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The recurrent goitre unusually located near the hyoid bone

Nietypowa lokalizacja wola nawrotowego w pobliżu kości gnykowej

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Abstract

Introduction: Recurrent goitre is a significant clinical problem among patients who have been operated due to benign lesions. An atypical localization of recurrent goitre — near the hyoid bone — poses additional difficulties as there are no data available on the clinical significance of such lesions.

The aim of this study was to analyze if this unusual localization of recurrence is related to any significant differences in the clinical course, and if it significantly increases the risk of thyroid neoplasm.

Material and methods: The outcomes of ultrasound (US) and cytological examinations of 62 patients presenting with a goitre recurrence localised as a focal lesion near the hyoid bone were analyzed (mean age 59.4 ± 12.4 years). The analysis included the period from the operation to the lesion-revealing US, the lesion's volume, the presence of ultrasound features of malignancy, the volume of residual thyroid tissue in the thyroid bed, the changes in volumes of examined structures, and the outcomes of cytological examinations.

Results: The mean period from the surgery to the US confirming the lesion presence was 16 years, the mean volume of lesion was 2.17 cm^3, and the mean period of observation was 3.2 years (ranging from 1 to 10). Fine needle aspiration biopsy was performed in 47 (76%) focal lesions. The cytological results were never suspicious or malignant. In 38% of patients in whom control US was done within the observation period, the lesions enlarged by 20% or more, in 21% of them — by 50%, and in 15% — by over 100%. The category of cytological result did not imply any significant change, even in the case of significant isolated increase in volume of the lesion near the hyoid bone.

Conclusions: Focal lesions near the hyoid bone, revealed in patients operated previously for benign goitre, are not related to increased risk of thyroid neoplasm, and their enlargement does not imply their malignancy.

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Key words: *thyroid, recurrent goitre, thyroidectomy, benign lesions*

Streszczenie

Wstęp: Wole nawrotowe u pacjentów po operacji tarczycy z powodu zmian łagodnych stanowi istotny problem kliniczny. Nietypowa lokalizacja wola w okolicy kości gnykowej stwarza dodatkowe trudności, ze względu na brak danych na temat klinicznego ryzyka takich zmian. Celem pracy była ocena czy taka nietypowa lokalizacja zmian wiąże się z odmiennym przebiegiem klinicznym oraz istotnym ryzykiem obecności nowotworu/raka tarczycy.

Materiał i metody: Analizie poddano kolejne wyniki badań ultrasonograficznych (USG) i biopsji aspiracyjnych cienkoigłowych (BAC) 62 pacjentów (śr. wieku 59,4 ± 12,4 lat). Oceniono czas jaki minął od operacji do ujawnienia zmiany w okolicy kości gnykowej, jej objętość, obecność ultrasonograficznych cech złośliwości w zmianie, objętość miąższu tarczycy w loży płatów, zmiany objętości powyższych struktur i wyniki badań cytologicznych ujawnionych zmian.

Wyniki: Średni czas od operacji do potwierdzenia obecności zmiany w USG wynosił 16 lat, średnia objętość zmiany — 2,17cm^3, średni okres obserwacji — 3,2 lat (1–10 lat). Biopsji aspiracyjnej cienkoigłowej poddano 47 zmian (76%), wynik badania w żadnym przypadku nie wskazywał na zmianę złośliwą bądź podejrzaną. Co najmniej 20-procentowy wzrost objętości zmiany obserwowano u 38% pacjentów poddanych kontrolnemu USG, 50-procentowy wzrost u 21% pacjentów, a ponad 100-procentowy — u 15% osób. Kontrolne biopsje nie przyniosły istotnej zmiany kategorii wyniku biopsji, nawet w przypadku izolowanego znacznego wzrostu objętości ogniska w okolicy kości gnykowej.

Wnioski: Zmiany ogniskowe okolicy kości gnykowej ujawnione u pacjentów operowanych wcześniej z powodu wola łagodnego nie wiążą się z wyższym ryzykiem obecności nowotworu/raka tarczycy, powiększanie się takich zmian nie jest dowodem ich złośliwego charakteru. **(Endokrynol Pol 2010; 61 (5): 448–453)**

Słowa kluczowe: *tarczyca, wole nawrotowe, tyreoidektomia, zmiany łagodne*

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Introduction

Recurrent goitre among patients who have been previously operated due to benign lesions of the thyroid gland is still an important clinical problem in Poland. It seems to be the result of several factors, among them a history of long-term insufficient iodine-prophylaxis and insufficient post-thyroidectomy treatment and follow-up. The decision regarding reoperation of patients with recurrent goitre should be based on particularly strong indications since the risk of complications after such treatment is significantly higher in comparison with primary surgery. It is also worth mentioning that referred patients often belong to the group of elderly people with co-existing diseases.

Particular diagnostic difficulties are encountered in patients with non-typically located recurrent goitre, e.g. at the upper frontal part of the neck near the hyoid bone. It has not been analyzed yet whether such localization of recurrent goitre results in a different risk of malignancy or different pattern of changes in lesion volume or cytological outcome in comparison to those of typical lateral lobe localization.

The aim of this study was to analyze the outcomes of ultrasound (US) and fine needle aspiration biopsy (FNAB) examinations performed in patients with recurrent goitre localized at the upper frontal part of the neck and to investigate if this unusual localization is related to any significant differences in the clinical course or to significant risk of malignancy.

Material and methods

The analysis was performed on the US and FNAB outcomes in a group of 62 patients (women only, aged 32–86 years, mean 59.4 ± 12.4) who had been previously operated due to benign goitre. The thyroid surgeries were performed at several clinics in Łódź. In general, the patients were referred for surgical treatment for reasons other than suspicious FNAB outcome — with the exception for only 4 patients (6.5%) (follicular neoplasm in 2 cases, oncocytic cell tumour in 1 case, and the presence of thyroid follicular cells with intranuclear grooves in 1 case) — usually because of nodular or toxic goitre, notwithstanding the benign outcome of FNAB. In the majority of cases the patients had previously undergone subtotal thyroidectomy, in 1 case hemithyroidectomy, and in 5 cases the extent of surgery was not determined because of the long period since the surgery and missing medical documentation. In the studied group, 9 patients were operated for the second time because of goitre recurrence within several years from the first thyroid surgery. The majority of patients (45–72.6%) had received levothyroxine treatment with substitutive doses (75–125 μg, the serum TSH levels were normal on the first and the following examinations), 4 patients (6.4%) had been treated with Thiamazole because of recurrent hyperthyroidism, and 13 patients (21.0%) had not received any pharmacological treatment as they were euthyroid during the observation period.

In all the patients, a focal lesion near the hyoid bone (FLNHB) was revealed in the postoperative US, and it showed no connection to the residual thyroid tissue located typically. The analysis included: the period from the operation to the lesion-revealing US, the lesion's volume, palpability, echo structure (solid, mixed, cystic), presence of ultrasound features of malignancy (such as marked hypoechogenicity, microcalcifications, increased internal blood flow, irregular or blurred margins), and the results of cytological examinations. All of the same parameters were assessed for the residual thyroid tissue in the thyroid bed and for any lesions found there. The study also included the control examination outcomes, and special attention was paid to the pattern of lesion volume change and to possible changes in cytological outcomes in control FNABs. Lesion volume was measured with the use of simplified elliptical shape volume formula: 1/2 × width × depth × length of the measured structure. In order to analyze the significance of the lesion growth, three threshold points were applied: 20%, 50%, and 100%.

All the US examinations were performed by a team of three physicians with at least five years experience, using the same equipment — an Elegra Advanced (Siemens Medical Systems Inc., Issaquah, WA, USA) with a 7.5 MHz linear transducer and power Doppler capability. All the biopsies were US guided. In order to obtain a sufficient amount of diagnostic material, usually two aspirations of each examined lesion were performed. Ten millilitre syringes mounted in the aspirating syringe holders with 25 gauge (0.5 or 0.42 mm) needles were used in the process. In the case of cystic lesions the cytocentrifugation technique was employed for aspirate preparation, enabling the cell condensation from any residual material which was left in the syringe. All smears were fixed in 95% ethanol and stained with haematoxylin and eosin. The guidelines formulated in the Bethesda system for reporting thyroid cytopathology were accepted as the criteria for non-diagnostic smears [1]. The precise methods of classifying FNAB outcomes into categories were fully described previously [2, 3]. The category 'benign lesions' included the outcomes with 'benign lesions' in conclusion or with 'nodular goitre', 'thyroiditis', or 'thyroid cyst' diagnosed – apart from haemorrhagic cysts. The category 'suspected lesions' included the outcomes with 'follicular neoplasm/ /suspicious for follicular neoplasm', 'oxyphilic neoplasm/ /suspicious for a follicular neoplasm, oxyphilic cell type',

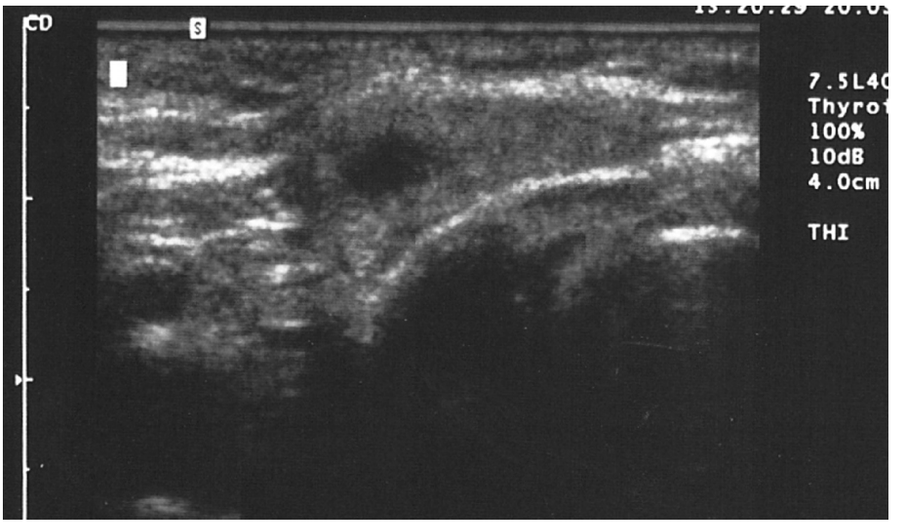

Figure 1. *Focal lesion in the upper-frontal part of the neck, thyroid follicular cells revealed in FNAB*

Rycina 1. *Zmiana ogniskowa ujawniona w badaniu USG w górnej części przedniej okolicy szyi, w BAC ujawniono komórki pęcherzykowe tarczycy*

Table I. *The categorization of fine-needle aspiration biopsy (FNAB) results of lesions located near the hyoid bone*

Tabela I. *Kategorie wyników badań cytologicznych zmian położonych w okolicy kości gnykowej*

Cytological results of lesions located near the hyoid bone	Categories of cytological outcomes	Number and % of FNABs	Echo structure of lesions
Non-suspected cytological picture (thyroid follicular cells or thyroid follicular cells with mild anisocytosis or admixture of follicular cells and Hürthle cells in a background of abundant colloid and macrophages)	Benign lesions	37 — 78.7	29 — solid, hypoechoic 1 — solid, hypoechoic with microcalcifications 7 — solid, normo-echoic
Chronic thyroiditis	Lesions of non-thyroidal origin	3 — 6.4	solid, hypoechoic
Postoperative granuloma		3 — 6.4	mixed:solid-cystic
Epidermal cyst		1 — 2.1	mixed:solid-cystic
Specimen lacking cytological material	Non-diagnostic	3 — 6.4	2 — mixed:solid-cystic 1 — solid, hypoechoic

and with disturbing, hardly diagnosable cytological picture — 'unclassified suspected lesions/suspicious for malignancy'. The category 'malignant lesions' included the outcomes with malignant tumour diagnosed.

Continuous variables were analysed by *t*-Student test. The comparison of frequency distributions was performed with χ^2 test. A value of 0.05 was assumed as the level of significance.

Results

The mean period from the surgical intervention to the ultrasound examination confirming FLNHB presence with no connection to the residual thyroid tissue located typically was 16 years (ranging from 3 months to 45 years). Those lesions were easily palpable in 22 out of 62 patients (35%). Their mean volume was 2.17 ± ± 2.12 cm^3 (mean ± SD) (Fig. 1). In 3 patients there was no residual thyroid tissue in the thyroid bed, and in the remaining group the mean volume of thyroid remnants was 11.9 ± 10.9 cm^3.

The echogenicity of FLNHB was similar to the regular thyroid tissue in 19 cases (30.6%), and it was slightly diminished in 37 cases (59.7%). In the remaining group (6 patients, 9.7%) the structure was solid-cystic and the solid part was non-homogenous. In one case, the US revealed microcalcifications in the examined lesion. Apart from that, none of the remaining FLNHB presented US features which might have implied a risk of malignancy (Table I).

Table II. *The volume changes of lesions located near the hyoid bone and thyroid remnants in its bed*

Tabela II. *Zmiany objętości struktur zlokalizowanych w okolicy kości gnykowej oraz miąższu resztkowego tarczycy w jej loży*

Cut-off point for volume enlargement	% of all monitored patients			
	Enlargement of lesion located near the hyoid bone	Enlargement of thyroidal residues in bed	Isolated enlargement of lesion located near the hyoid bone	Enlargement of both lesion located near the hyoid bone and thyroidal residues in bed
> 0%	22/64.7%	19/55.9%	10/29.4%	12/35.3%
> 20%	13/38.2%	13/38.2%	5/14.7%	8/23.5%
> 50%	7/20.6%	8/23.5%	5/14.7%	2/5.9%
> 100%	5/14.7%	6/17.6%	3/8.8%	2/5.9%

Fine needle biopsy was performed in 47 patients (75.8%). In all cases the lesions near the hyoid bone were examined, and additionally in 22 patients recurrent goitre in typical localization was biopsied. The cytological outcome of FLNHB revealed a post-surgical granuloma in 3 cases, epidermic cyst in 1 patient, and follicular thyroid cells in 40 cases. In 3 cases the outcome was non-diagnostic (Table I). The cytological outcome was not classified as suspicious or malignant in any of the cases. Cytological examination of focal lesions found in the thyroid bed in 1 patient revealed metastasis of non-microcellular lung cancer. In a biopsy of the FLNHB observed in this patient neoplastic cells were absent and only normal thyroid follicular cells, colloid, and macrophages were found. In other cases the outcomes of the FNAB of the recurrent goitre in the typical lateral lobe localization indicated the presence of benign thyroid lesions.

The control US examinations (1 to 4 control US examinations) were performed in 34 patients. This group included only patients with the presence of thyroid follicular cells in FLNHB, confirmed by FNAB. In all the patients, remnant thyroid tissues were present in the thyroid bed. The mean period of observation was 3.2 years (ranging from 1 to 10 years). No statistically significant differences in mean volume of examined structures between the first and last examination were found, neither in FLNHB (2.17 ± 2.12 cm^3 *v.* 2.28 ± 2.21 cm^3; mean ± SD) nor in the structures in the thyroid bed (11.9 ± 10.9 cm^3 *v.* 13.5 ± 12.41 cm^3). In 2 patients (5.9%) FLNHB volume remained constant between control US examinations, in 10 patients (29.4%) it decreased, and in 22 patients (64.7%) it increased. Different limits of volume change between control examinations were tested and the results are summarized in Table II. The FLNHB volume changed at least by 20% in 19 patients (55.9%); in 13 cases (38.2%) it increased. In 9 patients FLNHB changed in volume at least by 50%, and in 7 of them (20.6%) it increased. In 5 cases (14.7%) the lesion volume increased by more than 100%. The enlargement of thyroid remnants in the typical localization was found in a similar percentage of patients — the volume of thyroidal residues increased by at least 20% in 13 patients (38.2%) and by at least 50% in 8 patients (23.5%). In 6 cases the enlargement of the residual tissue exceeded 100%. In 8 out of 13 patients (61.5%) in whom FLNHB volume increased by at least 20% this change was accompanied by an analogous increase in the volume of the residual thyroid tissue in the thyroid bed. In 2 cases that enlargement was over 100%. Conversely, in 5 patients (14.7%) the 20% enlargement of FLNHB was isolated and was not accompanied by the enlargement of the residual thyroid. At least 50% isolated enlargement of FLNHB was found in 5 patients and at least 100% enlargement in 3 cases (Table II).

The control US examinations did not reveal changes in the echogenicity and echo structure of the examined lesions, nor did they show any evolution of features suggestive of malignancy. All the examined patients had normal TSH levels. The majority of them (30 out of 34) were treated with substitutive doses of levothyroxine. In none of the 4 patients without substitutive therapy was significant enlargement of goitre observed.

Control FNABs of FLNHB were performed in 18 patients including all 13 patients in whom its increase was above 20%. In 4 cases the cytological picture was slightly changed but the category of cytological outcome remained the same. In 1 patient (with FLNHB isolated enlargement above 20% but less than 50%) the cytological picture changed from 'normal follicular thyroid cells' to 'follicular cells with mild anisocytosis'. In 2 cases (with changes in lesion volume below 20%) the cytological picture changed in the opposite way. In the 1 remaining case (also with volume changes below 20%) the pic-

ture of benign non-inflammation lesion changed to 'chronic thyroiditis'. No patients examined in this study were referred to the repeated thyroidectomy due to goitre recurrence in the unusual localization.

Discussion

The reasons why a goitre starts growing in an abnormal localization are still the subject of research. There are several possible explanations of such a condition. It could be the result of some abnormalities during the embryogenesis [4, 5]. As a result of such disorders, the entire thyroid gland can be ill-positioned, and this can lead to so-called thyroid gland ectopy. Moreover, there can be a situation in which the thyroid gland is located in the right place but with co-existing gland-type tissue foci in some alternative locations — some authors call them split-off thyroid foci [4]. In none of the patients of the examined group were such disorders found in imaging examinations before the surgery.

Another, more probable explanation assumes the growth of previously invisible thyroid tissue in the localization tracking the embryonal route of thyroid anlage. In fact, a pyramidal lobe is present in some 50% of individuals, and in some of them it is long enough to reach the hyoid bone [6]. If not resected during primary surgery, it may be the source of recurrence. It may grow and may appear as a nodule, especially in conditions of hyperstimulation by TSH due to insufficient postoperative substitutive treatment [4]. The patients in the studied group had normal TSH levels during the observation, but no data was available on the sufficiency of substitutive treatment in the period before the study. It is reasonable to assume that such treatment was not optimal in some of the cases. Similarly, the relatively long mean period from the surgical intervention to the US confirming the presence of the lesion in unusual localization is — in our opinion — the result of delayed control US examination and does not reflect the true growth pattern of those lesions.

Some investigators have suggested that in patients with nodular goitre, some nodules may exist detached from the main gland although still connected to it by a vascular pedicle [7]. However, no connection was found in any of the patients in our study between the nodules located near the hyoid bone and the thyroid bed.

Other possible explanations are related to the surgical procedure itself and include the accidental transplant of some thyroid cells to the observed localization [7–9]. Harach et al. reported eight cases of thyroid implantation after surgery, of which only one was thyroid cancer and the others were related to benign lesions [7]. Koh et al. reported a patient with multiple palpable subcutaneous nodules after endoscopic hemithyroidectomy for a benign thyroid nodule by the breast approach [8]. The recent review by Moon et al. supports theories that surgery is more frequently the cause of extrathyroidal implantation of thyroid cells in the case of benign lesions and that FNAB is a possible cause of the implantation of cancer cells [9].

Moreover, Harach et al. suggested that a blunt trauma to the neck could be a possible aetiology of benign thyroid tissue deposits beyond the typical localization [7]. This shows that traumatic background should also be taken into consideration in the differential diagnosis. However, none of the examined patients in the studied group had a history positive for a neck trauma.

From a clinical point of view, it is important that — according to our results — lesions in the upper-frontal part of the neck in patients previously operated for benign goitre do not cause any significant differences in the clinical course, nor do they relate to increased risk of malignancy in comparison with the recurrent goitre in the thyroid bed. The changes in volume of those lesions have a similar pattern to those of thyroid remnants, and their enlargement does not seem to be an alarming issue if it is not accompanied by ultrasound features suggestive of increased risk of malignancy. Similarly, Alexander et al. found that the majority of solid benign thyroid nodules tend to grow. Therefore, an increase in nodule volume alone is not a reliable predictor of malignancy [10]. In this study we evaluated three thresholds of significant change of the focal volume — at least 20%, 50%, and 100%. The revised ATA Thyroid Cancer Guidelines recommend a 50% cutoff for nodule volume growth as the most appropriate and safe for making decisions on performing control FNAB [11]. It should be stressed that we did not observe any significant change in cytological outcome even in the case of isolated 50% or 100% enlargement of FLNHB. Thus, FLNHB enlargement, similarly to the enlargement of the goitre in the thyroid bed, is not evidence of the malignant character of the lesion if it is not accompanied by other features suggestive of malignancy.

Conclusions

In conclusion, patients who have been operated on due to benign goitre require systematic endocrinological care. The care should include not only substitutive levothyroxine treatment but also repeated ultrasound imaging in order to prompt diagnosis of possible recurrence of goitre. While performing a US examination one should take into consideration the possible presence of thyroid lesions outside the thyroid bed. Such lesions need cytological verification by fine needle aspiration biopsy. There is always a possibility of cancer being omitted during the postoperative histopathological ex-

amination of the thyroid excised during the primary intervention or of the malignant lesion growing in the recurrent goitre. However, lesions located near the hyoid bone are usually composed of normal thyroid tissue and are not related to any significant differences in the clinical course or to increased risk of malignancy in comparison with the recurrent goitre in the normal lateral lobe bed.

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