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CLINICAL MANIFESTATIONS OF POLYMYALGIA RHEUMATICA – A SINGLE CENTRE EXPERIENCE

KLINIČKA OBILJEŽJA REUMATSKE POLIMIALGIJE – ISKUSTVA JEDNOG CENTRA

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Abstract

Introduction. Polymyalgia rheumatica (PMR) is a chronic inflammatory rheumatic disease that occurs mainly in patients over the age of 50. It is characterised by pain and stiffness in the shoulder and pelvic girdle and neck. Some patients develop giant cell arteritis (GCA). The aim of our study was to present clinical characteristics of PMR patients diagnosed in the period from January 2015 to July 2020 at the Division of Rheumatology and Clinical Immunology, Split University Hospital Centre, Croatia. *Materials and methods.* We analysed available medical records of patients diagnosed with PMR in accordance with the 2012 EULAR/ACR classification criteria. Methods of descriptive statistics were used in the analysis. Forty-nine PMR patients were included in the study. The mean age of patients was 77, and 67.35% of included patients were female. *Results.* The most frequent PMR manifestation was joint pain, which was documented in 91.84% patients, followed by fever in 28.57% cases. GCA was diagnosed in 6 cases (12.24%). The most common comorbidities were arterial hypertension (73.47%), followed by type 2 diabetes (38.78%). In 3 cases (6.12%) the malignant disease was diagnosed in the period of one year before and after the diagnosis of PMR. All patients received glucocorticoid therapy (GC) and remission was achieved in 45 (91.84%) cases. *Conclusion.* In conclusion, PMR is a disease which commonly affects the elderly, and it is successfully treated with GC. As expected, the most common symptom was joint pain, and the most common comorbidity was arterial hypertension. We did not find a higher prevalence of malignant diseases, so PMR should not be viewed as part of the paraneoplastic syndrome, which was also confirmed by the results of the recently conducted studies.

Keywords: Polymyalgia rheumatica; Comorbidity; Paraneoplastic syndrome

Sažetak

Uvod. Reumatska polimialgija (lat. *polymialghia reumatica* – PMR) je kronična upalna reumatska bolest koja se javlja uglavnom kod bolesnika starijih od 50 godina. Najčešće se prezentira bolovima i ukočenošću u području ramenog i zdjeličnog obruča te vrata. U pojedinih bolesnika dolazi do razvoja arteritisa divovskih stanica (engl. *Giant Cell Arteritis* – GCA). Cilj ovoga istraživanja jest prikazati kliničke karakteristike bolesnika kojima je dijagnosticirana PMR u razdoblju od početka 2015. godine do srpnja 2020. godine na Zavodu za reumatologiju i kliničku imunologiju Kli-

ničkoga bolničkog centra (KBC-a) Split. *Materijali i metode.* U istraživanje su uključeni bolesnici kojima je dijagnosticirana PMR prema EULAR/ACR klasifikacijskim kriterijima iz 2012. godine. Podatci su prikupljeni pregledom dostupne medicinske dokumentacije. U analizi rezultata korištene su metode deskriptivne statistike. Ukupno je dijagnosticirano 49 bolesnika s PMR-om. Prosječna dob je 77 godina, a prevladavaju osobe ženskog spola (67,35%). *Rezultati.* PMR se najčešće manifestirala bolovima u zglobovima (u 91,84% bolesnika) te febrilitetom (u 28,57% bolesnika). U 6 bolesnika (12,24%) je naknadno dijagnosticiran GCA. Najčešći pridruženi komorbiditeti bili su arterijska hipertenzija (73,47%) i šećerna bolest tipa 2 (38,78%). U troje bolesnika (6,12%) maligna bolest je dijagnosticirana u periodu od jednu godinu prije i nakon postavljanja dijagnoze PMR-a. Liječenje glukokortikoidima (GC) provedeno je u svih bolesnika, a u njih 45 (91,84%) postignuta je remisija bolesti. *Zaključak.* Zaključno, PMR je bolest koja se javlja u starijoj životnoj dobi i uspješno se liječi GC. Najčešća klinička prezentacija u naših bolesnika bila je bol u zglobovima, dok je najčešći komorbiditet bila arterijska hipertenzija. Nije potvrđeno da je PMR paraneoplastična bolest, što se poklapa s podatcima dostupnim iz literature.

Ključne riječi: Reumatska polimialgija; Komorbiditeti; Paraneoplastički sindrom

INTRODUCTION

Polymyalgia rheumatica (PMR) is a chronic inflammatory rheumatic disease manifested by pain in the shoulder and pelvic girdle and neck, morning stiffness, and increased acute phase reactants such as C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR). Joint effusion is often present in shoulder and hip joints. This disease most commonly occurs in people over the age of 50 and its incidence increases with ageing (1,2).

Approximately 10 – 16% of PMR patients develop giant cell arteritis (GCA) (3). This is the most common form of large blood vessel vasculitis which predominantly affects the extracranial branches of the carotid arteries and aorta, and is followed by symptoms such as headache, fever and / or vision loss (3, 4). A clear aetiology of PMR is yet to be defined, but it is thought that the main cause of immune system modulation is associated with ageing in genetically predisposed individuals (3, 5). Given that the incidence of PMR increases in old age, when the incidence of malignancy also increases, PMR has long been considered part of paraneoplastic syndromes, but this has not been clearly confirmed (6–8).

One of the characteristics of this disease is an excellent therapeutic response to low doses of glucocorticoids (GC).

The aim of this study was to determine the clinical manifestations of PMR in patients treated at the Division of Rheumatology and Clinical Immunology of the Split University Hospital Centre, the frequency and type of comorbidities and the response to the therapy used.

SUBJECTS AND METHODS

The study included patients with a clear diagnosis of PMR in accordance with the 2012 EULAR / ACR classification criteria, who were treated at the Division of

UVOD

Reumatska polimialgija (lat. *polymialghia reumatica* – PMR) je kronična upalna reumatska bolest koja se manifestira bolovima u vratu, ramenom i zdjeličnom obruču, jutarnjom zakočenosti, povišenim reaktantima akutne upale kao što su C-reaktivni protein (CRP) i sedimentacija eritrocita (SE). Često su prisutni izljevi u zglobovima ramena i kukova. Gotovo isključivo se javlja u osoba starijih od 50 godina, a incidencija raste povećanjem životne dobi (1, 2).

U 10–16% bolesnika s PMR-om razvija se arteritis divovskih stanica (engl. *Giant Cell Arteritis* – GCA) (3). To je vaskulitis velikih krvnih žila s predominantnim zahvaćanjem ekstrakranijalnih ogranaka karotidnih arterija i aorte te posljedičnom glavoboljom, febrilitetima i/ili ispadima vida (3, 4). Jasna etiologija PMR-a još nije definirana, smatra se da je glavni uzrok modulacija odgovora imunološkog sustava povezana sa starenjem u genetski predisponiranih pojedinaca (3, 5). S obzirom na to da incidencija PMR-a raste u starijoj životnoj dobi, kada raste i incidencija zloćudnih bolesti, PMR se dulje vrijeme smatrala dijelom paraneoplastičnih zbivanja, što međutim nije jasno potvrđeno (6–8).

Jedna od značajki ove bolesti jest izvrstan terapijski odgovor na niske doze glukokortikoida (engl. *Glucocorticoids*, skr. GC).

Cilj ovog istraživanja bio je utvrditi klinička obilježja PMR-a u bolesnika liječenih na Zavodu za reumatologiju i kliničku imunologiju Kliničkoga bolničkog centra (KBC-a) Split, učestalost i vrstu komorbiditeta te odgovor na primijenjenu terapiju.

ISPITANICI I METODE

U istraživanje su uključeni bolesnici s jasnom dijagnozom PMR-a prema EULAR/ACR klasifikacijskim kriterijima iz 2012. godine, koji su liječeni na Zavodu za reumatologiju i kliničku imunologiju KBC-a Split (9).

Pregledana je dostupna medicinska dokumentacija bolesnika koji su liječeni ambulantno ili stacionarno u

Rheumatology and Clinical Immunology, Split University Hospital Centre (9).

We analysed available medical records of patients who have received outpatient or inpatient care in the period from January 2015 to July 2020. Apart from the demographic data, the manifestations of the disease and its duration were recorded as well. In addition to that, comorbidities and the occurrence of malignant neoplasms were recorded, as well as symptoms that would indicate the occurrence of GCA. The therapy used in the treatment of patients, the response to therapy used, the number of patients in remission, the number of patients who have experienced relapse and the number of patients with active disease were analysed. Methods of descriptive statistics were used in the analysis. The collected data were analysed in Microsoft Excel.

RESULTS

The study included 49 PMR patients. Out of the total number of patients, 33 (67.35%) were female and 16 (32.65%) were male. The mean age of patients was 77, ranging from 62 to 92, and the mean age at diagnosis was 74.5. The mean age for the diagnosis of PMR was 76 for women, and 71.5 for men. The cohort analysis revealed that the average duration of the disease was 2.5 years, with the average duration of the disease being slightly longer in women (2.79 years) than in men (1.88 years).

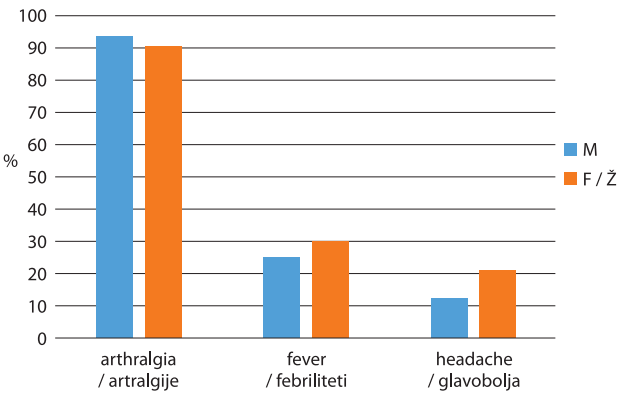
PMR manifested as joint pain in 91.84% of patients, fever (37.5 °C, axillary temperature) in 28.57% of patients, while headaches were recorded in 18.37% of patients (Figure 1). At the time of diagnosis, all patients reported pain and stiffness in the shoulders and shoulder girdle muscles, while 33 patients (67.4%) reported pain and stiffness in the hips and pelvic girdle muscles. Hand pain was recorded in 18 patients (36.7%), and knee pain was recorded in 13 patients (26.5%). A total of 43 patients (87.8%) reported significant morning stiffness lasting over 30 minutes. The headaches reported did not have GCA-specific characteristics, and patients with early-onset headaches did not meet the GCA criteria. None of the patients had positive antibodies to citrullinated proteins, while rheumatoid factor was detected in low titre in four patients (8.2%). Regarding the values of inflammatory parameters, the average value of erythrocyte sedimentation rate (ESR) at the time of diagnosis was 61 ± 25 mm/hr, and the average value of CRP was 74 ± 61.7 mg/dl. After treatment with low doses of glucocorticoids, the values decreased significantly and the average value of the last recorded ESR was 18 ± 13 mm/hr, and CRP 7.7 ± 4.4 mg/dl. As part of the diagnosis of PMR, ultrasound examination of the shoulder joints was performed in 10 patients (20.4%). The most common comorbidities

razdoblju od siječnja 2015. godine do srpnja 2020. godine. Osim demografskih podataka, zabilježeni su simptomi kojima se bolest prezentirala te trajanje bolesti. Uz to su evidentirani komorbiditeti i pojava zloćudnih novotvorina te simptomi koji bi upućivali na pojavu GCA. Analizirana je terapija kojom su bolesnici liječeni, odgovor na terapiju, udio bolesnika koji su u remisiji te udio onih koji su imali relaps bolesti ili je bolest još uvijek aktivna. U analizi su korištene metode deskriptivne statistike. Dobiveni podatci su analizirani u programu *Excel Microsoft Office*.

REZULTATI

U istraživanje je uključeno 49 bolesnika s PMR-om. Od ukupnog broja bolesnika njih 33 (67,35%) su bile žene, a 16 muškarci (32,65%). Prosječna životna dob oboljelih bila je 77 godina, uz raspon od 62 do 92 godine, a prosječna dob u trenutku postavljanja dijagnoze bila je 74,5 godine. U žena je u prosjeku dijagnoza PMR-a bila postavljena u dobi od 76 godina, a u muškaraca u dobi od 71,5 godina. Za analiziranu kohortu prosječno trajanje bolesti bilo je 2,5 godine, s tim da je u žena prosjek trajanja bolesti nešto dulji (2,79 godine) nego u muškaraca (1,88 godine).

PMR se u 91,84% bolesnika manifestirala bolovima u zglobovima, febrilitetom (37,5°C mjereno aksilarno) u njih 28,57%, dok su u 18,37% bolesnika evidentirane glavobolje (slika 1). Svi su bolesnici u trenutku dijagnoze navodili bolove i ukočenost u ramenima i mišićima ramenog obruča, dok su 33 bolesnika (67,4%) navela bolnost i ukočenost u kukovima i mišićima zdjeličnog obruča. U 18 bolesnika (36,7%) evidentirani su bolovi u šakama, a u 13 bolesnika (26,5%) evidentirani su bolovi u koljenima. Ukupno 43 bolesnika (87,8%) navelo je značajnu jutarnju zakočenost u trajanju preko 30 minuta. Zabilježene glavobolje nisu imale obilježja karakteristična za GCA, a bolesnici s glavobo-



Legend / Legenda: M – males / muški, F/Ž – females / ženski

FIGURE 1. Main presenting symptoms of polymyalgia rheumatica (PMR)
SLIKA 1. Glavni prezentirajući simptom reumatske polimijalgije (PMR)

Legend / Legenda:
M – males / muški, FŽ – females / ženski

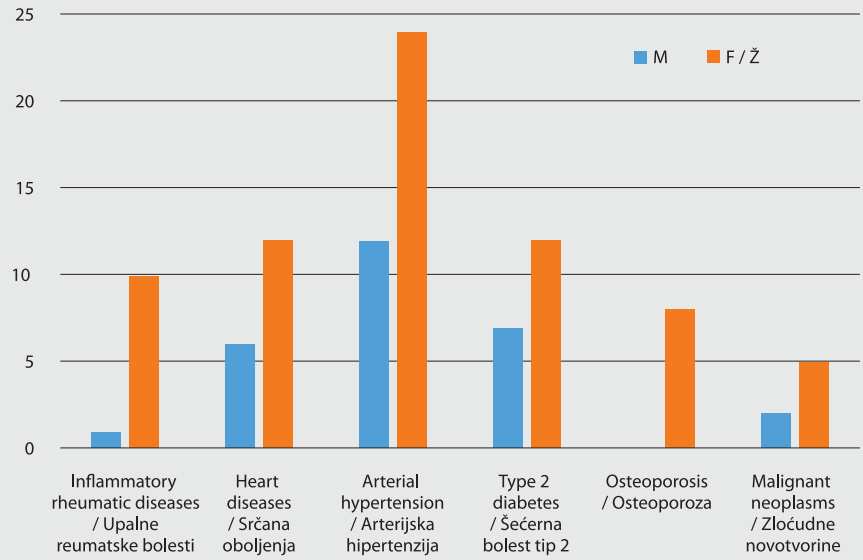


FIGURE 2. Comorbidities in patients with polymyalgia rheumatica (PMR)
SLIKA 2. Komorbiditeti u bolesnika s reumatskom polimijalgijom (PMR)

were arterial hypertension, found in 73.47% of cases, type 2 diabetes, found in 38.78% of cases, and various heart diseases such as ischemic or dilated cardiomyopathy, found in 36.73% of cases (Figure 2). Osteoporosis was recorded in 8 patients (16.33%). When it comes to concomitant inflammatory rheumatic diseases, GCA was diagnosed in 6 patients through additional diagnostic processing, while seronegative polyarthritis was diagnosed in three patients, rheumatoid arthritis was diagnosed in one patient and generalised osteoarthritis was diagnosed in one patient as well. Most cases of concomitant inflammatory rheumatic diseases as well as osteoporosis have been reported in women (Figure 2). Five patients had a previous diagnosis of malignancy at the time of diagnosis of PMR. In three of them, the malignancy occurred more than five years before the diagnosis of PMR. The most commonly diagnosed malignancies were breast cancer, which was diagnosed in three patients, malignant melanoma, which was diagnosed in one patient and smouldering multiple myeloma, which was also diagnosed in one patient. In two patients, the malignancy was diagnosed after the diagnosis of PMR, and these malignancies included cases of renal cell carcinoma and essential thrombocythemia.

All patients received oral glucocorticoid therapy at the time of data analysis. The initial daily dose of methylprednisolone was 12 to 16 mg. Synthetic antimalarials were used as treatment in 20.41% of cases, while methotrexate was used in 14.29% of cases, mostly in cases with concomitant inflammatory rheumatic diseases. Azathioprine was used for the treatment of concomitant GCA in one patient. In 47 (95.92%) patients, remission of PMR was achieved at the time of analysis, and the remaining two patients had recently been diagljama na početku bolesti nisu zadovoljavali kriterije za GCA. Niti jedan bolesnik nije imao pozitivna protutijela na citrulinirane proteine, dok je u njih četvero (8,2%) pronađen reumatoidni faktor u niskom titru. Što se tiče vrijednosti upalnih parametara, prosječna vrijednost sedimentacije eritrocita (SE) prilikom postavljanja dijagnoze bila je 61±25/h, a prosječna vrijednost CRP-a 74±61,7 mg/dl. Nakon provedenog liječenja niskim dozama glukokortikoida vrijednosti su se značajno snizile te je prosječna vrijednost posljednje zabilježene SE bila 18±13/h, a CRP 7,7±4,4 mg/dl. U sklopu dijagnoze PMR-a, ultrazvučni pregled ramenih zglobova napravljen je u 10 bolesnika (20,4%). Najčešće pridružene bolesti bile su arterijska hipertenzija, nađena u 73,47% slučajeva, šećerna bolest tipa 2 u 38,78%, a različita srčana oboljenja kao što su ishemijska ili dilatativna kardiomiopatija u 36,73% slučajeva (slika 2). Osteoporoza je bila zabilježena u 8 bolesnika (16,33%). Od pridruženih upalnih reumatskih bolesti u 6 bolesnika je dodatnom obradom dijagnosticiran GCA, seronegativni poliartritis u tri bolesnika, reumatoidni artritis u jednoga te generalizirani osteoartritis u jednoga bolesnika. Većina popratnih upalnih reumatskih bolesti kao i osteoporoza zabilježena je u žena (slika 2). Pet bolesnika imalo je već ranije postavljenu dijagnozu zloćudne bolesti u trenutku postavljanja dijagnoze PMR-a; u njih troje zloćudna bolest se javila više od pet godina prije dijagnoze PMR-a. Najčešće dijagnosticirane zloćudne bolesti bile su karcinomi dojke u tri bolesnice te maligni melanom u jednoga i asimptomatski multipli mijelom u još jednoga bolesnika. U dvoje bolesnika maligna bolest je dijagnosticirana nakon postavljanja dijagnoze PMR-a, a radilo se o karcinomu bubrega i esencijalnoj trombocitemiji.

Svi bolesnici su bili na terapiji peroralnim glukokortikoidima u trenutku analize podataka. Početna doza

nosed with PMR. Relapse was reported in two (4.08%) cases.

DISCUSSION

The results of our study confirmed that PMR is more common in women, like most inflammatory rheumatic diseases, and the most common symptom was joint pain (10). Given that this is a condition that commonly affects the elderly population, a high incidence of arterial hypertension is expected (11, 12). It is known that long-term glucocorticoid therapy may lead to the occurrence of new or dysregulation of existing diabetes in these patients, and in the case of prolonged treatment there is an increased risk of osteopenia and / or osteoporosis progression. Also, long-term use of glucocorticoids promotes accelerated atherosclerosis, despite the known fact that adequate control of systemic inflammation in inflammatory rheumatic diseases has a protective effect on the vascular endothelium (13–17). The incidence of osteoporosis, heart disease, and type 2 diabetes, despite relatively long-term glucocorticoid therapy, has been reported in approximately one-third of our patients. Similar results were presented in the study conducted by Shbeeb et al. after analysing the connection between glucocorticoid therapy and the occurrence of these comorbidities in patients with PMR. According to this study, the incidence of diabetes, atherosclerosis, and osteoporosis is similar in patients with PMR who received glucocorticoid therapy and the control group (18). Based on these data, it can be concluded that relatively small doses of glucocorticoids used in the treatment of PMR suppress systemic inflammation with a relatively low incidence of adverse effects and have a protective effect on inflammation-mediated endothelial and bone damage (19, 20).

A group of Italian authors showed, on a relatively small number of subjects, that 12.5 mg of prednisolone per day is a sufficient dose for the start of PMR treatment (21). These data indicate a good efficacy of glucocorticoid therapy in the treatment of PMR, which has also been confirmed in the case of our patients. The duration of glucocorticoid therapy should be at least 1–3 years, and in patients with high CRP and / or ESR levels, long-term treatment with minimal doses of prednisolone is recommended to prevent relapse (22, 23).

One of the aims of our study was to determine how often PMR occurs with malignancies. In the group of our patients, we recorded only three cases of malignancies that occurred in the period of one year before or after the diagnosis of PMR. One patient was diagnosed with multiple myeloma one year before she was diagnosed with PMR, while two other patients were diagnosed with essential thrombocythemia or kidney cancer several months after being diagnosed with PMR. Therefore, in our group of patients, PMR proved

bila je 12 do 16 mg metilprednizolona dnevno. Sintetskim antimalarikom liječeno je 20,41%, a metotreksatom 14,29% bolesnika, uglavnom s pridruženim upalnim reumatskim bolestima. U jednog bolesnika primijenjen je azatioprin za liječenje pridruženog GCA. U 47 (95,92%) bolesnika postignuta je remisija PMR-a u trenutku analize, a u preostala dva bolesnika radilo se o nedavno dijagnosticiranoj PMR. Relaps je zabilježen u dvoje (4,08%) bolesnika.

RASPRAVA

Rezultati našeg istraživanja potvrdili su da se PMR češće javlja u žena, poput većine upalnih reumatskih bolesti, a najčešći simptomi bili su bolovi u zglobovima (10). S obzirom na to da se radi o starijoj populaciji, očekivana je visoka učestalost arterijske hipertenzije (11, 12). Poznato je da dugotrajna terapija glukokortikoidima može dovesti do pojave nove ili disregulacije postojeće šećerne bolesti kod ovih bolesnika, a u slučaju produljenog liječenja raste rizik pogoršanja osteopenije i/ili osteoporoze. Također, dugotrajna primjena glukokortikoida potiče ubrzanu aterosklerozu, usprkos poznatoj činjenici da adekvatnom kontrolom sustavne upale u upalnim reumatskim bolestima ima protektivno djelovanje na krvožilni endotel (13–17). Učestalost osteoporoze, srčanih oboljenja i šećerne bolesti tipa 2, unatoč relativno dugotrajnoj terapiji glukokortikoidima, zabilježena je u otprilike trećine naših bolesnika. Slične rezultate prikazali su Shbeeb i sur. nakon analize povezanosti terapije glukokortikoidima i pojavnosti navedenih komorbiditeta u oboljelih od PMR-a. Prema toj studiji pojavnost šećerne bolesti, ateroskleroze i osteoporoze slična je u oboljelih od PMR-a koji su liječeni glukokortikoidima i u kontrolnoj skupini (18). Na temelju ovih podataka može se zaključiti da relativno male doze glukokortikoida koje se koriste u liječenju PMR-a suprimiraju sustavno upalno zbivanje uz relativno nisku učestalost štetnih učinaka te da protektivno djeluju na upalom posredovano oštećenje endotela i kostiju (19, 20).

Grupa talijanskih autora pokazala je na relativnom malom broju ispitanika da je 12,5 mg prednizolona dnevno dovoljna doza za početak liječenja PMR-a (21). Ovi podatci ukazuju na dobru učinkovitost terapije glukokortikoidima u liječenju PMR-a, što je potvrđeno i u naših bolesnika. Trajanje terapije glukokortikoidima trebalo bi biti barem 1–3 godine, a u bolesnika s povišenim nalazima CRP-a i/ili SE preporuča se i dugotrajnije liječenje minimalnim dozama prednizolona, čime se prevenira pojava relapsa bolesti (22, 23).

Jedan od ciljeva našeg istraživanja bio je ustanoviti koliko često se PMR javlja uz maligne bolesti. U skupini naših bolesnika zabilježili smo samo tri zloćudne bolesti koje su se pojavile u periodu od jedne godine prije ili nakon postavljanja dijagnoze PMR-a. Jednoj bolesnici je dijagnosticiran multipli mijelom jednu godinu prije

to be a paraneoplastic syndrome in only three patients, while malignancies that were diagnosed several years before the diagnosis of PMR can hardly be considered in this context. Since the elderly population was analysed in this study, we expected a more frequent occurrence of malignancies (24, 25), which in the end was not recorded. Therefore, we cannot state with certainty that PMR can be viewed as part of the paraneoplastic syndrome, which has also been concluded in some of the recently published reviews (7, 26). The suspected paraneoplastic syndrome should be confirmed by the atypical clinical features of PMR, which include, for example, the absence of prolonged morning stiffness, therapeutic response to glucocorticoids, or the absence of radiologically confirmed bursitis of the shoulders and hips (26). However, in a 2018 review by Partington et al., the connection of PMR with the occurrence of malignancies, especially haematological ones, was not rejected. In summary, a connection with malignancies was confirmed in seven studies, while in nine of the analysed studies no connection between PMR and malignancies was found (27). Two of our patients with malignancies that were diagnosed in the same period as PMR presented with typical clinical features which, in addition to pain and stiffness in the shoulder and pelvic girdle, manifested by hand swelling and pain with typical prolonged morning stiffness with a good response to glucocorticoid therapy. Further population research is needed to define a clear connection between PMR and occult malignant neoplasms.

The main challenge in the diagnosis of PMR is the early recognition of GCA symptoms to prevent the occurrence of disease complications such as vision loss. In addition to that, patients with concomitant GCA require higher doses of glucocorticoids (23). Literature data show that the incidence of GCA in PMR patients is 10 – 16%, which is in accordance with our results (3, 28). When it comes to other cases of concomitant inflammatory rheumatic diseases, three cases of seronegative arthritis, one case of rheumatoid arthritis and one case of generalised osteoarthritis have been reported, which is also in line with the current knowledge of the incidence of these diseases in PMR patients (26).

The disadvantage of this study is the small number of patients included, due to the fact that we have analysed data from only one hospital centre and performed only descriptive statistical analysis. In addition to that, it is a retrospective study based on the review of medical records, with no control group.

In conclusion, PMR is an inflammatory rheumatic disease which affects the elderly and is more common in women. In our group of patients, no significantly higher connection of the disease with the occurrence of malignancies nor with other inflammatory rheumatic diseases was found. Prospective population re-

nego joj je postavljena dijagnoza PMR-a, dok je kod još dva bolesnika dijagnosticirana esencijalna trombocitemija odnosno karcinom bubrega nekoliko mjeseci nakon što je dijagnosticirana PMR. Prema tome, u našoj skupini bolesnika PMR se pokazala kao paraneoplastični sindrom u svega tri bolesnika, dok zloćudne bolesti koje su utvrđene više godina prije dijagnosticiranja PMR-a teško možemo razmatrati u tom kontekstu. Budući da je analizirana populacija starije životne dobi, očekivali smo učestaliju pojavu zloćudnih bolesti (24, 25), koja u konačnici ipak nije zabilježena. Stoga PMR ne možemo sa sigurnošću smatrati dijelom paraneoplastičkog sindroma, što je zaključak i nedavno objavljenih preglednih članaka (7, 26). Sumnju na paraneoplastično zbivanje trebala bi pobuditi atipična klinička slika PMR-a, koja na primjer uključuje izostanak produžene jutarnje zakočenosti, terapijskog odgovora na glukokortikoide ili izostanak radiološki potvrđenog burzitisa ramena i kukova (26). Ipak, u preglednom članku Partingtona i sur. iz 2018. godine nije odbačena povezanost PMR-a s pojavom malignih oboljenja, pogotovo hematoloških. Sumarno, povezanost s malignim bolestima potvrđena je u sedam studija, dok u devet analiziranih studija nije pronađena povezanost PMR-a s malignim bolestima (27). Naša dva bolesnika sa zloćudnim bolestima koje su dijagnosticirane u periodu kada je postavljena i dijagnoza PMR-a prezentirala su se tipičnom kliničkom slikom koja se osim bolovima i ukočenošću u ramenom i zdjeličnom obruču manifestirala i oticanjem i bolovima u šakama uz pojavu tipične produžene jutarnje zakočenosti, s dobrim odgovorom na liječenje glukokortikoidima. Buduća populacijska istraživanja potrebna su kako bi se definirala jasna povezanost PMR-a s okultnim malignim neoplazmama.

Glavni izazov u dijagnostici PMR-a je rano prepoznavanje simptoma GCA kako bi se spriječile komplikacije ove bolesti kao što je gubitak vida. Uz to, bolesnici s pridruženim GCA zahtijevaju više doze glukokortikoida (23). U literaturi se navodi da učestalost GCA u oboljelih od PMR-a iznosi 10–16%, što odgovara i našim rezultatima (3, 28). Od ostalih pridruženih upalnih reumatskih bolesti zabilježena su tri slučaja seronegativnog artritisa, po jedan slučaj reumatoidnog artritisa i generaliziranog osteoartritisa, što je također u skladu s dosadašnjim saznanjima o pojavnosti ovih bolesti u oboljelih od PMR-a (26).

Nedostatak je ove studije mali broj uključenih bolesnika, budući da su analizirani podatci iz samo jednog centra te je provedena samo deskriptivna statistička obrada. Osim toga, radi se o retrospektivnoj studiji koja se temelji na pregledavanju medicinske dokumentacije, dok nije bilo kontrolne skupine.

Zaključno, PMR je upalna reumatska bolest starije životne dobi koja se češće javlja u žena. U našoj skupini bolesnika nije utvrđena značajno viša povezanost bolesti s malignim bolestima kao ni s drugim upalnim reu-

search is needed to define a clear connection between PMR and malignant neoplasms.

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matskim bolestima. Prospektivna populacijska istraživanja potrebna su kako bi se definirala jasna povezanost PMR-a s malignim neoplazmama.

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