KARAKTERISTIKE BOLESNIKA SA SEKUNDARNOM ERITROCITOZOM U ODNOSU NA BOLESNIKE SA POLICITEMIJOM VEROM

ORIGINALNI RAD

ORIGINAL ARTICLE

CHARACTERISTICS OF PATIENTS WITH SECONDARY ERYTHROCYTOSIS IN RELATION TO PATIENTS WITH POLYCYTHEMIA VERA

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SAŽETAK:

Uvod: Eritrocitoza predstavlja povišene vrednosti hemoglobina i hematokrita iznad opsega normalnih vrednosti. Primarnu eritrocitozu - policitemiju veru, karakteriše poremećaj na nivou multipotentne matične ćelije hematopoeze koštane srži koja dovodi do povećane produkcije eritrocita. Sa druge strane, sekundarna eritrocitoza (SE) je posledica stimulacije koštane srži spoljašnjim faktorom.

Cilj: Cilj našeg istraživanja bio je da se utvrde parametri koji su značajni u diferencijalnoj dijagnozi SE u odnosu na primarnu eritrocitozu – policitemiju veru (PV).

Materijal i metode: Ovo je retrospektivno istraživanje koje je obuhvatilo 108 bolesnika sa SE-om i 111 bolesnika sa PV-om, koji su dijagnostikovani i lečeni na Klinici za hematologiju, Univerzitetskog kliničkog centra Srbije (UKCS), u periodu: decembar 2005 – novembar 2018. Iz medicinske dokumentacije su prikupljeni podaci o demografskim i laboratorijskim parametrima, veličini jetre i slezine, celokupnoj masi eritrocita, prisustvu prethodnika hematopoeze (spontani rast *BFU-E* kolonija) i vrednosti eritropoetina (EPO) u serumu.

Rezultati: Bolesnici sa SE-om bili su mlađeg uzrasta, uz češću pojavu kod muškaraca, sa značajno višim vrednostima serumskog EPO-a, u odnosu na bolesnike sa PV-om. Bolesnici sa PV-om su imali značajno više vrednosti broja leukocita, broja trombocita, veličine slezine i vrednosti laktatne dehidrogenaze (LDH) kao i više vrednosti prethodnika eritrocitopoeze (BFU-E), u odnosu na bolesnike sa SE-om. Celokupna masa eritrocita nije pokazala diferencijalno dijagnostički značaj.

Zaključak: Normalna veličina slezine, normalne vrednosti broja leukocita, trombocita, i serumske LDH i povišena vrednost EPO-a, kod pacijenata, govore u prilog sekundarne eritrocitoze, dok nalaz splenomegalije, leukocitoze, trombocitoze, povišene vrednosti serumske LDH, nalaz snižene vrednosti EPO-a i prisutne spontane *BFU-E* kolonije, govore u prilog policitemije vere.

Ključne reči: sekundarna eritrocitoza, policitemija vera, diferencijalna dijagnoza

ABSTRACT:

Introduction: Erythrocytosis represents elevated hemoglobin and hematocrit levels above the range of normal values. Primary erythrocytosis - polycythemia vera, is characterized by increased erythrocyte production, due to a disorder at the level of the multipotent stem cell in the bone marrow. On the other hand, secondary erythrocytosis (SE) is the result of bone marrow stimulation by an external factor.

Aim: The aim of our study was to determine parameters which are significant in differentiating SE from primary erythrocytosis - polycythemia vera (PV).

Materials and methods: This is a retrospective study involving 108 patients with SE and 111 patients with PV, who were diagnosed and treated at the Clinic of Hematology of the Clinical Center of Serbia (CCS), in the period: December 2005 – November 2018. From the patient records, the following data were extracted: demographic characteristics, laboratory parameters, spleen size, total red cell mass, serum erythropoietin (EPO) level, and spontaneous growth of the BFU-E colony.

Results: Patients with SE were younger, with a predominance of the male gender and with significantly higher serum EPO values than patients with PV. Patients with PV had significantly higher values of BFU-E, leukocyte and platelet count, spleen size, and LDH level than patients with SE. Total red cell mass analysis did not show a differential diagnostic significance.

Conclusion: Findings of normal spleen size, normal leukocyte and platelet count, normal serum LDH level, and elevated EPO, in patients, refer to the diagnosis of secondary erythrocytosis, while the findings of splenomegaly, leukocytosis, thrombocytosis, elevated serum LDH level, decreased EPO, and the presence of spontaneous BFU-E colony speak in favor of the diagnosis of polycythemia vera.

Key words: secondary erythrocytosis, polycythemia vera, differential diagnosis

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UVOD

Eritrocitoza predstavlja povišene vrednosti hemoglobina i hematokrita iznad opsega normalnih referentnih vrednosti. Regulacija eritropoeze je kompleksan proces koji uključuje osetljivost koštane srži na kiseonik i eritropoetin (EPO). Pokazatelji eritrocitoze su broj eritrocita u perifernoj krvi, vrednost hemoglobina (Hb) i zapreminski odnos – hematokrit (Hct).

Apsolutna eritrocitoza je definisana kada je celokupna masa eritrocita veća od 125% u odnosu na referentne vrednosti predviđene za pol i telesnu masu, analizirano visoko specijalizovanim nuklearnim testom [1]. Analizom celokupne mase eritrocita može se diferencirati apsolutna od relativne eritrocitoze, koju karakteriše normalna masa eritrocita ali smanjen volumen plazme [2]. Eritrocitoza se deli na primarnu i sekundarnu. Primarnu eritrocitozu karakteriše poremećaj na nivou multipotentne matične ćelije hematopoeze koštane srži koja dovodi do povećane produkcije eritrocita [3]. Tada dolazi do spontanog rasta prethodnika eritropoeze u odsustvu eritropoetina (EPO) [3]. Primarna eritrocitoza, poznata kao policitemija vera – PV, jeste posledica pojave stečene mutacije u JAK2 genu [4,5]. JAK2-V617F mutacija je opisana kod 95% bolesnika, dok je JAK2 *exon* 12 mutacija, prisutna kod 3% bolesnika sa PV-om [4,5]. Ove mutacije dovode do stvaranja konstitutivno aktivne tirozin kinaze, koja aktivira eritropoetinski receptor i JAK-STAT signalni put, koji povećava produkciju eritrocita i često prateću produkciju leukocita i trombocita.

Sa druge strane, sekundarna eritrocitoza (SE) nastaje kao posledica stimulacije koštane srži spoljašnjim faktorom. Najčešća stanja koja dovode do sekundarne eritrocitoze su: hipoksemija usled pušenja, respiratornih ili kardiovaskularnih bolesti, kao i policistične bolesti bubrega ili ektopična sekrecija eritropoetina. Izražena gojaznost se navodi kao faktor rizika za sekundarnu eritrocitozu, u slučaju razvoja *spleep apnea*-e tj. hipoksemije tokom spavanja. Kada nijedan uzrok ne može biti definisan, takvo stanje se naziva idiopatskom eritrocitozom.

Cilj našeg istraživanja bio je da se utvrde parametri koji su značajni u diferencijaciji sekundarne eritrocitoze (SE) u odnosu na primarnu eritrocitozu – policitemiju veru (PV).

MATERIJAL I METODE

Ovo je retrospektivno istraživanje koje je obuhvatilo 108 bolesnika sa dijagnozom sekundarne eritrocitoze (SE) i 111 bolesnika sa dijagnozom policitemije vere (PV), koji su dijagnostikovani, praćeni i lečeni na Klinici za hematologiju, Univerzitetskog kliničkog centra Srbije, u periodu od decembra 2005. do novembra 2018.

INTRODUCTION

Erythrocytosis represents elevated hemoglobin and hematocrit levels above the range of normal values. The regulation of erythropoiesis is a complex process which includes bone marrow sensitivity to oxygen and erythropoietin (EPO). The indicators of erythrocytosis are the following: the number of erythrocytes in peripheral blood, the hemoglobin (Hb) level, and the volume ratio – hematocrit (Hct).

Absolute erythrocytosis is defined as the state where the total red blood cell mass is above 125%, as compared to the reference range defined for sex and body mass, as analyzed by a highly specialized nuclear test [1]. Analysis of the total red blood cell mass enables differentiation between absolute and relative erythrocytosis, which is characterized by normal red blood cell mass, but a decreased plasma volume [2]. Erythrocytosis can be primary and secondary. Primary erythrocytosis is characterized by increased erythrocyte production, due to a disorder at the level of the multipotent stem cell in the bone marrow [3]. This is when spontaneous growth of the erythropoiesis precursor occurs, in the absence of erythropoietin (EPO) [3]. Primary erythrocytosis, also known as polycythemia vera – PV, is the result of the occurrence of an acquired mutation on the JAK2 gene [4,5]. The JAK2-V617F mutation is described in 95% of patients, while the JAK2 exon 12 mutation is present in 3% of the patients with PV [4,5]. These mutations lead to the production of constitutively active tyrosine kinase, which activates the erythropoietin receptor and the JAK-STAT signaling pathway, which, in turn, increases the production of erythrocytes, and often the accompanying production of leucocytes and thrombocytes.

On the other hand, secondary erythrocytosis (SE) happens as the result of the stimulation of bone marrow by an external factor. The most common states leading to secondary erythrocytosis are the following: hypoxemia caused by smoking, respiratory or cardiovascular diseases, as well as polycystic kidney disease or ectopic production of erythropoietin. Marked obesity is stated as a risk factor for secondary erythrocytosis, in case of the development of sleep apnea, i.e., sleep hypoxemia. When no cause can be defined, such a state is called idiopathic erythrocytosis.

The goal of our research was to determine the parameters relevant for the differentiation of secondary erythrocytosis (SE) from primary erythrocytosis – polycythemia vera (PV).

MATERIALS AND METHODS

This is a retrospective study involving 108 patients with the diagnosis of secondary erythrocytosis (SE) and 111 patients with the diagnosis of polycythemia vera (PV),

godine. Kod bolesnika sa PV-om, dijagnoza je postavljena prema kriterijumima Svetske zdravstvene organizacije (SZO) iz 2016. godine [7], (Tabela 1).

Iz medicinske dokumentacije su prikupljeni sledeći podaci: 1) demografske karakteristike bolesnika; 2) parametri kompletne krvne slike i leukocitarne formule; 3) laboratorijske analize laktat dehidrogenaze; 4) veličina slezine i jetre (određene na osnovu ultrazvuka – UZ abdomena); 5) volumen eritrocita; 6) prisustvo prethodnika hematopoeze u koštanoj srži ili perifernoj krvi; 6) nivo eritropoetina (EPO) u serumu; 7) status JAK2V617F mutacije.

Medijana praćenja za bolesnike sa SE-om je bila 32 meseca (raspon: 1 – 151), dok je kod bolesnika sa PV-om bila 17 meseci (raspon: 1 – 62).

U statističkoj obradi podataka korišćene su metode deskriptivne statistike, zatim, u zavisnosti od distribucije podataka, za procenu značajanosti razlike između analiziranih podataka, korišćene su parametrijske (Studentov T test i analiza varijanse – ANOVA) i neparametrijske metode (Hi-kvadrat test, Man Vitnijev test i Kraskal Volisov test). Univarijantnim i multivarijantnim *Cox*-ovim regresionim modelom indentifikovani su prediktori sekundarne eritorcitoze u odnosu na policitemiju veru.

REZULTATI

Bolesnici sa sekundarnom eritrocitozom (SE)

Kod analiziranih 108 bolesnika sa SE-om bilo je 89 osoba muškog (82,4%) i 19 osoba ženskog pola (17,6%)

who were diagnosed, monitored and treated at the Clinic of Hematology of the Clinical Center of Serbia, in the period between December 2005 and November 2018. In patients with PV, diagnosis was established on the basis of the criteria of the World Health Organization (WHO) from 2016 [7], (Table 1).

The following data was collected from medical records: 1) patient demographic characteristics; 2) complete blood count and white blood cell count parameters; 3) lactate dehydrogenase laboratory analyses; 4) spleen and liver size (determined with abdominal ultrasound – US); 5) erythrocyte volume; 6) presence of the erythropoiesis precursor in bone marrow or peripheral blood; 6) serum level of erythropoietin (EPO); 7) JAK2V617F mutation status.

The median follow-up for patients with SE was 32 months (range: 1 – 151), while in patients with PV it was 17 months (range: 1 – 62).

In statistical data processing, descriptive statistics methods were employed, and, depending on data distribution, parametric (Student's t-test and analysis of variance – ANOVA) and nonparametric (the chi-squared test, the Mann-Whiteny test, the Kruskal-Wallis test) methods were employed for assessing the significance of the difference among the analyzed data. The univariate and multivariate Cox regression models were used to identify the predictors of secondary erythrocytosis in relation to polycythemia vera.

Tabela 1. SZO kriterijumi (2016) za dijagnozu PV*

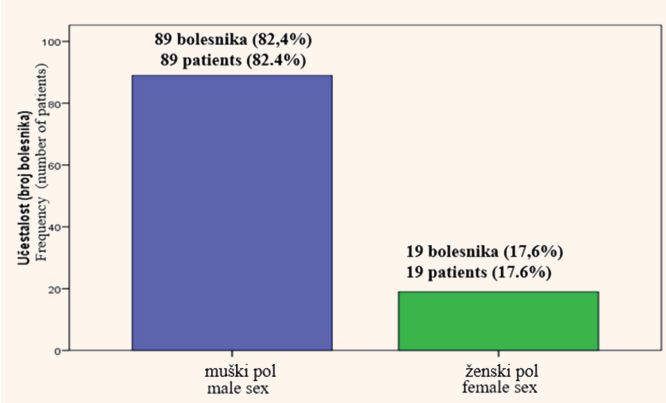
MAJOR KRITERIJUMI	*MINOR* KRITERIJUMI
1) Vrednost hemoglobina >165g/L kod muškaraca; vrednost hemoglobina > 160g/L kod žena ili vrednost hematokrita > 49% kod muškaraca ili vrednost hematokrita > 48% kod žena ili povećana masa eritrocita (više od 25% od prosečne normalne vrednosti)	**1)** Snižena serumska vrednost eritropoetina
2) Patohistološki nalaz bioptata koštane srži pokazuje hipercelularnost u odnosu na očekivanu za uzrast, sa trilinijskom proliferacijom (panmijelozom) uključujući eritroidnu, granulocitnu i megakariocitnu proliferaciju sa pleomorfnim, zrelim megakariocitima (razlike u veličini)	
3) Prisustvo *JAK2* ili *JAK2 exon* 12 mutacije	

Dijagnoza PV: prisustvo sva tri major kriterijuma ili prva dva major i minor kriterijuma
* Preuzeto iz: Barbui T, Thiele J, Gisslinger H, et al. Blood Cancer J. 2018;8(2):15.

Table 1. WHO criteria (2016) for PV diagnosis*

MAJOR CRITERIA	MINOR CRITERIA
1) Hemoglobin value > 165g / L in men; hemoglobin value > 160g / L in women or hematocrit value > 49% in men or hematocrit value > 48% in women or increased erythrocyte mass (more than 25% of the average normal value)	**1)** Decreased erythropoietin value
2) Pathohistological finding of bone marrow biopsy shows hypercellularity, as expected for the given age, with trilinear proliferation (panmyelosis), including erythroid, granulocyte, and megakaryocyte proliferation with pleomorphic, mature megakaryocytes (differences in size)	
3) The presence of the JAK2 or JAK2 exon 12 mutation	

PV diagnosis: presence of all three major criteria or first two major and minor criteria
* Taken from: Barbui T, Thiele J, Gisslinger H, et al. Blood Cancer J. 2018;8(2):15.



Grafikon 1. Raspodela bolesnika sa sekundarnom eritrocitozom prema polu (muški/ženski)

Figure 1. Distribution of patients with secondary erythrocytosis by sex (male/female)

(M:Ž = 4,7:1), (Grafikon 1). U celoj grupi ispitivanih bolesnika, medijana uzrasta bolesnika, u momentu postavljanja dijagnoze, bila je 55 godina (raspon: 19 – 88).

Medijana promera jetre je iznosila 135 mm (raspon: 130 – 174), dok je medijana promera slezine iznosila 100 mm (raspon: 90 – 150). Celokupna masa eritrocita je iznosila 136% (raspon: 105 – 269), (Grafikon 3). Povišena celokupna masa eritrocita od preko 125%, koja je karakteristična za policitemiju veru, bila je prisutna kod 90 bolesnika (83%). Medijana saturacije kiseonikom (SO2) je iznosila 96% (raspon: 89,4 – 99). Sniženu SO2 (< 92%) je imalo 5 bolesnika. Srednja vrednost EPO-a u serumu je iznosila 9,3 IU/mL (raspon: 3,3 – 32,4). Od 108 bolesnika sa SE-om, analiza JAK2V617F mutacije je urađena kod 42 bolesnika (38,8%), većinom tokom njihovog praćenja, i kod svih analiziranih bolesnika je bila negativna.

Bolesnici sa policitemijom verom (PV)

Ispitivanjima je obuhvaćeno ukupno 111 bolesnika sa policitemijom verom (PV), među kojima je bilo 65 osoba ženskog pola (58,5%) i 46 osoba muškog pola (41,5%) (Ž:M = 1,4:1), (Grafikon 2). U celoj grupi ispitivanih bolesnika, medijana uzrasta bolesnika u momentu postavljanje dijagnoze bila je 62 godine (raspon 24 – 85). Medijana promera jetre je iznosila 135 mm (raspon 120 – 180), dok je medijana promera slezine iznosila 121 mm (raspon: 90 – 255). Hepatomegaliju je imalo 15 bolesnika (13,3%), dok je splenomegaliju imalo 52 bolesnika (42%).

Srednja vrednost EPO-a u serumu je bila snižena i iznosila je 2 mU/mL (raspon: 0,06 – 31,8). Od 101 ispitivanog bolesnika, kod 95% je detektovano prisustvo JAK2V617F mutacije, dok 5% bolesnika nije imalo ovu mutaciju. Celokupna masa eritrocita ukazivala je na postojanje apsolutne eritrocitoze od 137% (raspon: 102 – 258), (Grafikon 3). Prisustvo apsolutne

RESULTS

Patients with secondary erythrocytosis (SE)

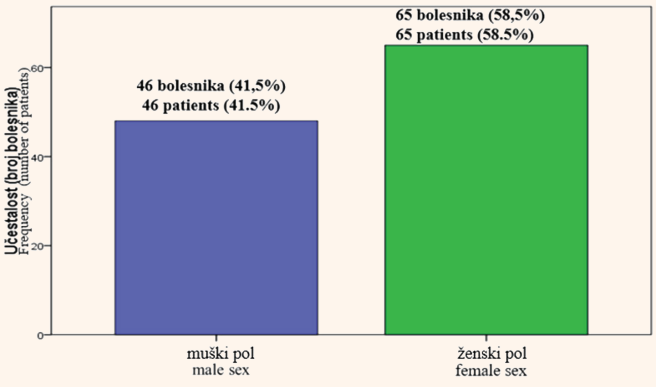
Among the 108 analyzed patients with SE, 89 were male subjects (82.4%), and 19 were female subjects (17.6%), (M:F = 4.7:1), (Figure 1). In the entire group of analyzed patients, the median age at the moment of diagnosis was 55 years (range: 19 – 88).

The median dimeter of the liver was 135 mm (range: 130 – 174), while the median diameter of the spleen was 100 mm (range: 90 – 150). The total erythrocyte mass was 136% (range: 105 – 269), (Figure 3). An elevated total erythrocyte mass of over 125%, which is characteristic of polycythemia vera, was present in 90 patients (83%). The median value of the oxygen saturation level (SO2) was 96% (range: 89.4 – 99). Below-normal SO2 (<92%) was noted in 5 patients. The median value of serum EPO was 9.3 IU/mL (range: 3.3 – 32.4). Among the 108 SE patients, analysis of the JAK2V617F mutation was carried out in 42 patients (38.8%), mostly during follow-up, and it was negative in all of the analyzed patients.

Patients with polycythemia vera (PV)

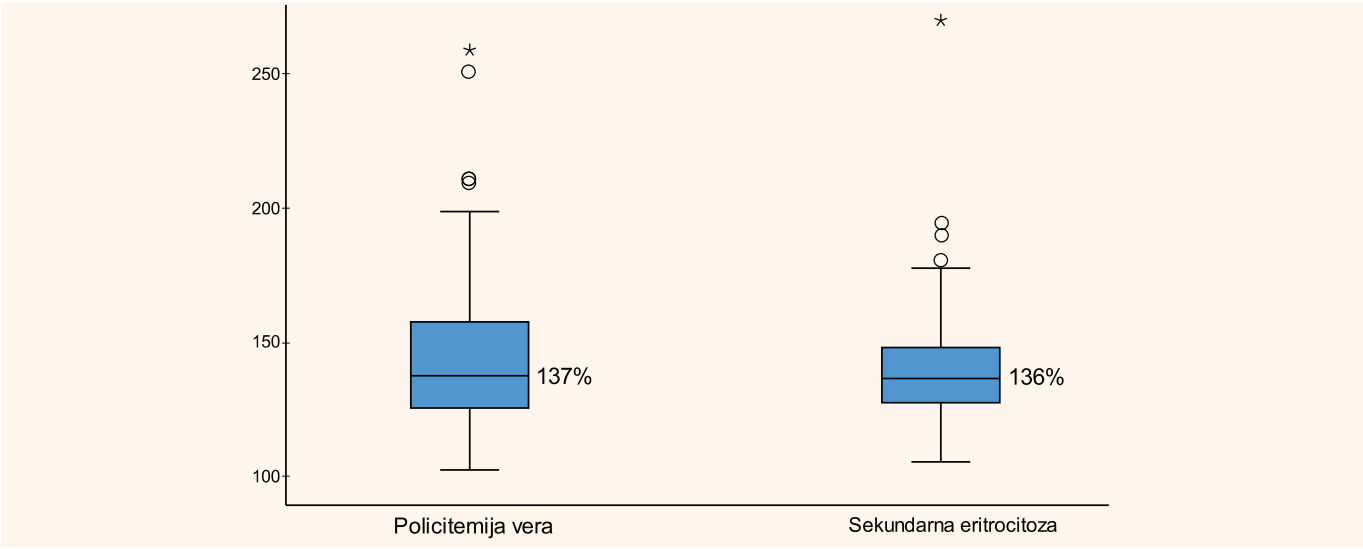
Among the 111 patients with polycythemia vera (PV) included in the study, 65 were female (58.5%) and 46 were male subjects (41.5%), (F:M = 1.4:1), (Figure2). In the entire group of analyzed patients, the median age at the moment of diagnosis was 62 years (range: 24 – 85). The median diameter of the liver was 135 mm (range 120 – 180), while the median diameter of the spleen was 121 mm (range: 90 – 255). A total of 15 patients (13.3%) were found to have hepatomegaly, while 52 patients (42%) had splenomegaly.

The median value of serum EPO was below-normal and amounted to 2 mU/mL (range: 0.06 – 31.8). Of the 101 analyzed patients, the JAK2V617F mutation was



Grafikon 2. Raspodela bolesnika sa policitemijom verom prema polu (muški/ženski)

Figure 2. Distribution of patients with polycythemia vera by gender (male/female)



Grafikon 3. Celokupna masa eritrocita kod bolesnika sa policitemijom verom i kod bolesnika sa sekundarnom eritrocitozom (%)

Figure 3. Total red cell mass in patients with polycythemia vera and in patients with secondary erythrocytosis (%)

eritrocitoze, tipične za policitemiju veru, potvrđeno je kod 88 bolesnika (79,2%).

Bolesnici sa PV-om, u odnosu na bolesnike sa SE-om, bili su značajno stariji (p = 0,001), sa većim promerom slezine (p < 0,001), većim brojem leukocita (12 ± 5,2x10^9/L naspram 7,7 ± 2,8 x10^9/L, p < 0,001), većim brojem trombocita (718 ± 354x10^9/L naspram 221 ± 61x10^9/L, p < 0,001), povišenom LDH u serumu (559 ± 183 U/L naspram 360 ± 64 U/L, p < 0,001), sniženim eritropoetinom (EPO) u serumu (2,5 ± 0,4 ml/mL naspram 13,8 ± 1,3 ml/mL, p < 0,001) i prisutnim spontanim *BFU-E* kolonijama (45±12 naspram 0, p = 0,011).

DISKUSIJA

Ova studija je analizirala demografske, kliničke i laboratorijske karakteristike bolesnika sa SE-om i PV-om. Rezultati su pokazali da bolesnici sa PV-om imaju značajno veći broj leukocita, veći broj trombocita, veće LDH vrednosti, veću veličinu slezine i prisutne spontane *BFU-E* kolonije, u odnosu na bolesnike sa SE-om. Kod bolesnika sa eritrocitozom, koji imaju uredan broj leukocita i trombocita, uredan nalaz LDH i normalnu veličinu slezine, savetuje se prvo isključivanje uzroka sekundarne eritrocitoze.

U našoj studiji, celokupna masa eritrocita nije pokazala statistički značajnu razliku između bolesnika sa SE-om u odnosu na pacijente sa PV-om, i najverovatnije se značaj celokupne mase eritrocita ogleda u diferencijaciji apsolutne i relativne eritrocitoze [1,3]. Vrednosti EPO-a u serumu kod bolesnika sa SE-om su normalne ili povišene, dok su kod bolesnika sa PV-om obično snižene, *što ukazuje* na značaj EPO analize u diferencijaciji sekundarne eritrocitoze od policitemije vere. Snižena vrednost EPO-a u serumu predstavlja *minor* kriterijum za postavljanje dijagnoze PV-a [6]. Kod bolesnika

detected in 95% of the subjects, while 5% of the patients did not have this mutation. The total erythrocyte mass indicated the presence of absolute erythrocytosis amounting to 137% (range: 102 – 258), (Figure 3). The presence of absolute erythrocytosis, typical for polycythemia vera, was confirmed in 88 patients (79.2%).

As compared to SE patients, patients with PV were significantly older (p = 0.001), they had a larger spleen diameter (p < 0.001), a higher leukocyte count (12 ± 5.2x10^9/L vs. 7.7 ± 2.8 x10^9/L, p < 0.001), a higher platelet count (718 ± 354x10^9/L vs. 221 ± 61x10^9/L, p < 0.001), elevated serum LDH (559 ± 183 U/L vs. 360 ± 64 U/L, p < 0,001), lower serum erythropoietin (EPO) (2.5 ± 0.4 ml/mL vs. 13.8 ± 1.3 ml/mL, p < 0.001) and the presence of spontaneous BFU-E colonies (45±12 vs. 0, p = 0.011).

DISCUSSION

The present study analyzed demographic, clinical and laboratory characteristics of patients with SE and PV. The results have shown that patients with PV have a significantly higher white blood cell count, higher platelet count, higher LDH values, larger spleen size, and the presence of spontaneous BFU-E colonies, as compared to patients with SE. In patients with erythrocytosis, with a normal white blood cell count and platelet count, with a normal LDH level and a normally sized spleen, it is advised that the causes of secondary erythrocytosis should first be excluded.

In our study, the total erythrocyte mass did not demonstrate a statistically significant difference between SE patients and PV patients, and the significance of the total erythrocyte mass is reflected, most probably, in the differentiation between absolute and relative erythrocytosis [1,3]. Serum EPO values in patients with SE are either normal or above-normal, while in patients with PV

sa eritrocitozom savetuje se da se prvo isključe uzroci sekundarne eritrocitoze. Međutim, ukoliko je bolesnik nepušač i nema prateće komorbiditete, a ima leukocitozu i/ili trombocitozu, kao i povišenu LDH vrednost, može se razmotriti i inicijalna analiza EPO-a u serumu.

Vrednosti *BFU-E* kolonija su bile prisutne kod bolesnika sa PV-om, u odnosu na bolesnike sa SE-om, kod kojih su bile odsutne. JAK2V617F mutacija je detektovana kod 95% bolesnika sa PV-om, što je u skladu sa prethodno objavljenim literaturnim podacima, dok kod bolesnika sa SE-om, kod kojih je analizirana ova mutacija, ona nije detektovana, što ukazuje na to da njena analiza može imati značaja u diferencijaciji policitemije vere od sekundarne eritrocitoze [4]. Međutim, u našoj studiji, JAK2V617F mutacija je analizirana kod 39% bolesnika, što predstavlja ograničavajući faktor za donošenje definitivnog zaključka.

ZAKLJUČAK

Celokupna masa eritrocita nije pokazala dijagnostički značaj u diferencijaciji sekundarne u odnosu na primarnu eritritrocitozu. Nalaz splenomegalije, leukocitoze, trombocitoze, povišene serumske LDH vrednosti i snižene vrednosti EPO-a u serumu govore u prilog policitemije vere. Sa druge strane, normalna veličina slezine, normalan broj leukocita i trombocita, normalne vrednosti serumske LDH i povišene vrednosti EPO-a, govore u prilog sekundarne eritrocitoze. Prema tome, kod bolesnika sa eritrocitozom, koji imaju uredan broj leukocita i trombocita, urednu LDH vrednost i normalnu veličinu slezine, savetuje se da se prvo isključe uzroci sekundarne eritrocitoze, a da se zatim uradi analiza EPO-a u serumu i razmotri potreba za daljom hematološkom obradom u pravcu policitemije vere.

SPISAK SKRAĆENICA:

BFU-E – burst forming unit-erythroid
EPO – eritropoetin
Hb – hemoglobin
Hct – hematokrit
LDH – laktat dehidrogenaza
PV – policitemija vera
SE – sekundarna eritrocitoza
SO2 – saturacija kiseonikom
SZO – Svetska zdravstvena organizacija
UZ – ultrazvuk
UKCS – Univerzitetski klinički centar Srbije

Sukob interesa: Nije prijavljen.

these values are typically below-normal, which indicates the significance of EPO analysis in the differentiation between secondary erythrocytosis and polycythemia vera. Below-normal serum EPO value is a minor criterion for diagnosing PV [6]. In patients with erythrocytosis it is recommended that secondary erythrocytosis causes should first be excluded. However, if the patient is a non-smoker without associated comorbidities, but has leukocytosis and/or thrombocytosis, as well as an above-normal LDH level, initial analysis of serum EPO can also be considered.

BFU-E colony values were present in patients with PV, as compared to SE patients, where these values were absent. The JAK2V617F mutation was detected in 95% of the patients with PV, which is in keeping with the above stated data from literature, while in SE patients, in whom this mutation was tested, it was not detected, which indicates that the analysis of this mutation can be significant in the differentiation between polycythemia vera and secondary erythrocytosis [4]. However, in our study, the JAK2V617F mutation was analyzed in 39% of the patients, which is a limiting factor for reaching a definitive conclusion.

CONCLUSION

Total erythrocyte mass did not demonstrate diagnostic significance in the differentiation of between primary and secondary erythrocytosis. The findings of splenomegaly, leukocytosis, thrombocytosis, above-normal serum LDH levels and below-normal serum EPO values, speak in favor of polycythemia vera. On the other hand, a normally sized spleen, a normal white blood cell count and platelet count, normal values of serum LDH and elevated EPO values, indicate secondary erythrocytosis. Therefore, in patients with erythrocytosis, who have a normal white blood cell and platelet count, a normal LDH value and a normally sized spleen, it is recommended that causes of secondary erythrocytosis should be excluded first, upon which serum EPO analysis should be performed, and the need for further hematological analysis considered, in relation to polycythemia vera.

LIST OF ABBREVIATIONS AND ACRONYMS:

BFU-E – burst forming unit-erythroid
EPO – erythropoietin
Hb – hemoglobin
Hct – hematocrit
LDH – lactate dehydrogenase
PV – polycythemia vera
SE – secondary erythrocytosis
SO2 – oxygen saturation
WHO – World Health Organization
US – ultrasound
KCS – Clinical Center of Serbia

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