რეზიუმე

ძლიერი ტკივილი და ტანჯვა, როგორც წამების შედეგები: დადგენის სამედიცინო-სამართლებრივი პრაქტიკა (მიმოხილვა)

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კვლევის მიზნას წარმოადგენდა ძლიერი ტკივილის და ტანჯვის, როგორც წამების შედეგების დადგენა სამედიცინო და იურიდიული (საგამოძიებო და სასამართლო) პრაქტიკებს შორის ურთიერთკავშირის აღმოჩენა და თავისებურებების გამოვლენა. კვლევა ეძღვნება სისხლის სამართლის პრობლემატიკას ძლიერი ტკივილის და ტანჯვის, როგორც წამების შედეგების, დადგენის დროს. კვლევაში გამოყენებულია წამების მსხვერპლთა სარეაბილიტაციო ცენტრების პუბლიკაციები, პროფილური სამედიცინო ჟურნალები, ექიმების დამხმარე სახელმძღვანელოები, ტკივილის შემსწავლელი საერთაშორისო ასოციაციისა და უკრაინული ასოციაციის პუბლიკაციები, ა.ბოგომოლცის სახ. ეროვნული სამედიცინო უნივერსიტეტის (კიევი,უკრაინა),დანილა გალიცკის სახ. ლვოვის ეროვნული სამედიცინო უნივერსიტეტის (ლვოვი, უკრაინა) წამყვანი სპეციალისტების განმარტებები, გაეროს შეტყობინებები, გაეროს ადამიანის უფლებათა უმაღლესი კომისრის სამმართველოს ოფიციალური განმარტებები, საერთაშორისო ხელშეკრულებები წამების აკრძალვის შესახებ, პოსტსაბჭოთა ქვეყნების სისხლის სამართლის კოდექსები. კვლევის ემპირიულ ბაზას წარმოადგენდა 2014-დან 2019 წწ. გამოტანილი 41 საბოლოო სასამართლო გადაწყვეტილება წამების გამოყენების საქმეებზე. დასახული მიზნის მისაღწევად გამოყენებულია ანალიზის, ინდუქციის, სტატისტიკური და სისტემური მეთოდები.

კვლევის შედეგების მიხედვით გამოტანილია დასკვნა იმის შესახებ, რომ მხოლოდ ძლიერი ტკივილისა და ტანჯვის სამედიცინო-სამართლებრივი დადგენა არის წამების შედეგების არსებობის ან არარსებობის შესახებ საკითხის სწორი გადაწყვეტის საწინდარი. აღნიშნულია, რომ არც სამედიცინო, არც სამართლებრივი შეფასება არ არის თვითკმარი და მოითხოვს ურთიერთ კონტექსტებით დამატებებს. ყურადღება გამახვილებულია, რომ ძლიერი ტკივილისა და ტანჯვის სამედიცინო-სამართლებრივი დადგენის მეთოდიკური რეკომენდაციების შემუშავება წარმოადგენს ერთ-ერთ ძირითად ამოცანას სამეცნიერო საზოგადოებისთვის.

დამტკიცებულია, რომ წამების შედეგების კონსტატაციის სამედიცინო პრაქტიკის თავისებურებას წარმოადგენს ამ დანაშაულის, როგორც ნორმატიულად განსაზღვრული (ძლიერი ტკივილი და ტანჯვა), ასევე „შორეული“ (ფიზიკური, ფსიქოსომატური და ფსიქიკური) შედეგების დადგენა. არგუმენტირებულია, რომ ძლიერი ტკივილისა და ტანჯვის, როგორც წამების შედეგების, კონსტატაციის საგამოძიებო და სასამართლო პრაქტიკის სპეციფიკა დაკავშირებულია ფართო სპექტრის ინსტრუმენტების გამოყენების საჭიროებასთან: ძლიერი ტკივილისა და ტანჯვის დადგენის სამეცნიერო-სამართლებრივი მეთოდიკა, სამედიცინო დასკვნები ტკივილისა და ტანჯვის სიძლიერის შესახებ, წამების „შორეული“ შედეგების ფიქსაციის სამედიცინო დოკუმენტაცია, სასამართლო-სამედიცინო და ფსიქოლოგიურ-ფსიქიატრიული ექსპერტიზების დასკვნები, დაზარალებულის, მოწმეების დაკითხვის ოქმები და ჩვენებები, ჩადენილი დანაშაულის ადგილის დათვალიერების, ჩხრეკის, საგამოძიებო ექსპერიმენტის ჩატარების, ნივთიერი მტკიცებულების დათვალიერების ოქმები.

DISTRIBUTION OF SEX HORMONES AND LYMPHOCYTES IN REPRODUCTIVE WOMAN WITH THYROID PAPILLARY CARCINOMA AND HASHIMOTO'S THYROIDITIS

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The incidence of papillary thyroid carcinoma is increasing around the world [11]. During last years the incidence of thyroid carcinoma has been increased to 16.3% per 100.000 women. It also represents the fifth most common cause of cancer mortality amongst women [1]. In Georgia, thyroid carcinoma moved from 20th place to 2nd place according to the data of national cancer registry. It is recorded in all age groups and unfortunately it represents the number one malignancy in puberty age girls [8]. The reason for increased incidence is unknown.

Papillary thyroid cancer is the most common subtype of thyroid carcinoma [5]. Its incidence is markedly higher in women compared to men and the female male ratio represents 4:1 [5]. The causative factor of papillary thyroid carcinoma is unknown. However, familial adenomatous polyposis [1], Gardner's disease [9] Cowden disease [7] and Carney complex I [2] spotty skin pigmentation, and endocrine overactivity (of the adrenal, the pituitary, and the testis are considered as pathogenic factors. One of the causes of the development of papillary thyroid carcinoma might be Hashimoto's thyroiditis. However, this association is not very well studied. Although, there are number of pathologies associated with papillary thyroid carcinoma, the most frequently the association with Hashimoto's thyroiditis has been seen [3]. Hashimoto's thyroiditis represents the autoimmune disease, which is mediated by organ-specific T lymphocytes. It is characterised with the presence of lymphoid infiltrate,

including germinal centre formation [6]. There are number of cell groups in Hashimoto's thyroiditis which are characterised with hypochromasia and papillary cancer like features. They express epithelial marker CK19 and mesothelial cell marker HMBE1 similar to papillary thyroid carcinoma [6]. However, the relationship between Hashimoto's thyroiditis and papillary thyroid cancer is still obscure. In addition, there is no information about the role of sex hormone receptor expression or the proliferative characteristics in Hashimoto's thyroiditis and papillary carcinoma.

Therefore, the aim of our study was to analyse the expression of steroid sex hormone receptors, including oestrogen receptor (ER) and progesterone receptors (PR), lymphocytic infiltration and thyreocyte/lymphocyte proliferation index in different types of papillary carcinoma, in Hashimoto's thyroiditis and in co-occurrence of Hashimoto's thyroiditis and papillary carcinoma.

Material and methods. Study included 115 formalin-fixed and paraffin-embedded tissue material from the teaching, research and diagnostic laboratory of Tbilisi State Medical University. Study material was divided into following groups: normal thyroid gland (15 cases), Noninvasive Follicular Thyroid Neoplasm with Papillary-Like Nuclear Features (NIFTP) (15 cases), classic papillary carcinoma (20 cases), follicular variant of papillary carcinoma (17 cases), cylindric-cell variant of papillary carcinoma (9 cases), Hashimoto's thyroiditis (25 cases) and the co-occurrence of Hashimoto's thyroiditis and papillary carcinoma (14 cases).

4μ FFPE tissue sections were deparaffinized in xylene, rehydrated by using serial dilutions of ethanol (96%, 80%, 70%) and heat mediated antigen retrieval has been performed. Ready to use antibodies against the following antigens were used: ER, PR, Ki67, CK19, CD56. Staining and visualization has been performed using Bond polymer refine detection system. The number of positive cells were counted in 20HPF and the percentage of marker positive cells were estimated. For ER and PR absence of staining considered as negative, 1-10% of positively stained nuclei was considered as weak expression and >10% positively stained nuclei was considered as strong expression. Thyreocyte and lymphocyte proliferation index was made based on the percentage of Ki67 positive thyreocytes and lymphocytes in 20HPF respectively. In addition thyreocyte/lymphocyte proliferation index was made as the ratio of Ki67 positive thyreocytes to Ki67 positive lymphocytes.

Non-germinal centre lymphocytes were counted in standard haematoxylin and eosin stained specimens as the percentage of lymphocytes covering total area of the lesion. The absence of lymphocytic infiltration considered as negative. Lymphocytic infiltration ≤10% considered as low and lymphocytic infiltration >10% considered as high.

Comparisons between groups were made using Kruskal-Wallis test. The Kruskal-Wallis test is a nonparametric (distribution free) test, and is used when the assumptions of one-way ANOVA are not met. The Kruskal-Wallis test can be used for both continuous and ordinal-level dependent variables. Correlations were assessed using Spearman's rank correlation. The Spearman's rank correlation is also used when data is non-parametrically distributed. P values <0.05 were considered as significant. All statistical tests were performed using SPSS software V19.00.

Results and discussion. 9/15 (60%) cases of normal thyroid gland were negative for ER and there was weak ER expression present in 6/15 (40%) cases of normal thyroid gland. Strong ER expression was not detected in normal thyroid gland. ER negativity was not detected in any of the NIFTP cases, weak ER expression was detected in 10/15 (70%) of the NIFTP cases and strong ER expression was detected in 5/15 (30%) of NIFTP cases. ER negativity was detected in 9/20 (45%) classic papillary carcinoma cases, weak ER expression was detected in 5/20 (25%) classic papillary carcinoma cases and strong ER expression was detected in 6/20 (30%) classic papillary carcinoma cases. In follicular variant of papillary carcinoma ER negativity was detected in 7/17 (41.2%) cases, weak ER expression was detected in 3/17 (17.6%) cases and strong ER expression was detected in 7/17 (41.2%) cases. In cylindric-cell variant of papillary carcinoma 3/9 (33.3%) cases were negative for ER expression, 1/9 (11.1%) case revealed weak ER expression and 5/9 (55.6%) cases revealed strong ER expression. In Hashimoto's thyroiditis 12/25 (48%) cases were negative for ER and 13/25 cases showed weak ER (52%) expression. In cases with the co-occurrence of Hashimoto's thyroiditis and papillary carcinoma, ER negativity was not detected when evaluated both lesions together, weak expression was detected in 5/14 (35%) cases and strong expression was detected in 9/14 (65%) cases. When evaluated separately ER negativity was detected in 6/14 (42.9%) cases of Hashimoto's thyroiditis component and 5/14 (35.7%) cases of Hashimoto's thyroiditis component revealed weak ER positivity and 3/14 (21.4%) Hashimoto's thyroiditis component revealed strong ER positivity. In papillary carcinoma component weak expression was detected in 5/14 (35%) cases and strong expression was detected in 9/14 (65%) cases.

13/15 (86.7%) cases of normal thyroid gland were negative for PR and there was weak ER expression present in 2/15 (13.3%) cases of normal thyroid gland. Strong PR expression was not detected in normal thyroid gland. PR negativity was not detected in any of the NIFTP cases, weak PR expression was detected in 9/15 (60%) of the NIFTP cases and strong PR expression was detected in 6/15 (40%) of NIFTP cases. PR negativity was detected in 5/20 (25%) classic papillary carcinoma cases, weak PR expression was detected in 6/20 (30%) classic papillary carcinoma cases and strong PR expression was detected in 9/20 (45%) classic papillary carcinoma cases. In follicular variant of papillary carcinoma PR negativity was detected in 4/17 (23.5%) cases, weak PR expression was detected in 4/17 (23.5%) cases and strong PR expression was detected in 9/17 (52.9%) cases. In cylindric-cell variant of papillary carcinoma 2/9 (22.2%) cases were negative for PR expression, 1/9 (11.1%) case revealed weak PR expression and 6/9 (66.7%) cases revealed strong ER expression. In Hashimoto's thyroiditis 20/25 (80%) cases were negative for PR and 5/25 (20%) cases showed weak PR expression. In cases with the co-occurrence of Hashimoto's thyroiditis and papillary carcinoma, PR negativity was detected in 4/14 (28.6%) cases when evaluated both lesions together, weak expression was detected in 3/14 (21.4%) cases and strong expression was detected in 7/14 (50%) cases. When evaluated separately PR negativity was detected in 7/14 (50%) cases of Hashimoto's thyroiditis component, and 3/14 (21.4%) cases of Hashimoto's thyroiditis component revealed weak PR positivity and 4/14 (28.6%) Hashimoto's thyroiditis component revealed strong PR positivity. In papillary carcinoma component weak negative expression was detected in 4/14 (28.6%) cases, weak expression was detected in 3/14(21.4%) cases and strong expression was detected in 7/14 (50%) cases.

Table 1. Distribution of ER and PR percentage values in groups. Green cells represent highest percentage of cases and red cells represent the lowest percentage of cases, yellow, orange and light green cells represent the moderate percentage of cases

	ER			PR		
	Negative	**Weak**	**Strong**	**Negative**	**Weak**	**Strong**
Normal Thyroid Gland	60.0%	40.0%	0.0%	86.7%	13.3%	0.0%
NIFTP	0.0%	70.0%	30.0%	0.0%	60.0%	40.0%
Classic Papillary Carcinoma	45.0%	25.0%	30.0%	25.0%	30.0%	45.0%
Follicular Variant of Papillary Carcinoma	41.2%	17.6%	41.2%	23.5%	23.5%	52.9%
Cylindric-cell Variant of Papillary Carcinoma	33.3%	11.1%	55.6%	22.2%	11.1%	66.7%
Hashimoto's Thyroiditis	48.0%	52.0%	0.0%	80.0%	20.0%	0.0%
Hashimoto's Thyroiditis + Papillary Carcinoma	0.0%	35.0%	65.0%	28.6%	21.4%	50.0%

Table 2. The distribution of lymphocytic infiltration in groups

	Lymphocyte count			
	<10% N/%		**≥10% N/%**	
Normal Thyroid Gland	15	100.0%	0	0.0%
NIFTP	8	53.3%	7	46.7%
Classic Papillary Carcinoma	12	60.0%	8	40.0%
Follicular Variant of Papillary Carcinoma	11	64.7%	6	35.3%
Cylindric-cell Variant of Papillary Carcinoma	7	77.8%	2	22.2%
Hashimoto's Thyroiditis	0	0.0%	25	100.0%
Hashimoto's Thyroiditis + Papillary Carcinoma	0	0.0%	14	100.0%

The study of lymphocyte distribution showed following results: in normal thyroid gland all cases were characterised with <10% lymphocytes. In NIFTP 8/15 (53.3%) of cases were characterised with <10% lymphocytes and 7/15 (46.7%) cases were characterised with ≥10% lymphocytes. In classic papillary carcinoma 12/20 (60%) cases were characterised with the presence of <10% lymphocytes and 8/20 (40%) of cases were characterised with the presence of ≥10% lymphocytes. In follicular variant of papillary carcinoma 11/17 (64.7%) of cases were characterised with <10% lymphocytic infiltrate and 6/17 (35.3%) of cases were characterised with ≥10% lymphocytic infiltrate. In cylindric-cell variant of papillary carcinoma 7/9 (77.8%) cases showed <10% lymphocytic infiltrate and 2/9 (22.2%) cases showed ≥10% lymphocytic infiltrate. When examined together none of the cases of Hashimoto's thyroiditis or combined Hashimoto's thyroiditis with papillary carcinoma showed <10% lymphocytic infiltrate. When examined as separate components, Hashimoto's thyroiditis component does not show <10% lymphocytic infiltrate in any of the cases. In papillary carcinoma component 9/14 (64.3%) cases were characterised with <10% lymphocytic infiltrate and 6/14(35.7%) of cases were characterised with ≥10% lymphocytic infiltrate.

The study of thyreocyte Ki67 proliferation index distribution in groups showed the following results: in normal thyroid gland Ki67 activity was not detected. In NIFTP average Ki67 proliferation index was 2±0.3; In classic papillary carcinoma average Ki67 proliferation index was 3±0.7; In Follicular variant of papillary carcinoma the average Ki67 proliferation index was 4±1.1; In Cylindric-cell variant of papillary carcinoma the average Ki67 proliferation index was 5±1.8; In epithelial component of Hashimoto's thyroiditis the average Ki67 proliferation index was 7±2.4 and in combined Hashimoto's thyroiditis and papillary carcinoma cases the average Ki67 proliferation index was 10±3.1 when examined both components together. When each component examined separately the average Ki67 proliferation index in Hashimoto's thyroiditis component was 8±3.2 and in papillary carcinoma component was 6±2.5.

The study of lymphocyte Ki67 proliferation index distribution in groups showed the following results: in normal thyroid gland Ki67 activity in lymphocytes was not detected. In NIFTP average lymphocyte Ki67 proliferation index was 3 ± 0.9; In classic papillary carcinoma average lymphocyte Ki67 proliferation index was 2.5±0.6; In Follicular variant of papillary carcinoma the average lymphocyte Ki67 proliferation index was 2±0.4; In Cylindric-cell variant of papillary carcinoma the average lymphocyte Ki67 proliferation index was 1.7±0.2; In epithelial component of Hashimoto's thyroiditis the average lymphocyte Ki67 proliferation index was 4.5±1.7 and in combined Hashimoto's thyroiditis and papillary carcinoma cases the average lymphocyte Ki67 proliferation index was 4±1.3 when examined both components together. When each component examined separately the average lymphocyte Ki67 proliferation index in Hashimoto's thyroiditis component was 4±2.2 and in papillary carcinoma component was 2±0.8.

The study of thyreocite/lymphocyte proliferation index (Ki67 thyr/lymph IND) in groups showed following results: in normal thyroid gland the Ki67 thyr/lymph IND was 0.00; In NIFTP the Ki67 thyr/lymph IND was 0.67±0.3; In classic papillary carcinoma the average Ki67 thyr/lymph IND was 1.2±1.1; In follicular variant of papillary carcinoma the average Ki67 thyr/lymph IND was 2±1.75; In Cylindric-cell variant of papillary carcinoma the average Ki67 thyr/lymph IND was 2.94±1.98; In Hashimoto's thyroiditis the average Ki67 thyr/lymph IND was 1.56±0.94; In combined Hashimoto's thyroiditis and papillary carcinoma the average thyr/lymph IND was 2.50±1.7 when examined together. When examined separately, the average thyr/lymph IND was 2±1.9 in Hashimoto's thyroiditis component and 3±2.1 in papillary carcinoma component.

Table 3. The distribution of Ki67 thyreocyte index, Ki67 lymphocyte index and Ki67 thyreocyte/lymphocyte index in groups

	Ki67/Thyr.	Ki67/Lymph.	Ki67 Thyr/Lymph IND
Normal Thyroid Gland	0.00%	0.00%	0.00
NIFTP	2%±0.3	3%±0.9	0.67±0.3
Classic Papillary Carcinoma	3% ± 0.7	2.5%±0.6	1.20±1.1
Follicular Variant of Papillary Carcinoma	4%±1.1	2%±0.4	2.00±1.75
Cylindric-cell Variant of Papillary Carcinoma	5%±1.8	1.7%±0.2	2.94±1.98
Hashimoto's Thyroiditis	7%±2.4	4.5%±1.7	1.56±0.94
Hashimoto's Thyroiditis + Papillary Carcinoma	10%±3.1	4%±1.3	2.50±1.7

Table 4. The distribution of CK19 and CD56 staining in groups.

	CK19		CD56	
	Negative	Positive	Negative	Positive
Normal Thyroid Gland	100.00%	0.00%	0.00%	100.00%
NIFTP	60.00%	40.00%	53.30%	46.70%
Classic Papillary Carcinoma	0.00%	100.00%	100.00%	0.00%
Follicular Variant of Papillary Carcinoma	29.50%	70.50%	100.00%	0.00%
Cylindric-cell Variant of Papillary Carcinoma	44.50%	55.50%	100.00%	0.00%
Hashimoto's Thyroiditis	76.00%	24.00%	24.00%	74.00%
Hashimoto's Thyroiditis + Papillary Carcinoma	42.90%	57.10%	57.10%	42.90%

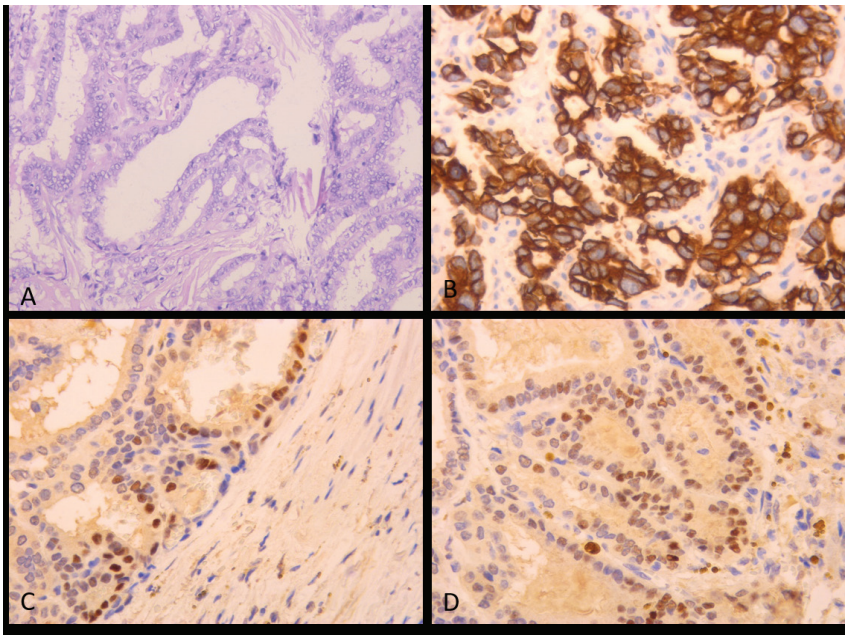


Fig. 1. A. Papillary thyroid carcinoma, H&E, x100, B. CK19 expression, IHC, x200, C. ER expression, IHC, x200 and D. PR expression, IHC, x200

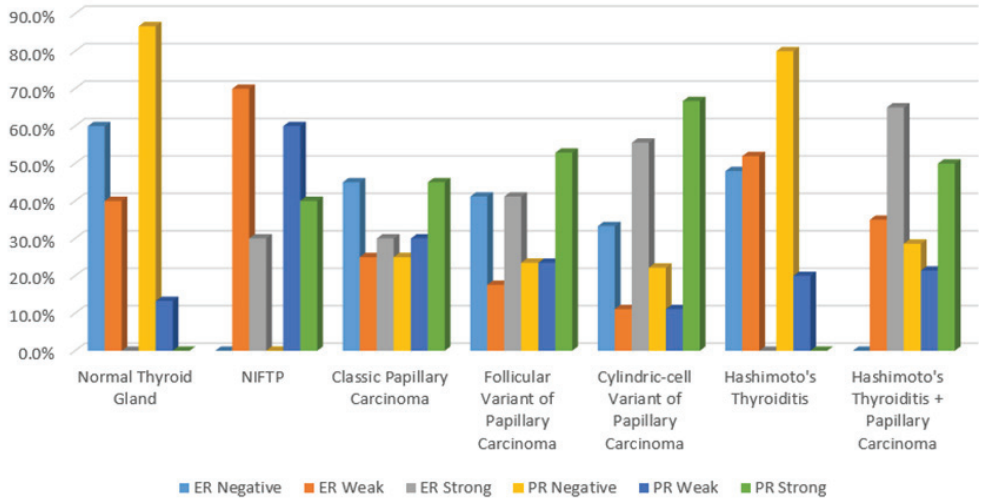
The study of the distribution of CK19 in groups showed following results: in normal thyroid gland all 15/15 (100%) cases were negative for CK19 expression. In NIFTP 9/15 (60%) cases were negative for CK19 expression and 6/15 (40%) of cases were positive for CK19 expression. In classic papillary carcinoma 0/20 (0%) were negative and 20/20 (100%) of cases were positive for CK19 expression. In follicular variant of papillary carcinoma 5/17 (29.5%) cases were negative and 12/17 (70.5%) cases were positive for CK19 expression. In cylindric-cell variant of papillary carcinoma 4/9 (44.5%) cases were negative and 5/9 (55.5%) cases were positive for CK19 expression. In Hashimoto's thyroiditis 19/25 (76%) was negative for CK19 expression and 6/25 (24%) was positive for CK19 expression. In combined Hashimoto's thyroiditis and papillary carcinoma 6/14 (42.9%) of cases were negative for CK19 expression and 8/14 (57.1%) of cases were positive for CK19 expression when evaluated together.

The study of the distribution of CD56 in groups showed the following results: in normal thyroid gland all 15/15 (100%) cases were positive for CD56. In NIFTP 8/15 (53.3%) cases were negative and 7/15 (46.7%) cases were positive for CD56. In classic papillary carcinoma 20/20 (100%) cases were negative for CD56. Similarly, in follicular variant of papillary carcinoma and cylindric-cell variant of papillary carcinoma all 17/17 (100%)

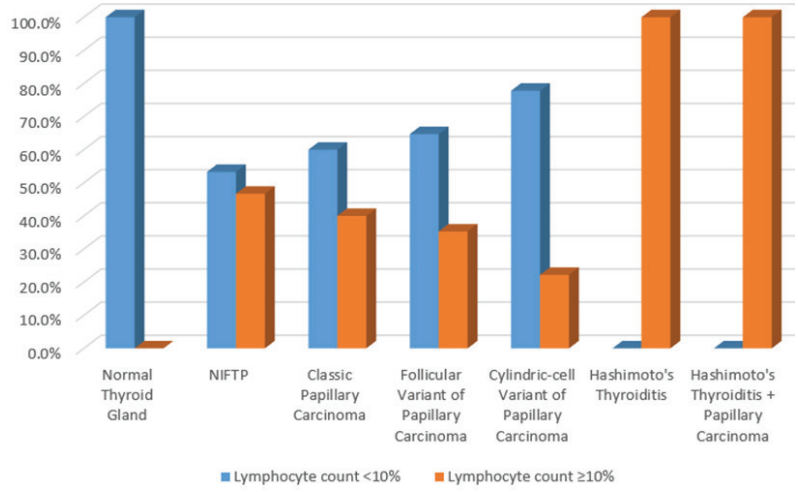
and 9/9 (100%) of cases were negative for CD56 respectively. In Hashimoto's thyroiditis 6/25 (24%) of cases were negative and 19/25 (74%) of cases were positive for CD56 staining. In combined cases of Hashimoto's thyroiditis and papillary carcinoma 8/14 (57%) cases were negative and 6/14 (43%) of cases were positive for CD56 staining.

The analysis of results showed that the lowest ER expression is seen in normal thyroid gland and the highest ER expression is seen in papillary carcinoma component of combined Hashimoto's thyroiditis and papillary carcinoma. Also, amongst three types of papillary carcinoma, including: classic, follicular and cylindric-cell variants, the expression of ER is gradually increased and reaches it's maximum in cylindric-cell variant, which is considered as the most aggressive type of thyroid papillary carcinoma amongst others. The lowest rates of PR expression are seen in normal thyroid gland and in Hashimoto's thyroiditis. Similarly, to ER the PR expression is also gradually increased amongst classic, follicular and cylindric-cell variant of papillary carcinoma and reaches it's maximum in cylindric-cell variant.

The comparative analysis of lymphocyte counts in groups showed that the highest amount of lymphocytic infiltrate was present in Hashimoto's thyroiditis and the lowest amount was present in normal thyroid gland. In NIFTP there was an average lymphocyte count present. Interestingly, lymphocyte count was markedly decreased between classic, follicular and cylincric-cell variant of papillary carcinoma, showing the lowest amount of lymphocytic infiltration in cylindric-cell variant of papillary carcinoma.



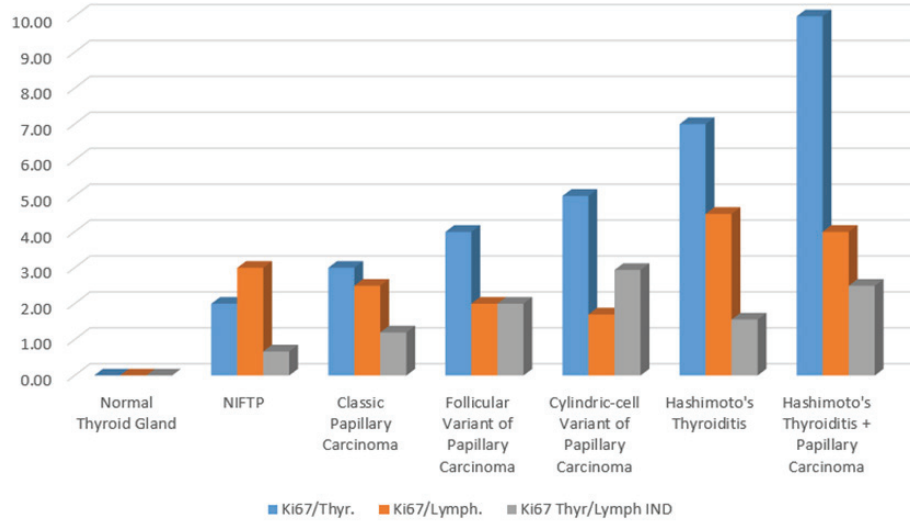
Graph 1. The distribution of ER and PR in groups



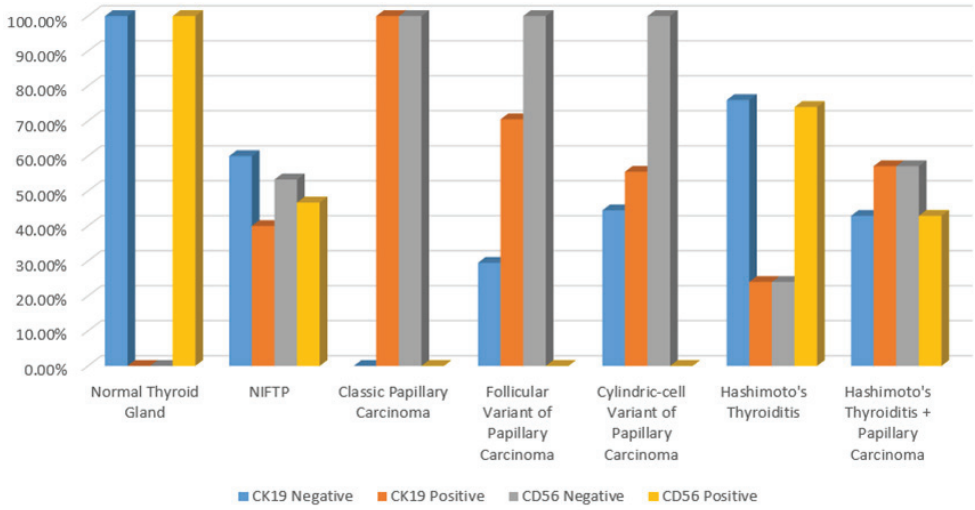
Graph 2. The distribution of lymphocyte count in groups

The comparative analysis of Ki67 thyreocyte proliferation index showed that it is gradually increased from NIFTP to papillary carcinoma and its variants. The highest Ki67 thyreocyte proliferation index was seen in Hashimoto's thyroiditis and in combined cases of Hashimoto's thyroiditis and papillary carcinoma. The comparative analysis of lymphocyte Ki67 proliferation index showed that the highest lymphocyte Ki67 proliferation index is seen in Hashimoto's thyroiditis, followed by co-occurrence of Hashimoto's thyroiditis and papillary carcinoma cases. In cases of classic papillary carcinoma, folicullar and cylindric-cell variants it is gradually decreased, with the minimal lymphocyte KI67 proliferation index in cylindric-cell variant of papillary carcinoma.

The comparative analysis of Ki67 thyreocyte/lymphocyte proliferation index (Ki67 Thyr/lymph IND), showed that it is gradually increased from NIFTP, to papillary carcinoma and it variants, showing the maximum degree in cylincric-cell variant of papillary carcinoma. In Hashimoto's thyroiditis Ki67 Thyr/lymph IND is relatively low compared to combined cases of Hashimoto's thyroiditis and papillary carcinoma.



Graph 3. The distribution of Ki67 thyreocyte, Ki67 lymphocyte and Ki67 Thyreocyte/lymphocyte index (Ki67 Thyr/lymph IND) in groups



Graph 4. The distribution of CK19 and CD56 in groups

The analysis of CK19 and CD56 showed that CK19 is significantly and negatively correlates with the expression of CD56 in all groups ($p<0.001$). Meaning that in cases with high CK19 expression CD56 shows lowest expression and in cases of low CK19 expression or negativity CD56 shows highest expression.

Previously Rajoria et al. evaluated thyroid cells for the presence of ER and also cell response to estrogen, showing the important role of estrogen in cell division, migration and invasion [10]. Kansakar et al. found that the expression of ER and PR in thyroid neoplasms was higher in comparison with normal thyroid tissue and our study results are in line with the findings of Kansakar et al., we have also found the marked increase of ER and PR in carcinoma cases compared to normal thyroid tissue [4]. To the best of our knowledge we are first who examined ER and PR status in co-occurrence of Hashimoto's thyroiditis and papillary carcinoma. Also, to the best of our knowledge we are first who examined thyreocite/lymphocyte proliferation index.

Conclusions. The expression level of ER and PR is even higher in cases where Hashimoto's thyroiditis and papillary carcinoma co-occur. Therefore, we can conclude that Hashimoto's thyroiditis may play an important role in the development of papillary thyroid carcinoma.

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SUMMARY

DISTRIBUTION OF SEX HORMONES AND LYMPHOCYTES IN REPRODUCTIVE WOMAN WITH THYROID PAPILLARY CARCINOMA AND HASHIMOTO'S THYROIDITIS

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The incidence of papillary thyroid carcinoma is characterised with increasing tendency, with unknown reasons. Frequently the co-occurrence of papillary thyroid carcinoma and Hashimoto's thyroiditis has been observed.

The aim of our study was to analyse the expression of hormone receptors, lymphocytic infiltration and thyreocyte/lymphocyte proliferation index in thyroid papillary carcinoma and in Hashimoto's thyroiditis.

Study included 115 formalin-fixed and paraffin-embedded tissue material from the teaching, research and diagnostic laboratory of Tbilisi State Medical University. Study material was divided into following groups: normal thyroid gland (n=15), Non-invasive Follicular Thyroid Neoplasm with Papillary-Like Nuclear Features (NIFTP) (n=15), classic papillary carcinoma (CPC)(n=20), follicular variant of papillary carcinoma (FPC) (n=17), cylindric-cell variant of papillary carcinoma (CCPC)(n=9), Hashimoto's thyroiditis (HT) (n=25) and the co-occurrence of Hashimoto's thyroiditis and papillary carcinoma (HTPC) (n=14). Standard immunohistochemistry was used to detect ER, PR, Ki67, CK19, CD56. In addition, lymphocytic infiltration was evaluated in H&E stained specimens. Study results showed that ER and PR expression is higher in FPC, CCPC and HTPC compared to CPC ($p<0.001$), whilst lymphocytic infiltrate is lower in FPC and CCPC compared to CPC ($p<0.05$). In addition, ER and PR expression is higher in HTPC compared to HT only ($p<0.001$). The thyreocyte/lymphocyte proliferation index is increased in FPC and CCPC compared to CPC and it is also higher in HTPC compared to only HT and CPC ($p<0.05$). The expression of sex steroid hormones plays an important role in the pathogenesis of papillary thyroid carcinoma. The expression level of ER and PR is even higher in cases where Hashimoto's thyroiditis and papillary carcinoma co-occur. Therefore, we can conclude that Hashimoto's thyroiditis may play an important role in the development of papillary thyroid carcinoma.

Keywords: papillary-papillary thyroid carcinoma, Hashimotos's thyroiditis, sex hormones.

РЕЗЮМЕ

ОСОБЕННОСТИ РАСПРЕДЕЛЕНИЯ ПОЛОВЫХ ГОРМОНОВ И ЛИМФОЦИТАРНОЙ ИНФИЛЬТРАЦИИ ПРИ СОСУЩЕСТВОВАНИИ ТИРЕОИДИТА ХАСИМОТО И ПАПИЛЛЯРНОГО РАКА ЩИТОВИДНОЙ ЖЕЛЕЗЫ У ЖЕНЩИН РЕПРОДУКТИВНОГО ВОЗРАСТА

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Инцидентность папиллярной карциномы щитовидной железы характеризуется тенденцией к увеличению. Часто отмечается сосуществование папиллярного рака щитовидной железы и тиреоидита Хасимото. Целью исследования явилось изучение гормональных рецепторов, лимфоцитарной инфильтрации и тиреоцит-лимфоцитарного пролиферативного индекса при папиллярной карциноме щитовидной железы и тиреоидите Хасимото.

Исследование проводилось в "Учебной, научной и диагностической лаборатории Тбилисского государственного медицинского университета" на 115 тканевых образцах, фиксированных в формалине и залитых в парафин. Материал разделён на следующие группы: нормальная ткань щитовидной железы (n=15), неинвазивная неоплазия щитовидной железы с ядрами, похожими на папиллярный рак (NIFTP, n=15), классическая папиллярная карцинома (CPC, n=20), фолликулярный вариант папиллярной карциномы (FPC, n=17), цилиндр-клеточный вариант папиллярной карциномы (CCPC, n=9), тиреоидит Хасимото (HT, n=25) и случаи сосуществования тиреоидита Хасимото и папиллярного рака щитовидной железы (HTPC, n=14). Стандартным иммуногистохимическим методом изучены следующие молекулярные маркеры: ER, PR, Ki67, CK19, CD56. В препаратах, окрашенных стандартным гематоксилином и эозином, оценена лимфоцитарная инфильтрация. Результаты исследования показали, что экспрессия ER и PR высокая в FPC, CCPC и HTPC в сравнении с CPC ($p<0,001$), а лимфоцитарная инфильтрация низкая в FPC, CCPC и HTPC в сравнении с CPC ($p<0.05$). Экспрессия ER и PR высокая при HTPC в сравнении с HT и CPC ($p<0,05$). Следует заключить, что повышенная экспрессия гормональных рецепторов играет значимую роль в патогенезе папиллярной карциномы и тиреоидита Хасимото и представляет один из главных риск факторов развития папиллярной карциномы.

რეზიუმე

სასქესო ჰორმონების და ლიმფოციტური ინფილტრაციის განაწილების თავისებურებები რეპროდუქციული ასაკის ქალებში ჰასიმოტოს თირეოიდიტით და ფარისებრი ჯირკვლის პაპილური კარცინომით

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ფარისებრი ჯირკვლის პაპილური კარცინომის ინციდენტობა ხასიათდება მზარდი ტენდენციით. ხშირ

შემთხვევაში აღინიშნება ფარისებრი ჯირკვლის პაპილური კარცინომისა და ჰასიმოტოს თირეოიდიტის თანაარსებობა.

კვლევის მიზანს წარმოაგენდა ჰორმონული რეცეპტორების, ლიმფოციტური ინფილტრაციის და თირეოციტ-ლიმფოციტური პროლიფერაციის ინდექსის შესწავლა ფარისებრი ჯირკვლის პაპილურ კარცინომასა და ჰასიმოტოს თირეოიდიტში.

კვლევა მოიცავდა 115 ფორმალინში დაფიქსირებულ და პარაფინში ჩაყალიბებულ ქსოვილოვან მასალას თსსუ სასწავლო, სამეცნიერო და დიაგნოსტიკური ლაბორატორიიდან. საკვლევი მასალა დაყოფილი იყო შემდეგ ჯგუფებად: ფარისებრი ჯირკვლის ნორმალური ქსოვილი (n=15), ფარისებრი ჯირკვლის არაინვაზიური ნეოპლაზია პაპილურის მსგავსი ბირთვებით (NIFTP - n=15), კლასიკური პაპილური კარცინომა (CPC - n=20), პაპილური კარცინომის ფოლიკულური ვარიანტი (FPC - n=17), პაპილური კარცინომის ცილინდრულ უჯრედული ვარიანტი (CCPC - n=9), ჰასიმოტოს თირეოიდიტი (HT - n=25) და შემთხვევები ჰასიმოტოს თირეოიდიტის და პაპილური კარცინომის თანაარსებობით (HTPC - n=14). სტანდარტული იმუნოჰისტოქიმიური მეთოდით გამოვლენილია ER, PR, Ki67, CK19, CD56. ჰემატოქსილინით და ეოზინით შეღებილ ანათლებში შეფასდა ლიმფოციტური ინფილტრაცია.

კვლევის შედეგებმა აჩვენა, რომ ER და PR ექსპრესია მაღალია FPC, CCPC და HTPC-ში შედარებით CPC-თან ($p<0,001$), ხოლო ლიმფოციტური ინფილტრაცია დაბალია FPC, CCPC და HTPC-ში შედარებით CPC-თან ($p<0,05$). ER და PR ექსპრესია მაღალია HTPC-ში შედარებით HT-თან და CPC-თან ($p<0,05$). კვლევის შედეგად გამოტანილია დასკვნა, რომ ჰორმონული რეცეპტორების მომატებული ექსპრესია მნიშვნელოვან როლს თამაშობს პაპილური კარცინომის პათოგენეზში და ჰაშიმოტოს თირეოიდიტი შესაძლებელია წარმოადგენდეს პაპილური კარცინომის განვითარების ერთ-ერთ მთავარ რისკ-ფაქტორს.

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