.

Financial support and sponsorship
Nil.

Conflicts of interest

There are no conflicts of interest.

REFERENCES

1. Di Crescenzo V, Garzi A, Petruzziello F, Cinelli M, Catalano L, Zeppa P, et al. Nodular goiter with amyloid deposition in an elderly patient: Fine-needle cytology diagnosis and review of the literature. BMC Surg 2013;13 Suppl 2:S43.
2. Gigerli O, Unal AD, Panldar H, Demiralay F, Tarcan O. Amyloid goiter due to familial Mediterranean fever in a patient with Byler syndrome: A case report. Balkan Med J 2014;31:261-3.
3. Palladini G, Merlini G. Current treatment of AL amyloidosis. Haematologica 2009;94:1044-8.
4. Siddiqui MA, Gertz M, Dean D. Amyloid goiter as a manifestation of primary systemic amyloidosis. Thyroid 2007;17:77-80.
5. Ibrahimov M1, Yilmaz M, Kilic E, Akil F, Rasidov R, Karaman E. Rapidly progressive thyroid mass: Amyloid goiter. J Craniofac Surg 2012;23:e555-6.
6. Villa F, Dionigi G, Tanda ML, Rovera F, Boni L. Amyloid goiter. Int J Surg 2008;6 Suppl 1:S16-8.
7. Lester D, Thompson R, Goldblum JR. In: Endocrine Pathology. Philadelphia, US: Churchill Livingstone; 2006. p. 46-8
8. Kazdaghli Lagha E, Msakni I, Bougrine F, Laabidi B, Ben Ghachem D, Bouzian A. Amyloid goiter: First manifestation of systemic amyloidosis. Eur Ann Otorhinolaryngol Head Neck Dis 2010;127:108-10.
9. Amado JA, Ondiviela R, Palacios S, Casanova D, Menzanos J, Freijanes J. Fast growing goiter as the first clinical manifestation of systemic amyloidosis. Postgrad Med 1982;58:171-2.
10. Mache CJ, Schwinghangl J, Ring E, Pfeifer A, Borkenstein MH. Amyloid goiter in a child with familial Mediterranean fever. J Pediatr Endocrinol 1994;7:371-2.
11. Naveen Kumar BJ, Santosh KV. Amyloid tumor of thyroid, amyloid goiter: A case report with a stress on importance of preoperative diagnosis. Thyroid Res Pract 2012;9:58-9.
12. Yildiz L, Kefeli M, Kose B, Baris S. Amyloid goiter: Two cases and a review of the literature. Ann Saudi Med 2009;29:138-41.
13. Mohammed R, Yassin E, Radwan M, Ahmed B, Ettouny I, Abozied A. Amyloid Goiter: Clinicopathological assessment of two cases and review of literature. Open J Pathol 2015;5:20-7.
14. Cannizzaro MA, Lo Bianco S, Saliba W, D’Errico S, Pennella F, Buttafuoco G, et al. A rare case of primary thyroid amyloidosis. Int J Surg Case Rep 2018;53:179-81.
15. Aksu AO, Ozmen MN, Oguz KK, Akinci D, Yasavun U, Firat P. Diffuse fatty infiltration of the thyroid gland in amyloidosis: Sonographic, computed tomographic, and magnetic resonance imaging findings. J Ultrasound Med 2010;29:1251-5.