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## POVEĆANJE BROJA LIMFOCITA U OSOBA SA B-HRONIČNOM LIMFOMOM NISKOG STEPENA MALIGNOSTI PA U RAZLIKOVANJE LIMFOMA NISKOG STEPENA MALIGNOSTI OD B-HRONIČNE LIMFOCITNE LEUKEMIJE

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## INCREASING OF LYMPHOCYTES NUMBER AND CHARACTERISTIC IMMUNOPHENOTYPE IN DIFFERENTIATION OF LOW GRADE LYMPHOMAS FROM B-CHRONIC LYMPHOCYTIC LEUKEMIA

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### SAŽETAK

Limfomi malih limfocita su grupa limfoma niskog stepena malignosti (low grade). Ovi limfomi se morfološki ne razlikuju od B-hronične limfocitne leukemije, ali imaju sposobnost da se transformišu u B-leukeiju. Limfomi niskog stepena rizika imaju sporu progresiju bolesti, bez simptoma dugi niz godina. Kako je povećanje broja limfocita znak prelaska u leukemijsku fazu, mi smo pratili povećanje broja limfocita i određivali imunofenotip kod ovih bolesnika. Statistički značajno povećanje broja limfocita od  $2.9$  do  $23.4 \times 10^9/l$  tokom nekoliko godina praćenja zajedno sa uvećanjem jetre, slezine, uvećanjem limfnih čvorova je korišćeno kao pokazatelj transformacije limfoma u B-hroničnu leukemiju. Za razliku od većine B-CLL pacijenata koji su imali HLA-DR, CD5, CD19, CD20, CD22, CD23, CD25, CD38 pozitivne markere a CD3, CD10 and SmIg negativne, mi smo imali i slučajeve sa drugim imunofenotipskim karakteristikama; viska ekspresija za HLA-DR, CD19, CD20, CD22 CD23 tj pozitivni markeri a CD3, CD5, CD10, CD14, CD25 CD38 negativni markeri. Ovi klinički slučajevi još jednom pokazuju sklonost non-Hodgkin'skih limfoma da se transformišu u B-CLL pri čemu ne mora uvek da dođe do bitne izmene kliničkog toka bolesti. To svedoči o njihovoj međusobnoj bliskoj povezanosti pri čemu mogu da imaju različite imunofenotipske karakteristike.

**Ključne reči:** imunofenotip, limfom, HLL

### ABSTRACT

Small lymphocyte lymphoma is form of low grade lymphoma patients. This group of lymphomas was morphologically indistinguishable from chronic lymphocytic leukemia (CLL) and these patients have possibility to progress into B-CLL. The indolent lymphomas was low grade NHL group that have a long history of disease usually without symptoms over many. Since increase of peripheral lymphocyte number is characteristic of B-CLL, in this study we monitored immunophenotype in patients with transformation of small lymphocytic lymphoma to B-CLL. Significant increase ( $p < 0.05$ ) of mean values of absolute lymphocyte number from  $2.9 \times 10^9/l$  to  $23.4 \times 10^9/l$  after several years of follow-up, involvement of bone marrow, liver, spleen and rapidly enlarging asymmetric lymph nodes were used as indicator of disease transformation. Contrary to most patients with immunophenotype characteristic for B cell type lymphoma: HLA-DR, CD5, CD19, CD20, CD22, CD23, CD25, CD38 positivity and CD3, CD10 and SmIg negativity, in this report we also present a case of small lymphocytic lymphoma with HLA-DR, CD19, CD20, CD22 CD23 positive and CD3, CD5, CD10, CD14, CD25 CD38 negative antigens. Coexpression of CD5- antigen that originates from postgerminal center, CD10- from marginal zone and D23+ representing activation antigen in these patients we conclude that these antigens are not characteristic of mantle cell, follicular, and other form in low grade lymphoma group. Heterogeneity of immunophenotypes suggest that different type of low grade lymphoma underwent transformation into B-CLL, with similarity in their clinical course.

**Key words:** immunophenotype, lymphoma, CLL



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## KONCENTRACIJA TIROKSINA I TRIJODTIRONINA KOD OSOBA SA HIPERTIREOZOM

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## THYROXINE AND TRIIODOTHYRONINE IN PATIENTS WITH HYPERTHYROIDISM

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### SAŽETAK

U štitastoj žlezdi se u normalnim uslovima sintetiše ukupna količina tiroksina (T4) i samo 20% trijodtironina (T3). Balans između koncentracije tiroksina i trijodtironina u plazmi ostvaruje se kontrolom sekrecije ovih hormona iz štitaste žlezde i nivoa tkivne dejodinacije T4 i pretvaranja u T3. Cilj ovog rada bio je da se ispita koliko je povećanje slobodnih koncentracija tiroidnih hormona, slobodnog tiroksina (FT4) i slobodnog trijodtironina (FT3) kod osoba sa povećanom funkcijom štitaste žlezde. Mi smo analizirali serumske koncentracije tiroidnih i tireostimulirajućeg hormona kod 105 pacijenata sa hipertireozom. Svi pacijenti su imali sniženo ili suprimovano lučenje TSH (koncentracije manje od  $0.25 mIU/L$ ). Kod 67 pacijenata (63.8%) koncentracija oba tiroidna hormona bila je povećana, kod 24 pacijenata (22.9%) bila je povećana koncentracija samo FT4, a kod 14 pacijenata (13.3%) samo koncentracija FT3. Iako je u serumu obolelih od hipertireoze uvek mnogo veća koncentracija FT4 nego FT3, njihovo relativno povećanje (izraženo kao odnos između detektovane i gornje granične vrednosti) je ispitivano. U grupi pacijenata sa hipertireozom kod kojih je povećana koncentracija FT4 i FT3, samo 14 pacijenata (20.9%) imalo je veće relativno povećanje FT3 nego FT4. S obzirom na to da terapija može uticati na nivo ekstratireoidne dejodinacije tiroksina, ispitivali smo relativno povećanje koncentracije FT4 i FT3 kod 30 pacijenata kod kojih je po prvi put dijagnostifikovana hipertireoza. Pokazano je da je kod samo 6 pacijenata (16.7%) bilo veće relativno povećanje FT3 nego FT4. Naši rezultati su pokazali da je kod pacijenata sa hipertireozom veće relativno povećanje koncentracije FT4 nego FT3, što bi moglo da ima zaštitni efekat kod osoba sa povećanom funkcijom štitaste žlezde.

**Ključne reči:** tiroksin, trijodtironin, hipertireoza

### ABSTRACT

All thyroxine (T4) comes from the thyroid gland, but under usual circumstances, only about 20% of triiodothyronine (T3). The balance between plasma levels the T4 and the T3 is maintained by the level of thyroid gland secretion and the tissue rates of T4 and T3 deiodination. The aim of this study was to estimate the increase of free T4 (FT4) and free T3 (FT3) in patients with hyperthyroidism. We analyzed the sera concentrations of thyroid hormones and thyrotropin (TSH) in 105 patients with hyperthyroidism. All patients had hyperthyroidism with suppressed TSH level (less than  $0.25 mIU/l$ ). In 67 patients (63.8%) the levels of both free thyroid hormones were increased, 24 patients (22.9%) had only FT4 and 14 patients (13.3%) had only FT3 increase. Although there is always much more T4 than T3 in serum of hyperthyroid patients, their relative increase (expressed by ratio to upper limit of normal range T4 or T3) was investigated. In the group of hyperthyroid patients with both thyroid hormones elevated, only 14 patients (20.9%) had the greater increase of FT3 than FT4. Because the therapy might influence the level of extrathyroidal T4 deiodination we analysed the relative increase of free T4 and T3 in the subgroup of 30 new diagnosed patients. It was shown that only 6 patients (16.7%) had higher relative increase of FT3 than FT4. Our results show the higher relative increase of FT4 than FT3 indicating that this might protect the organism from excess of FT3 in hyperthyroid patients.

**Key words:** thyroxine, triiodothyronine, hyperthyroidism





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## UPOREDNE ANALIZE PATO-HISTOLOŠKOG I ULTRAZVUČNOG NALAZA KOD TUMORA DOJKE

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## COMPARATIVE ANALYSES OF PATHO-HISTOLOGY FINDINGS WITH ULTRASOUND ANALYSES IN BREAST CANCER PATIENTS

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### SAŽETAK:

Različite metode se koriste sa ciljem da se tumori dojke što pre otkriju, postavi pravilna dijagnoza i otpočne adekvatno liječenje. Međutim i pored toga, tumori dojke predstavljaju i dalje vodeći uzrok smrti kod nas i u svetu. Zbog toga se postavlja pitanje kako što pre tačno dijagnostikovati tumore dojke u opštoj bolnici i uputiti ih blagovremeno u odgovarajuću ustanovu. U ovom radu je ispitivano u kom procentu se u opštoj bolnici može postaviti rana i odgovarajuća dijagnoza tumora dojke. Ispitivanje je bazirano na uporednoj analizi palpatornog i ultrazvučnog ispitivanja, sa pato-histološkim nalazom biopsijskog materijala. U ovom ispitivanju obuhvaćeno je 59 žena sa tumorima dojke, starosti od 16 do 69 godina. Najveća zastupljenost tumora dojke u ispitivanoj grupi bila u starosnoj dobi preko 61 godine, mada je veliki procenat tumora bio u starosnoj grupi od 21 do 50 godina. Benigni tumori -fibroadenom su bili najčešće zastupljeni (40.68%), dok su maligni tumori -carcinoma ductale iznosili 13.56%. U najvećem broju slučajeva je pokazano da se rezultati pato-histološkog nalaza podudaraju sa ultrazvučnim ispitivanjima kod benignih tumora što iznosi 86.05%. Kod malignih tumora taj procenat podudarnosti iznosi još više, 93.33%. Rezultati pokazuju visoku podudarnost dobijenih nalaza u ovoj grupi ispitanika. Ipak, postoje razlike u veličini tumorskog tkiva opisanog na osnovu ex tempore analiza. U uporednim nalazima mamografskih ispitivanja i ultrazvučnog ispitivanja se poklapaju u najvećem broju slučajeva, pri čemu su uvek analize mamografije pokazivale da se radi o većoj rasprostranjenosti tumora. I pored utvrdjene statistički značajne korelacije postoje problemi u dijagnostikovanju i razlikovanju malignih od benignih tumora dojke, pa se sugerise primena savremenih metoda baziranih na molekularnom nivou, određivanje hormonskih receptora, kako bi se okarakterisali pojedini histološki oblici tumora dojke, koje zahtevaju savremeno hormon zavisno liječenje.

**Cljučne reči:** tumori dojke, pato-histološki nalaz, ultrazvučno ispitivanje, rana dijagnoza

### ABSTRACT

Different methods were used in early diagnosis of breast cancer, with aims to appropriate diagnosis confirmation and early therapy of applied. However, breast cancer is really one from tumor with highest mortality in this country as well as in the word. Based on this, combination of established methods was applied with aims to confirm a proper diagnosis in general hospital. This research estimated also in what percentage early diagnosis is possible to make in general hospital for breast cancer patients. Research included comparative analyses of palpatory findings with ultrasound analyses and pathohistology analyses obtained after extempore biopsy, in 59 women with breast cancer aged from 16 to 69. The highest incidence was obtained in women in age over 61, although high rate of breast cancer was found in patients aged from 21 to 50 years. Benign tumors (fibroadenoma) were founded with 40.68% of all patients, while malignant carcinoma ductale was expressed in 13.55%. Comparative analyses between pathohistology findings and ultrasound findings indicated that statistical significance exists. For fibroadenoma this correlation was found in 86.05%, while in malignant lesions this percentage was highest (93.33). Results indicated high correlation between our analyses ( $p < 0.05$ ). However, difference in tumor size described by ultrasound and analyses described after extempore biopsy was found. Simultaneous analyses between mammography and ultrasound correlates in high rate. Mammography result showed some times enlargements of tumors in comparison to ultrasound analyses in patients, since results dependent on patient age and breast consistency. We concluded that apart of two or more analyses applied for early diagnosis in general hospital and obtained statistical significance in diagnosis, new techniques based on molecular level (hormone receptor status) for subtype of breast cancer diagnosis confirmation, must be used for hormone appropriate therapy application.

**Key words:** Breast cancer, pathohistology, ultrasound, early diagnosis



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## MAKROFAZI KOSTNE SRŽI KAO ANTIGEN-PREZENTUJUĆE ČELIJE

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## ANTIGEN-PRESENTING ABILITY OF BONE MARROW-DERIVED MACROPHAGES

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### SAŽETAK

U ovom radu je ispitivana sposobnost makrofaga izolovanih iz kostne srži da prezentuju antigen specifičnim T limfocitima. Pošto su prethodno uklonjene dendritične čelije koje su privremeno atherirale za podlogu, atherentne čelije kostne srži su izolovane i obojene po metodi May-Grünvald Giemsa. Pokazano je da više od 95% atherentnih čelija kostne srži ima morfologiju makrofaga. Izolovani makrofazi su pretrčani mitomicinom C kako bi se ispitala njihova sposobnost prezentovanja antigena u testu proliferacije T limfocita. Makrofazi su inkubirani sa T limfocitima izolovanim iz limfnih čvorova C57Bl/6 miševa koji su prethodno imunizovani ovčjim eritrocitima (OE) u prisustvu antigena (OE) tokom 96 sati. Proliferacija T limfocita u uslovima in vitro merena je ugradnjom radioaktivnog 3H-timidina u novosintetisanu DNK. Pokazano je da makrofazi izolovani iz kostne srži mogu da pomognu antigen-specifičnu proliferaciju T limfocita u uslovima in vitro. Sa povećanjem broja makrofaga izvestan inhibicioni efekat na proliferaciju T limfocita je pokazan.

**Cljučne reči:** makrofazi, kostna srž, prezentovanje antigena, ovčji eritrociti, T limfociti

### ABSTRACT

In this study the antigen-presenting ability of bone marrow-derived macrophages was analyzed. Macrophage enrichment was achieved by a simple one-step adherence procedure to eliminate the transiently-adherent dendritic cells. For morphology analysis bone marrow-derived adherent cells were stained with May-Grünvald Giemsa and it was shown that more than 95% of cells possess the morphology of macrophages. The antigen-presenting ability of mytomycin C-pretreated macrophages was tested in T cell proliferation assay. The macrophages were cocultured with T lymphocytes isolated from lymph nodes of C57Bl/6 mice immunized with sheep red blood cells (SRBC) in the presence of antigen (SRBC) for 96 hours. T cell proliferation was measured by 3H-thymidine incorporation in new synthesized DNA. It was demonstrated that bone marrow-derived macrophages supported antigen specific proliferation of T lymphocytes in vitro. By increasing the number of macrophages cocultured with T cells, certain inhibitory effect on T cell proliferation was obtained.

**Keywords:** macrophages, bone marrow, antigen-presenting, sheep red blood cells, T lymphocytes