

¹MI «Kyiv Regional Clinical Hospital»

²The P.L. Shupyk National Medical Academy of Postgraduate Education, Kyiv

DIAGNOSTIC OF THYROID MICROCARCINOMAS WITH HIGH RISK OF EXTRAORGAN INVASION



A. Reyti¹, V.Ye. Medvediev²

Correspondence:

Reyti Andrian Ostapovych
04107, Kyiv, 1 Baggovutivska str.
MI «Kyiv Regional Clinical Hospital»
E-mail: a.reyti@gmail.com

80

Key words: thyroid cancer, thyroid incidentaloma, US investigation, chromatic lymphography, lymph node dissection, thyroidectomy.

There was carried out an analysis of the effectiveness of integrated use of different diagnostic methods for papillary thyroid cancer up to 10 mm, in the largest diameter, depending on the functional morphological subtype. There was proposed use of chromatic lymphography, which objectifies and simplifies searching the affected local lymph nodes that significantly reduces the operation time in case of microcarcinomas with high risk of extraorgan invasion according to ultrasound investigation.

The development and implementation of modern diagnostic methods in theriology at the end of 20th century led to an increase in detection of small nidus of the thyroid gland. The frequency of the detection of 1 cm nidus among all the focal lesions amounts to 78%. Numerous studies show that the share of microcarcinomas accounts for 30% of all the cases of thyroid cancer [5, 7]. The main task of diagnosis is to determine the identity of nidus to malignant or benign type, which in turn determines the treatment strategy. Benign focal lesions in the absence of compression or uncontrolled thyrotoxicosis do not require surgery. Malignant focal lesions should be treated according to the canons of oncological principles, regardless of the size. However, in early 21st century the views on nature, and thus on treatment strategy of small malignant focal lesions including microcarcinomas divided [2]. In 2007 Y. Ito and A. Miyauchi published data on monitoring of microcarcinomas for 5-year period; aggression factors were revealed only in 1.7% that is why the researcher believes it possible to observe without an active surgical approach. In 2008 S. Noguchi et al. published entirely another data, indicating a more aggressive course of microcarcinomas of regional and distant metastasis in 40%, and pointed to the need of fine-needle aspiration biopsy (FNAB) and early surgical treatment [12–15, 17]. In modern scientific view of the problem of microcarcinomas there is a tendency of microcarcinomas division into two subtypes: microcarcinomas with high risk of extra-organ invasion, which should be treated as microcarcinomas [6, 8], and microcarcinomas of low risk of extra-organ invasion, for which there can be used conservative treatment [3, 11]. Objective criteria for determining such identity is a genetic test, but that method is still under development and is far from its implementation.

We analysed the tumours detected incidentally during histological examination regarding operated benign thyroid pathology or autopsy, which had minimal invasive properties and had not manifested themselves over a long period and microcarcinomas with aggressive course, which actually led to operations [1, 4, 7, 11].

In our study, we tried to determine the phenotypic manifestations of both subtypes of microcarcinomas using available implemented research methods, i.e. ultrasonography, FNAB, intra- and postoperative histological examination.

MATERIALS AND METHODS

The study is based on the comparison of clinical and morphological features of microcarcinomas, which displayed aggression factors and required surgical treatment, and microcarcinomas, which were detected incidentally (incidentalomas) during surgery for benign thyroid disease. The study was conducted on the basis of a retrospective analysis of disease histories, outpatient cards, protocols, ultrasound, cytological and histological studies of patients operated at Kyiv Regional Clinical Hospital № 1 in 2003–2013. The patients who had thyroid microcarcinomas at the preoperative stage underwent chromatic lymphography in 0.5% sterile solution of methylene blue to determine lymphatic basin, define regional spread, which was not diagnosed during ultrasound investigation and determine lymph node dissection volume.

RESULTS AND DISCUSSION

157 patients with microcarcinomas were divided into two groups: Group I, which included 39 patients with low risk of extra-organ invasion (24.8%), and Group II, which consisted of 118 patients with high risk of extra-organ invasion (75.2%).

Localization of thyroid microcarcinomas in Group I and II did not significantly vary in the study groups, but in the isthmus of thyroid gland the formations dominated in Group I (Table 1).

Table 1. Localization and invasive factors of thyroid microcarcinomas

Microcarcinomas localization	Group I, n (%)	Group II, n (%)
Left lobe of thyroid gland	16 (41.0)	54 (45.8)
Right lobe of thyroid gland	17 (43.6)	53 (44.9)
Isthmus of thyroid gland	6 (15.4)	11 (9.3)

Among the patients of Group I ultrasonography revealed all foci, among the patients of Group II ultrasonography did not reveal focus in 2 cases (1.7%); in both cases the focus was 3 mm. In Group I 35 focal lesions (89.7%) were interpreted as malignant, 4 focal lesions (10.3%) — as doubtful; in Group II 18 focal lesions (15.3%) were interpreted as malignant, 89 focal lesions (75.4%) — as suspicious and 11 foci (9.3%) — as benign ones. In both groups the definition of basic ultrasound criteria of focus identity to a particular morphofunctional type was carried out according to the recommendations of the American Thyroid Association (ATA) Professional Guidelines (2013). There were significant differences in ultrasonic characteristics ($p < 0.05$) in Group I and Group II, i.e. shape taller-than-wide (66.7 and 10.2%), even, smooth contour (74.4 and 25.4%), distinct border (30.8 and 81.4%), halo rim (76.9 and 27.9%). Microcalcification and the presence of enlarged lymph nodes were observed only in macrocalcification with an aggressive course. There were detected no significant differences in the following ultrasound signs ($p > 0.05$): hypoechogenicity (74.4 and 76.3%), inhomogeneous structure (25.7 and 15.3%), the presence of cystic component (25.7 and 11.9%) and I score elastometry on the Rago scale (Table 2).

Among microcarcinomas of Group I only 12 (30.8%) cases were found during the preoperative examination, while

in Group II there were detected 115 (97.5%) cases. All the undetected small cancers at preoperative stage were incidental findings during the routine histological examination.

In Group I the female to male ratio was 7:1, in Group II it was 9:1, and the average age in Group I was 62 ± 5.2 , Group II — 48 ± 5.2 . In Group I cancer without background diseases was in 8 (20.5%) cases. Comorbidity in Group I was observed in 79.5%, including 1 case of toxic goiter (2.6%), 13 cases of focal adenomatous hyperplasia (33.3%), 6 cases of toxic adenoma of the thyroid gland (15.4%), 11 cases of autoimmune thyroiditis (28.2%). In Group II thyroid microcarcinomas without background diseases made up 23 (19.5%) cases, microcarcinomas in combination with focal adenomatous hyperplasia were found in 23 (19.5%) cases, microcarcinomas in combination with thyroid adenomas were registered in 10 (8.5%) cases and microcarcinomas in combination with autoimmune thyroiditis were in 35 (29.7%) cases. The average size of tumours in Group I was 4 ± 0.72 mm, in Group II it was 8 ± 1.2 mm. FNAB was performed in 78.2% of patients in Group II and in 26.5% of patients in Group I.

The postoperative histological examination in Group I detected papillary microcarcinoma in 35 (89.7%) cases, follicular variant of papillary microcarcinoma in 3 (7.7%) cases and sclerosing microcarcinoma in 1 (2.6%) case; in Group II there were found papillary microcarcinoma in 93 (78.8%) cases, follicular variant of papillary microcarcinoma in 8 (6.8%) cases and sclerosing microcarcinoma in 18 (15.3%) cases. During the histological examination in the group with low risk of extra-organ invasion the nidi were of smaller diameter, and only in 2 cases (5.1%) had invasive

properties, resulting in capsular invasion. In Group II in 84 (71.2%) patients there were revealed invasive properties (Table 3).

Comparing data on postoperative histological examination and preoperative ultrasound examination there was determined correlation between ultrasound signs of malignancy and invasive properties of microcarcinomas. This makes it possible to determine the group with low risk and delay surgery at the preoperative stage.

The operated patients underwent chromatic lymphography in 0.5% methylene blue to determine the characteristics of regional metastasis. It was established that in case of microcarcinomas localization in the upper third part there were observed metastatic lesions of the upper prelaryngeal and jugular lymph nodes (II and VI segments). In case of microcarcinomas localization in the middle third part of the thyroid there were involved pre- and paratracheal, medium jugular lymph nodes (III and VI segments). In case of microcarcinomas localization in the lower third part there were lesions of lymph nodes only of segment VI. The ways of metastasis of the thyroid isthmus microcarcinomas also depend on the location, so the focal lesions of the upper third part involved prelaryngeal lymph nodes, and upper jugular lymph nodes (II and VI segments); middle third part involved both prelaryngeal and pre- and paratracheal lymph nodes (VI segment). The focal lesions in the lower third part involved pre- and paratracheal lymph nodes; in 50% only Delphian lymph node had metastatic lesions.

Preventive lymph node dissection of the unstained lymph nodes did not detect metastatic lesions. Therefore, we believe that the use of chromatic lymphography in patients with microcarcinomas enables objective substantiation of the volume of lymph node dissection under visual control. The method makes it possible to apply less traumatic selective “pick up” lymphadenectomy (affecting only Delphian lymph node) instead of routine central lymph node dissection, or *vice versa* requires expanding the volume when affecting deep lateral cervical (jugular) lymph nodes that are not included to the volume of the central lymph node dissection.

In our research we have established morphofunctional inhomogeneity of microcarcinomas. In low risk group the tumors manifest themselves rather as benign tumors, having no clinical symptoms, with benign ultrasound signs, with the absence of blood vessels and metastasis invasion. Such microcarcinomas are mainly detected incidentally and have a favorable prognosis, thus this group does not require active surgical treatment and should be monitored until the tumor does not show aggressive characteristics. In 2004 Y. Ito et al. in their study stated that in 70% of cases of monitoring of microcarcinomas there was noted a decrease or no change in the size of the tumor, however, the researcher notes that in 6.7% of microcarcinomas of “high risk

Table 2. Ultrasonic characteristics of microcarcinomas

Ultrasound signs	Group I (n=39)		Group II (n=118)	
	n	%	n	%
Shape:				
• PZD/PD > 1 – (taller-than-wide shape)	26	66.7	12	10.2
Contour:				
• smooth, even	29	74.4	30	25.4
• unregular, uneven	10	25.6	88	74.6
Border:				
• distinct	12	30.8	96	81.4
• indistinct	27	69.2	22	18.6
Echogenicity:				
• hypo-	30	76.9	70	59.4
• hyper-	4	10.3	22	18.6
• iso-	5	12.8	26	22.0
Echostructure:				
• homogeneous	29	74.4	100	84.7
• inhomogeneous	10	25.6	18	15.3
Cystic component:				
• present	10	25.6	14	11.9
• absent	29	74.4	104	88.1
Halo rim:				
• present	30	76.9	33	28.0
• absent	9	23.1	85	72.0
Calcification:				
• micro-	—	—	25	21.2
• macro-	—	—	93	78.8
Dorsal signal change:				
• enhancement or decay	3	7.7	11	9.3
Enlarged lymph nodes:				
• regional on one side	—	—	15	12.7
• regional on both sides	—	—	4	3.4

Table 3. Invasive properties of thyroid microcarcinomas

Diameter of cancer focus, mm	4±0.72	8±12
Capsular invasion	2 (5.1%)	25 (21.1%)
Pericapsular, thyroid capsular or blood vessels invasion	–	18 (15.3%)
Multifocal cancer foci	–	23 (19.5%)
Regional lymph nodes metastasis	–	18 (15.3%)

group” there have been registered aggressive growth in the size during 5-year observation. The group of high risk of the development of cancer aggression is characterized by rapid growth, a tendency to extrathyroid extension by capsular invasion and thyroid capsular invasion, lymphatic and blood vessels invasion leading to regional and/or remote metastasis. Aggressive behavior of this group is correlated with some signs which can be revealed at the preoperative stage (taller-than-wide shape (irregular shape), hypoechogenicity, inhomogeneous, indistinct boundaries and no halo rim, microcalcification), that allows us to refer these signs to prognostic parameters. These lesions require extrafascial thyroidectomy, as in 20% there can be observed multifocal growth [9], but the issue of advisability and volume of lymph node dissection still remains contentious. In our research the smallest cancer focus with regional metastases was 7 mm, metastasis appeared in 6.7% of focal lesions with a high risk of aggression. Most of them involved segment VI, but there were registered the cases with metastases in segment II and III, that needs the expansion of lymph node dissection. In 50.0% of the thyroid isthmus

microcarcinomas there were observed metastases only in Delphian lymph node, enabling less traumatic selective lymphadenectomy.

CONCLUSIONS

As can be seen from the above the division of patients with thyroid microcarcinomas as to the risk of extra-organ invasion is important for prognosis of the disease course and determination of treatment regimens. The features of widely-accepted diagnostic methods (ultrasonography, FNAB and histological examination) are still not completely developed; a comprehensive assessment of survey results in most cases makes it possible to determine the need for surgical treatment of microcarcinomas and intraoperative chromatic lymphography identifies advisability and volume of lymph node dissection, especially in doubtful cases.

REFERENCES

1. Avetisyan I.L., Samoilo A.A., Gulchiy N.V., Yarovoy A.O. (2001) Frozen section examination of thyroid diseases: six-year experience of surgical department. *Ukr. Med. J.*, 6(26): 125–131 (in Russian).
2. Gulchiy M.V., Oleinik O.B., Stashuk A.V. et al. (2001) Features of thyroid cancer in the background of other thyroid diseases. *Endocrinology*, 6: 75.
3. Palamarchuk V.I. (2004) Methods of preventing specific complications in the surgical treatment of thyroid cancer: Abstract. Thesis. Candidates work. Science: 19.

4. Fedorenko Z.P., Haysenko A.V. (2012) Cancer in Ukraine, 2010–2011. *Bulletin of the National Cancer Registry of Ukraine*. Ed. 13 (<http://www.ucr.gs.com.ua/dovidb0/index.htm>) (in Ukrainian).
5. Cherenko S.M., Larin A.S. (2006) Random detection of thyroid cancer in patients with surgery on tumors not authority. *Clinical Surgeon*, 7: 9–11.
6. Cherenko S.M. (2014) Diagnosis, trends and pathomorphosis incidence, prognosis and surgical treatment of focal thyroid gland. Abstract. Thesis. Dr. Med. Sciences: 124.
7. Jemal A., Siegel R., Ward E. et al. (2008) Cancer statistics. *CA Cancer J. Clin*; 58: 71–96.
8. de Matos P.S., Ferreira A.P., Ward L.S. (2006) Prevalence of papillary microcarcinoma of the thyroid in Brazilian autopsy and surgical series. *Endocr. Pathol.*, 17: 165–173.
9. Arora N., Turbendian H.K., Kato M.A. et al. (2009) Papillary thyroid carcinoma and microcarcinoma: is there a need to distinguish the two? *Thyroid*, 19: 473–477.
10. Ito Y., Tomoda C., Uruno T. et al. (2004) Papillary microcarcinoma of the thyroid: how should it be treated? *World J. Surg.*, 28: 1115–1121.
11. Yu X.M., Wan Y., Sippel R.S., Chen H. (2011) Should all papillary thyroid microcarcinomas be aggressively treated? An analysis of 18,445 cases. *Ann. Surg.*, 254: 653–660.
12. Sorrentino F., Atzeni J., Romano G. et al. (2010) Differentiated microcarcinoma of the thyroid gland. *G. Chir.*, 31: 277–278.
13. Shaha A.R., DiMaio T., Webber C., Jaffe B.M. (1990) Intraoperative decision making during thyroid surgery based on the results of preoperative needle biopsy and frozen section. *Surgery*, 108: 964–967.
14. Yang G.C., LiVolsi V.A., Baloch Z.W. (2002) Thyroid microcarcinoma: fine-needle aspiration diagnosis and histologic follow-up. *Int. J. Surg. Pathol.*, 10: 133–139.
15. Lin H.S., Komisar A., Opher E., Blaugrund S.M. (2007) Follicular variant of papillary carcinoma: the diagnostic limitations of preoperative fine-needle aspiration and intraoperative frozen section evaluation. *Laryngoscope*, 110: 1431–1436.
16. Ito Y., Miyauchi A. (2007) A therapeutic strategy for incidentally detected papillary microcarcinoma of the thyroid. *Nat. Clin. Pract. Endocrinol. Metab.*, 3: 240–248.
17. Noguchi S., Yamashita H., Uchino S., Watanabe S. (2008) Papillary microcarcinoma. *World J. Surg.*, 32: 747–753.

Діагностика мікрокарцином щитоподібної залози з високим ризиком екстраорганної інвазії

A.O. Peimi¹, B.E. Medvedev²

¹КУ «Київська обласна клінічна лікарня»

²Національна медична академія післядипломної освіти імені П.Л. Шупика, Київ

Резюме. Проведено аналіз ефективності комплексного застосування різних методів діагностики раку щитоподібної залози розмірами до 10 мм, залежно від його морфофункціонального підтипу. Для мікрокарцином з високим, за даними ультразвукового дослідження, ризиком екстраорганної агресії запропоновано застосування хроматолимфографії, яка об'єктивізує і значно спрощує пошук уражених регіонарних лімфовузлів, що відчутно скорочує час операції.

Ключові слова: рак щитоподібної залози, інциденталом щитоподібної залози, ультразвукове дослідження, хроматолимфографія, лімфодисекція, тироїдектомія.

Диагностика микрокарцином щитовидной железы с высоким риском экстраорганной инвазии

A.O. Peimi¹, B.E. Medvedev²

¹КУ «Киевская областная клиническая больница»

²Национальная медицинская академия последипломного образования имени П.Л. Шупика, Киев

Резюме. Проведен аналіз ефективності комплексного застосування різних методів діагностики раку щитовидної залози розміром до 10 мм, в залежності від його морфофункціонального підтипу. Для мікрокарцином з високим, по даним ультразвукового дослідження, ризиком екстраорганної агресії пропонується застосування хроматолимфографії, яка об'єктивізує і значительно упрощає пошук уражених регіонарних лімфовузлів, що ощутимо скорочує час операції.

Ключевые слова: рак щитовидной железы, инциденталом щитовидной железы, ультразвуковое исследование, хроматолимфография, лимфодиссекция, тироидэктомия.