Sanja Medenica,* Božo Trbojević,**

ZNAČAJ ANTIPEROKSIDAZNIH ANTITELA KOD PACIJENATA SA TIREOIDNOM NODOZNOM STRUMOM

Sažetak: *Uvod*: Tireoidna nodozna struma je klinički prepoznatljiva ograničena promena građe štitaste žlezde. Brojne studije pokazuju vezu između tireoidne autoimunosti i diferentovanog tireoidnog karcinoma kod pacijenata sa nodoznom strumom. Jedan od klinički značajnih markera u definisanju tireoidne autoimunosti jesu antitela na tireoidnu peroksidazu.

Cilj: Cilj rada je da se analizira veza između antiperoksidaznih antitela i tireoidnog maligniteta kod osoba sa nodozno izmenjenom štitastom žlezdom.

Materijal i metode: Retrospektivno je pregledano 248 tireoidnih FNA citoloških izveštaja uzoraka, dobijenih punkcijom pacijenata sa tireoidnom nodoznom bolešću Odeljenja za štitastu žlezdu, Klinike za endokrinologiju, dijabetes i bolesti metabolizma Kliničkog centra Srbije u Beogradu u periodu od oktobra 2007. do januara 2010. godine. Analiziran je odnos između dijagnostičkih kategorija citopatoloških nalaza i antiperoksidaznih antitela. Podaci su statistički obrađeni pomoću kompjuterskog programa SPSS 12.0 softverskog paketa.

Rezultati: Od 248 pacijenta, 148 pacijenata (59,7%) imalo je vrednosti anti TPO antitela u referentnim granicama (do 30 IU/ml), a 40,3% povišene vrednosti anti TPO antitela (preko 30 IU/ml). U grupi pacijenata sa povišenim vrednostima anti TPO antitela bilo je čak 7% (7/100) pacijenata sa malignim citološkim nalazom, a u grupi pacijenata sa vrednostima anti TPO antitela u referentnim granicama svega 1.4% (2/148) sa malignim citološkim nalazom.

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Zaključak: Definisanje veze između tireoidne autoimune bolesti i diferentovanog tireoidnog karcinoma pruža nova saznanja na polju imunoterapije tireoidnog karcinoma. Prosvetljavanje molekularnih mehanizama povezanosti tireoidne autoimune bolesti i razvoja tireoidnog karcinoma kod pacijenata sa nodoznom strumom pomaže otkrivanju novih terapeutskih strategija protiv tireoidnog karcinoma.

Ključne reči: nodozna struma, antiperoksidazna antitela, tireoidna autoimunost, aspiracija tankom iglom

Abstract: *Introduction*: Thyroid nodular goiter Nodular goiter is clinically recognizable restricted structure changes of the thyroid gland. Numerous studies show the relationship between thyroid autoimmunity and differentiated thyroid cancer in patients with nodular thyroid goiter. One of the important clinical marker in defining thyroid autoimmunity are antibodies to thyroid peroxidase.

Objective: The aim of this study was to analyze the relationship between antibodies anti peroksidaznih ii thyroid malignancies in patients with thyroid altered thyroid.

Material and Methods: We retrospectively reviewed the 248 reports of thyroid FNA cytology of samples obtained by puncture of patients with nodular thyroid goiter, at Department of thyroid gland, Department of Endocrinology, Diabetes and Metabolic Diseases, Clinical Center of Serbia in the period from October 2007. by January 2010. year. We analyzed the relationship between findings of cytopathological diagnostic categories and serum concentrations of anti peroxidase antibodies. The data were statistically processed using the computer program SPSS 12.0 software package.

Results: Of total 248 patients, 148 patients (59.7%) had anti-TPO antibody values in a reference limits (30 IU / ml), and 40.3% elevated anti-TPO antibodies (over 30 IU / ml). In the group of patients with elevated values of anti-TPO antibodies 7% (7/100) of patients had malignant cytologic findings, and in the group of patients with anti-TPO antibody values in the normal range only 1.4% (2/148) of pateints had malignant cytologic findings.

Conclusion: Defining the relationship between thyroid autoimmune disease and differentiated thyroid cancer, providing new insights in the field of immunotherapy of thyroid carcinoma. Enlightening the molecular mechanisms link autoimmune thyroid disease and thyroid cancer development in patients with thyroid nodule help find new therapeutic strategies against thyroid cancer.

Key words: thyroid nodule, anti peroxidase antibodies, thyroid autoimmunity, fine needle aspiration

Uvod

Tireoidna nodozna struma je klinički prepoznatljiva ograničena promena građe štitaste žlezde. Oko 2–6% slučajeva ove bolesti otkriveni su palpacijom, 19–35% pomoću osetljivih postupaka, kao što je ultrazvuk, i 8–65% na autopsiji. Prevalenca se linearno povećava godinama, izloženošću radijaciji i deficijenciji joda. Može se javiti endemski u područjima s deficijencijom joda. Žene obolevaju češće nego muškarci (1).

Kliničke forme bolesti uključuju netoksičnu nodoznu strumu, multinodoznu toksičnu strumu i toksični tireoidni adenom (Plummer-ova bolest).

Uzroci tireoidne nodozne bolesti mogu biti benigni (koloidni nodus, Hashimoto tireoiditis, obična ili hemoragijska cista, folikularni adenom, subakutni tireoiditis) i maligni (primarni porekla folikularnih ćelija–papilarni, folikularni i anaplastični tireoidni karcinom, porekla C-ćelije tireoideje-medularni tireoidni karcinom, limfomi i sekundarni metastatski karcinomi).

Dijagnoza bolesti se postavlja na osnovu fizikalnog pregleda, laboratorijskih ispitivanja, aspiracione punkcije tankom iglom (FNA) i metoda vizuelizacije (scintigrafija, ultrazvuk i ultrazvučna elastografija, CT, MR i PET).

Aspiraciona punkcija tankom iglom (FNA) ključna je dijagnostička procedura i prva linija dijagnostičkih testova tireoidne nodozne bolesti. Klasifikacija dijagnostičkih kategorija tireoidne FNA najčešće podrazumeva sledeće kategorije: 'maligno', 'benigno', 'neodređeno', 'neuspešno'. Pojam neodređeno odnosi se na lezije koje se na osnovu citološkog izgleda nisu mogle sa sigurnošću svrstati u jednu od grupa benigno ili maligno, a tu spadaju folikularne, oksifilne lezije (Hurthle cell) i suspektni nalazi. Kategorija neuspešno odnosila se na one uzorke koji nisu imali dovoljno materijala ili isti nije bio adekvatan za dijagnozu.

Terapija je najčešće hirurška ili ablacija radiojodom, dok se u novije vreme u za to indikovanim slučajevima primenjuju terapija rekominantnim humanim tireotropinom, perkutana injekcija etanola, laser termal ablacija i radiofrekventna ablacija.

Klinički značaj tireoidne nodozne bolesti, pored estetskih izmena, kao što je zadebljanje vrata, lokalnih kompresivnih sindroma i tireoidne disfunkcije – jeste mogućnost razvoja maligniteta u 5% slučajeva. Godišnja incidenca tireoidnog karcinoma je 1–2 na 100.000 ljudi, što čini 90% maligniteta celog endokrinog sistema, 1% svih maligniteta kod ljudi i 0,5% smrtnosti zbog maligniteta (1,2).

Brojne studije pokazuju vezu između tireoidne autoimunosti i diferentovanog tireoidnog karcinoma kod pacijenata sa nodoznom strumom.

Jedan od značajnih kliničkih markera u definisanju tireoidne autoimunosti jesu antitela na tireoidnu peroksidazu.

Cilj rada

Cilj rada je da se analizira veza između antiperoksidaznih antitela i i tireoidnog maligniteta kod osoba sa nodozno izmenjenom štitastom žlezdom.

Materijal i metode

Ispitivanje je sprovedeno u Klinici za endokrinologiju, dijabetes i bolesti metabolizma, Kliničkog centra Srbije u Beogradu. Retrospektivno je pregledano 248 tireoidnih FNA citoloških izveštaja uzoraka, dobijenih punkcijom pacijenata sa tireoidnom nodoznom bolešću Odeljenja za štitastu žlezdu, u periodu od oktobra 2007. do januara 2010. god.

Pacijenti su ambulantno pregledani, uzeta je anamneza i urađena laboratorijska ispitivanja (biohemija, krvna slika i hormonski status), urađen je EKG i ultrazvuk, a nekim pacijentima i scintigrafija štitaste žlezde. Nakon toga izvedena je aspiraciona punkcija tankom iglom (FNA), a dobijeni preparati analizirani u Institutu za patologiju Kliničkog centra Srbije u Beogradu.

Citološki nalazi uzoraka FNA su klasifikovani pomoću sheme dijagnostičkih kategorija tireoidne FNA i to: benigno, maligno, neodređeno i neuspešno.

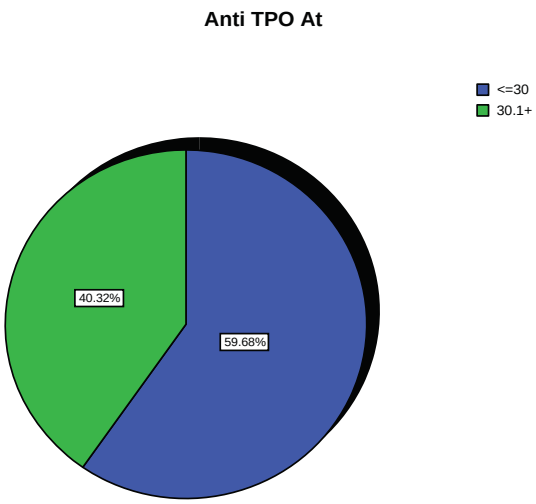
Analiziran je odnos između dijagnostičkih kategorija i serumske koncentracije antiperoksidaznih (TPO) antitela.

Podaci su statistički obrađeni pomoću kompjuterskog programa SPSS 12.0 softverskog paketa.

Rezultati

Od 248 pacijenata, 148 pacijenata (59.7%) je imalo vrednosti antitela u referentnim granicama (do 30 IU/ml), a 40,3% povišene vrednosti anti TPO antitela (preko 30 IU/ml). Rezultati su grafički prikazani na grafikonu 1.

Grafikon 1. Distribucija anti TPO antitela



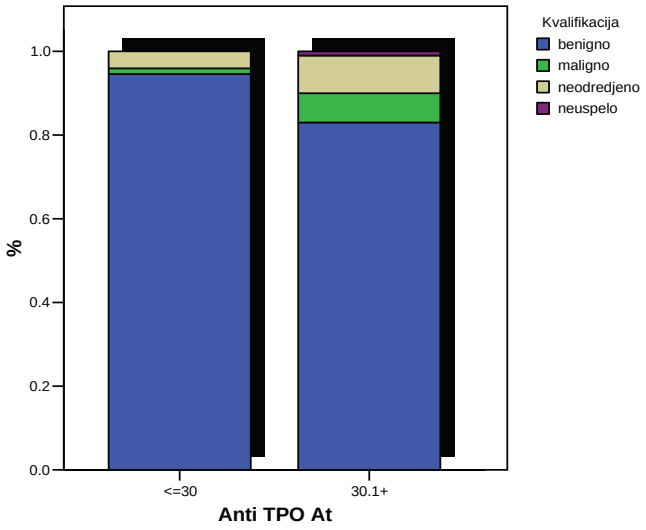
Ispitivana je vrednost anti TPO antitela u odnosu na dijagnostičke kategorije. Vrednosti anti TPO antitela podeljene su u dve grupe i to prva (do 30 IU/ml), koja obuhvata normalne vrednosti antitela i druga (preko 30 IU/ml), koja obuhvata povišene vrednosti antitela. U tabeli 1 prikazana je vrednost anti TPO antitela po dijagnostičkim kategorijama.

Tabela 1. Dijagnostičke kategorije zavisno od vrednosti anti TPO antitela

			Dijagnostičke kategorije				Ukupno
			Benigno	**maligno**	**neodređeno**	**neuspešno**	
Anti TPO At	*<=30*	N	140	2	6	0	148
		%	94.6%	1.4%	4.1%	.0%	100.0%
	30.1+	N	83	7	9	1	100
		%	83.0%	7.0%	9.0%	1.0%	100.0%
Ukupno		*N*	*223*	*9*	*15*	*1*	*248*
		%	*89.9%*	*3.6%*	*6.0%*	*.4%*	*100.0%*

Iz tabele se vidi da je među pacijentima sa povišenim vrednostima anti TPO antitela čak 7% pacijenata sa malignim citološkim nalazom, a u grupi pacijenata sa vrednostima anti TPO antitela u referentnim granicama svega 1.4% sa malignim citološkim nalazom. Rezultati su i grafički prikazani na grafikonu 2.

Grafikon 2. Vrednost anti TPO antitela zavisno od dijagnostičkih kategorija (kvalifikacija)



Diskusija

Hashimoto tireoiditis i Graves-ova bolest su dvije najčešće forme tireoidne autoimunosti, koje karakteriše limfocitna infiltracija i autoreaktivnost protiv tireoidnih autoantigena (3).

Tireoidna peroksidaza je glavni enzim uključen u tireoidnu hormogenezu, prvobitno identifikovan kao mikrozomalni antigen. Smatra se da su antitela na ovaj enzim glavni uzrok zapaljenja štitaste žlijezde. Ova antitela nalaze se u serumu kod pacijenata sa autoimunim bolestima štitaste žlezde. Prisutna su kod skoro svih pacijenata sa Hashimoto tireoiditisom, kod dvije trećine pacijenata sa postpartalnim tireoiditisom i skoro 75% pacijenata sa Graves-ovim hipertireoidizmom. Antiperoksidazna antitela produkuju limfociti koji u stanju zapaljenja infiltriraju žlezdu, a manjim delom limfociti porekla regionalnih limfnih žlezda i kostne srži. Antitela oštećuju ćelije štitaste žlezde indukcijom antitelo zavisne ćelijski posredovane citotoksičnosti.

Hashimoto tireoiditis vodi razvoju hipotireoidizma i porastu serumske koncentracije tireotropnog hormona (TSH), dok, nasuprot tome, Graves-ova bolest, takođe autoimunske prirode, u osnovi patogeneze ima porast TSH koncentracije preko stimulacije TSH receptora. Iz navedenog bi se moglo pretpostaviti da se veza između humoralne tireoidne autoimunosti i tireoidnog maligniteta ostvaruje preko TSH receptora.

Rezultati naše studije pokazuju da je od 248 pacijenata, 148 pacijenata (59,7%) imalo vrednosti anti TPO antitela u referentnim granicama (do 30 IU/ml), a 40,3% povišene vrednosti anti TPO antitela (preko 30 IU/ml). U grupi pacijenata sa povišenim vrednostima anti TPO antitela čak 7% (7/100) pacijenata je sa malignim citološkim nalazom, a u grupi pacijenata sa vrednostima anti TPO antitela u referentnim granicama nalazi se svega 1.4% (2/148) sa malignim citološkim nalazom.

Na osnovu navedenih rezultata može se uočiti značajno veća proporcija pacijenata sa malignim citološkim nalazom i povišenim vrednostima antiperoksidaznih antitela u odnosu na proporciju pacijenata sa malignim citološkim nalazom i normalnim vrednostima antiperoksidaznih antitela.

Brojne rađene studije ispitivale su povezanost autoimune tireoidne bolesti i diferentovanog tireoinog karcinoma.

Iako ne postoji slaganje svih, metaanaliza 10 studija Singh-a i saradnika pokazala je da kod pacijenata sa Hashimoto tireoiditisom postoji čak 2.77 puta veći rizik za pojavu tireoidnog maligniteta u poređenju sa kontrolnom grupom.

Boelaert i sar., u studiji rađenoj 2006. godine pokazali su signifikantno veću učestalost kod karcinoma sa pacijentima sa prisutnim antiperoksidaznim antitelima u poređenju sa pacijentima kod kojih nisu bila prisutna antitela.

Nasuprot gorenavedenim, studija Fiore i sar. pokazuje da među pacijentima sa antiperoksidaza pozitivnim i negativnim antitelima nema razlike u učestalosti tireoidnog maligniteta.

Studija Rebuffat i sar. pokazala je da anti TPO antitela ostvaruju ćelijski posredovanu citotoksičnost i antiproliferativnu aktivnost na ćelijama papilarnog tireoidnog karcinoma (4).

Na osnovu brojnih ispitivanja prihvaćeno je da fokalni hronični limfocitni tireoiditis (bilo nespecifični ili Hashimoto) vodi razvoju maligniteta, dok veza između za difuznog hroničnog limfocitnog tireoiditisa i tireoidnog maligniteta ostaje još uvek nerazjašnjena.

Zaključak

Definisanje veze između tireoidne autoimune bolesti i diferentovanog tireoidnog karcinoma pruža nova saznanja na polju imunoterapije tireoidnog karcinoma. Prosvetljavanje molekularnih mehanizama povezanosti tireoidne autoimune bolesti i razvoja tireoidnog karcinoma kod pacijenata sa nodoznom strumom pomaže otkrivanju novih terapeutskih strategija protiv tireoidnog karcinoma.

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Sanja Medenica,* Božo Trbojević,**

THE IMPORTANCE OF ANTI PEROXIDASE ANTIBODIES IN PATIENTS WITH NODULAR THYROID GOITER

Abstract: *Introduction*: Thyroid nodular goiter is clinically recognizable restricted structure changes of the thyroid gland. Numerous studies show the relationship between thyroid autoimmunity and differentiated thyroid cancer in patients with nodular thyroid goiter. One of the important clinical marker in defining thyroid autoimmunity are antibodies to thyroid peroxidase. Objective: The aim of this study was to analyze the relationship between anti peroxidase antibodies and thyroid malignancy in patients with nodular thyroid goiter.

Material and Methods: We retrospectively reviewed the 248 reports of thyroid FNA cytology of samples obtained by puncture of patients with nodular thyroid goiter, at Department of thyroid gland, Department of Endocrinology, Diabetes and Metabolic Diseases, Clinical Center of Serbia in the period from October 2007. by January 2010. year. We analyzed the relationship between findings of cytopathological diagnostic categories and serum concentrations of anti peroxidase antibodies. The data were statistically processed using the computer program SPSS 12.0 software package.

Results: Of total 248 patients, 148 patients (59.7%) had anti-TPO antibody values in a reference limits (30 IU / ml), and 40.3% elevated anti-TPO antibodies (over 30 IU / ml). In the group of patients with elevated values of anti-TPO antibodies 7% (7/100) of patients had malignant cytologic findings, and in the group of patients with anti-TPO antibody values in the normal range only 1.4% (2/148) of pateints had malignant cytologic findings.

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Conclusion: Defining the relationship between thyroid autoimmune disease and differentiated thyroid cancer, providing new insights in the field of immunotherapy of thyroid carcinoma. Enlightening the molecular mechanisms link autoimmune thyroid disease and thyroid cancer development in patients with thyroid nodule help find new therapeutic strategies against thyroid cancer.

Key words: thyroid nodule, anti peroxidase antibodies, thyroid autoimmunity, fine needle aspiration

Introduction:

Thyroid nodular goiter is clinically recognizable restricted structure changes of the thyroid gland. About 2-6% of the cases in this dIsease are discovered by palpation,19-35% are discovered by sensitive procedures like ultrasound and 8-65% by autopsy. Prevalence is linearly increasing for years by exposure to radiation and iodine deficiency.It can occur endemically in areas with iodine deficiency.Women fall sick more often than man (1).

Clinical forms of the dIsease include non-toxic nodular goiter,multinodular toxical goiter and toxical thyroid adenoma (Plummer`s desease).

Causes of the thyroid nodular dIsease can be benign (coloid nodules,Hashimoto`s thyroiditis,simple or hemorrhagic cysts,follicular adenoma,subacute thyroiditis) and malignant (primary follicular cell origin-papillary,follicular and anaplastic thyroid carcinoma,origin of C-cell thyroid-modular thyroid carcinoma,lymphoma and secondary metastatic carcinomas).

Diagnose of the dIsease is based on physical examination,laboratory testing, fine needle aspiration (FNA) and by visualization method (scintigraphy, ultrasound and ultrasound elastography,CT,MR and PET).

Fine needle aspiration (FNA) is crucial diagnostic procedure and first line of nodular thyroid goiter diagnostic tests. Qualification of diagnostic categories of thyroid FNA usually involves the following categories: `malignant` , `benign` , `unspecified` , `unsuccessful`. The term refers to the indefinite lesions which based on cytological appearance couldn`t be classified with certainty in one of the groups benign or malignant,and these include follicular,Hurthle cell and suspicious findings.Category was unsuccesfuly related to those samples which didn`t have enough material or the same material wasn`t adequate for diagnosis.

Therapy is usually surgical or radioiodine ablation, while recently in indicated cases for that is applying recombinant therapy with human thyrotropin,,percutaneous ethanol injection,laser thermal ablation and radiofrequency ablation.

Clinical significance of thyroid nodular diseas beside esthetic changes,such as neck thickening,local compressive syndromes and thyroid dysfunction is possibility

of developing malignancy in 5% cases. Annual incidence of thyroid carcinoma is 1-2 on 100.000 people,which makes 90% malignancy of the entire endocrine system,1%of all malignancies in humans and 0,5% of mortality due to malignancy. (1,2).

Numerous studies show the relationship between thyroid autoimmunity and differentiated thyroid cancer in patients with nodular thyroid goiter.

One of the important clinical marker in defining thyroid autoimmunity are antibodies to thyroid peroxidase.

Objective

The aim of this study was to analyze the relationship between anti peroxidase antibodies and thyroid malignancy in patients with nodular thyroid goiter.

Material and methods

The study was conducted at the Clinic for Endocrinology, Diabetes and Metabolic Diseases of the Clinical Center of Serbia in Belgrade. 248 reports of thyroid FNA cytology of samples obtained by puncture of patients with nodular thyroid goiter are retrospectively reviewed, at Department of thyroid gland, Clinic of Endocrinology, Diabetes and Metabolic Diseases, Clinical Center of Serbia in the period from October,2007 to January,2010.

The patients were ambulatory examined,medical history is taken and laboratory tests were performed (biochemistry,blood test and hormonal status) ECG and ultrasound were performed and some patients had scintigraphy of the thyroid gland.After that (FNA) fine needle aspiration is performed ,obtained preparations analysed in the Institute of Pathology in Clinical centre of Serbia in Belgrade.

Cytological examination of samples FNA are qualified by diagnostic category seed of thyroid FNA like:benign,malignant,unspecified and unsuccessful.

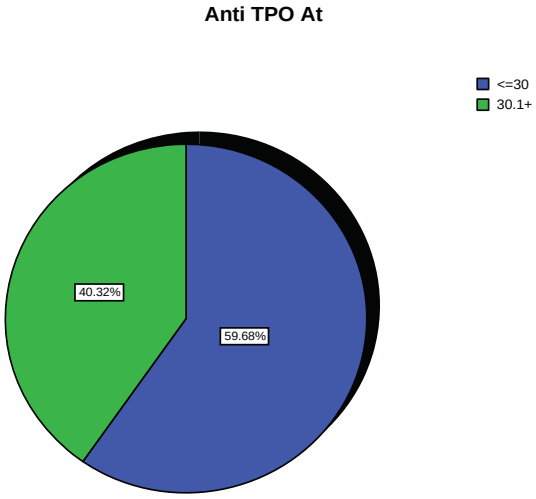
We analyzed the relationship between findings of cytopathological diagnostic categories and serum concentrations of anti peroxidase antibodies.

The data were statistically processed using the computer program SPSS 12.0 software package.

Results

Of total 248 patients, 148 patients (59.7%) had anti-TPO antibody values in a reference limits (30 IU / ml), and 40.3% elevated anti-TPO antibodies (over 30 IU / ml). The graphical results are shown in graph 1.

GRAPH 1: Distribution of antibodies TPO



The value of antibodies is examined in regard to diagnostic categories. Anti TPO antibodies values are divided in two groups and the first (to 30IU/ml) which includes normal values of antibodies and second (over 30IU/ml) which includes increased values of antibodies Table 1 shows the value of anti TPO antibodies by diagnostic categories.

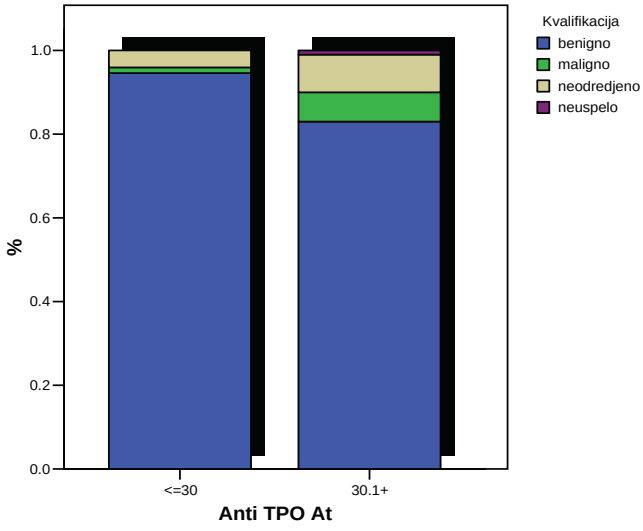
Table 1. Diagnostic categories depending on the value of anti TPO antibodies

			Diagnostic categories				Total
			benign	malignant	unspecified	unsuccessful	
Anti TPO Ab	<=30	N	140	2	6	0	148
		%	94.6%	1.4%	4.1%	.0%	100.0%
	30.1+	N	83	7	9	1	100
		%	83.0%	7.0%	9.0%	1.0%	100.0%
Total		N	223	9	15	1	248
		%	89.9%	3.6%	6.0%	.4%	100.0%

The table shows that between patients with increased values of anti TPO antibodies even 7% of patients had malignant cytological findings, but in group of patients

with anti-TPO antibody values in the normal range only 1.4% (2/148) of pateints had malignant cytologic findings. Results are graphically presented in the graph 2.

GRAPH 2. Anti TPO antibodies value depending on diagnostic categories (qualification)



Discussion

Hashimoto`s thyroiditis and Graves' disease are two most common forms of thyroid autoimmunities,which characterize lymphocytic infiltration and auto-reactivity against thyroid autoantigenes (3).

Thyroid peroxidase is the major enzyme involved in thyroid hormonal geneticks,primarily identified like microsomal antigen.It`s considered that these antibodies on this enzyme are the major cause of the thyroid gland inflammation.These antibodies are found in serum of patients with autoimmune diseases of thyroid gland. They are present in nearly all patients with Hashimoto`s thyroiditis,in two-thirds of patients with postpartum thyroiditis and almost 75% of patients with Graves` hyperthyroidism.Anti peroxidase antibodies are produced by lymphocytes that in the state of inflammation infiltrate the gland,to a lesser extent lymphocytes that have origin of regional lymph glands and bone marrow.Antibodies damage the cells of the thyroid gland by induction antibody dependent cell mediated citotoxicity.

Hashimoto`s thyroiditis leads to development of hypothyroidism and to serum concentration and increase of thyrotropin hormone (TSH),while on the contrary of that Graves` desease,also with autoimmune nature,anderlying the pathogenesis we have the growth of TSH concentration through TSH receptors stimulation.From referred

it could be assumed that the connection between humoral thyroid autoimmunity and thyroid malignity is made through TSH receptors.

The results of our study show that from 248 patients,148 of patients (59,7%) had anti TPO antibody values in the normal limits (to 30IU/ml),but 40,3% had the increased values of anti TPO antibodies (over 30IU/ml).In the group of patients with increased values of anti TPO antibodies even 7% (7/100) of patients is with malignant cytological findings,and in group of patients with anti TPO antibody values in normal limits is only 1.4% (2/148) with malignant cytological findings.

Based on the results it may be note significantly higher proportion of patients with malignant cytological findings and with increased values of anti peroxidase antibodies. Numerous studies that have been done examined the connection between autoimmune thyroid disease and differentiated thyroid carcinoma.

Even if there isn`t an agreement of all,target analysis of 10 studies by Singh and collaborators has shown that with patients who have Hashimoto`s thyroiditis have even 2.77 times higher risc for appearance of thyroid malignancy compared with the control group. Boelaert and collaborators in study done in 2006 have shown significantly higher frequency of cancer in patients with the present anti peroxidase antibodies in comparison with patients where were present antibodies.

Contrary to already specified,the study of Fiore and collaborators shows that between the patients with anti peroxidase positive and negative antibodies there is no difference in frequency of thyroid malignancy. The study Rebuffat with collaborators has shown that anti TPO antibodies achieve cell-mediated cytotoxicity and antiproliferative activity in papillary thyroid carcinoma cells (4).

Based on numerous studies it`s accepted that focal chronic lymphocytic thyroiditis (whether it`s nonspecific or Hashimoto`s) leads to the development of malignancy,while the connection between diffuse chronic thyroiditis and thyroid malignancy still remains unclarified.

Conclusion

Defining the relationship between thyroid autoimmune disease and differentiated thyroid cancer, providing new insights in the field of immunotherapy of thyroid carcinoma. Enlightening the molecular mechanisms link autoimmune thyroid disease and thyroid cancer development in patients with thyroid nodule help find new therapeutic strategies against thyroid cancer.

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