PRIMARNI PLAZMOCITOM LIMFNOG ČVORA – REDAK KLINIČKI ENTITET

PRIKAZ SLUČAJA

CASE REPORT

PRIMARY LYMPH NODE PLASMACYTOMA – A RARE CLINICAL ENTITY

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SAŽETAK

Uvod: Ekstramedularna lokalizacija plazmocitoma u regiji glave i vrata čini manje od 1% tumora te regije. Primarna solitarna lokalizacija u limfnom čvoru, bez proliferacije plazmocita na bilo kojoj drugoj lokalizaciji, kao jedina manifestacija plazmocitoma, izuzetno je retka. Do sada je referisano manje od 50 slučajeva.

Prikaz slučaja: Muškarac, star 58 godina, zbog uvećane bezbolne žlezde na vratu, bez temperature, preznojavanja i gubitka u težini, obratio se lekaru. Tretiran je antibioticima širokog spektra u trajanju od 10 dana, ali nije bilo promene. Urađena kompletna krvna slika je imala uredan nalaz. Biohumoralni zapaljenski sindrom je bio negativan, a kompletna biohemija u referentnom opsegu. Urađen je eho vrata i registrovana jedna limfna žlezda promera 30 mm x 15 mm. Pacijent je upućen maksilofacijalnom hirurgu, žlezda je u celosti ekstirpirana i poslata na histopatološku analizu. Dobijen je sledeći patohistološki nalaz (PH): difuzna infiltracija plazmocitoidnim tumorskim ćelijama visoke pozitivnosti za: OCT2, BOB1, CD38, MUM1, lambda, CD31,VIM i CD79 alfa; negativne na kapa; Ki67 pozitivne u 30%. Zaključak patohistološkog nalaza je bio: plazmocitom lambda pozitivan. Biopsija koštane srži (BK) dala je sledeći patohistološki nalaz: plazmociti 4%. Snimanjem multislajsnim skenerom (*MSCT*) grudnog koša, abdomena i male karlice dobijen je uredan nalaz. Radiografski pregled skeleta je bio uredan. M komponenta u serumu i urinu je bila negativna. Virusologija je pokazala HBsAg pozitivnost, dok su HCV i HIV bili negativni. Indikovana je lokalna zračna terapija uz aktivno lečenje antiviroticima.

Zaključak: Svaka limfadenopatija zahteva ozbiljan i detaljan pristup kliničara. Da li je HBV infekcija bila okidač za nastanak plazmocitoma, ostaje za razmatranje.

Ključne reči: plazmocitom, limfni čvor, HBV infekcija

ABSTRACT

Introduction: Extramedullary plasmacytoma localized in the region of the head and neck represents less than 1% of tumors found in that region. Primary solitary localization of plasmacytoma in the lymph node, as the only manifestation of plasmacytoma, is rare, with less than 50 cases reported so far.

Case report: A 58-year-old man came to the physician because of a painless swollen lymph node in the neck, afebrile, reporting no night sweats or weight loss. He was treated with broad-spectrum antibiotics for 10 days, but his health status did not change. A complete blood count (CBC) was performed, and normal test results were obtained. The patient tested negative for biohumoral inflammatory syndrome. The ultrasound examination of the neck showed a lymph gland, 30 mm x 15 mm in size. The patient was referred to a maxillofacial surgeon; total lymph node extirpation was performed, and the excised node was sent for histopathological analysis. The following pathohistological finding was obtained: diffuse infiltration by plasmacytoid tumor cells stronlgly positive for: OCT2, BOB1, CD38, MUM1, lambda, CD31, VIM, and CD79 alpha; negative for kappa; positive for Ki67 in 30%. The conclusion of the pathohistological examination was lambda positive plasmacytoma. Bone biopsy showed the following: plasmocytes 4%. The findings of multi-slice computed tomography (MSCT) of the thorax, abdomen, and lesser pelvis were normal. Radiographic imaging of the skeleton also showed normal findings. The M protein, in both serum and urine, was negative. Virology tests showed that the patient was HBsAg positive, while he was HCV and HIV negative. Local radiation therapy was indicated along with active antiviral therapy.

Conclusion: Each case of lymphadenopathy demands a serious and thorough approach to be established by the clinician. The question is whether an infection caused by the Hepatitis B virus may have served as a trigger for the development of plasmacytoma.

Keywords: plasmacytoma, lymph node, HBV infection

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UVOD

Multipli mijelom čini oko 1% svih malignih neoplazmi. Njegova incidencija raste sa godinama i doseže maksimum u sedmoj deceniji života [1–4]. To je drugi po učestalosti hematološki malignitet iza limfoma, čineći 10% ukupnog broja obolelih od malignih hematoloških bolesti, a sa učestalošću od 47% je najčešći tumor kostiju [5–7]. Za razliku od mijeloma, ekstramedularni plazmocitom može biti lokalizovan i u mekim tkivima, po celom organizmu, zahvatajući gornje partije respiratornog sistema, ždrelo, nazalnu regiju – sinuse, larinks, gastrointestinalni trakt, dojke, čak i mozak. Dijagnoza se postavlja biopsijom tumora. Bolesnici sa plazmocitomom imaju normalan radiološki nalaz na koštanom sistemu i normalan nalaz biopsije koštane srži.

Ekstramedularni plazmocitom u regiji glave i vrata čini manje od 1% svih tumora te regije [8]. Zahvaćenost limfne žlezde solitarno, kao jedina manifestacija plazmocitoma, izuzetno je retka – do sada je referisano manje od 50 slučajeva [9,10]. Dijagnoza primarnog plazmocitoma u limfnom čvoru, kao ekstramedularne lokalizacije, izuzetno je retka, ali oko 15% plazmocitoma lociranih u gornjim partijama respiratornog trakta može da metastazira u limfne čvorove vrata. Multipli mijelom visokog kliničkog stadijuma takođe može, u skoro 40% slučajeva, da metastazira u limfne čvorove. Oboleli od plazmocitoma su, u dve trećine slučajeva, muškarci starosnog doba od 39 do 76 godina, a plazmocitom često zahvata žlezde cervikalne regije. Preživljavanje kod onih pacijenata kod kojih su zahvaćene limfne žlezde je slično kao i kod drugih ekstramedularnih plazmocitoma, a koji nisu progredirali u multipli mijelom [9]. Primarni plazmocitom limfnog čvora je vrlo retka hematološka neoplazma, koja se manifestuje uvećanim limfnim čvorom vrata, bez drugih diskrazija plazma ćelija [10].

PRIKAZ SLUČAJA

Muškarac, star 58 godina javio se lekaru zbog uvećanog palpabilnog tumefakta na vratu desno, a bez izmene na koži iznad izrasline. Fizikalnim nalazom ustanovljen je palpabilan tumefakt – limfna žlezda, tvrde konzistencije, bezbolan, iza sternokleidomastoidnog mišića, u gornjoj trećini. Bolesnik nije imao povišenu temperaturu, preznojavanje, niti gubitak u telesnoj težini. Uključen je antibiotik širokog spektra dejstva, *per os,* tokom 10 dana, ali nije bilo nikakve promene.

Kako se tumefakcija nije smanjivala, urađene su laboratorijske analize. Kompletna krvna slika je bila u referentnom opsegu, kao i biohemijske analize, uz negativan biohumoralni zapaljenski sindrom. Urađen je ultrazvučni pregled vrata, koji je rezultirao sledećim opisom: uvećana limfna žlezda promera 30 mm x 15

INTRODUCTION

Multiple myeloma accounts for about 1% of all malignant neoplasms. Its incidence increases with age and reaches its maximum in people in their sixties [1–4]. It is the second most common hematological malignancy after lymphoma, accounting for 10% of the total number of patients with malignant hematological diseases, and with a frequency of 47% it is the most common bone tumor [5–7]. Unlike myeloma, extramedullary plasmacytoma can also be localized in soft tissues, throughout the body, affecting the upper segments of the respiratory system, the pharynx, the nasal region – sinuses, the larynx, the gastrointestinal tract, the breasts, and even the brain. Diagnosis is established by tumor biopsy. Radiological findings of the skeleton are normal in patients with plasmacytoma. They also have normal bone marrow biopsy findings.

Extramedullary plasmacytoma located in the region of the head and neck accounts for less than 1% of all tumors in that region [8]. Involvement of the lymphatic gland alone, as the only manifestation of plasmacytoma, is extremely rare – less than 50 cases have been reported so far [9,10]. The diagnosis of primary plasmacytoma in a lymph node, as an extramedullary localization, is extremely rare. Nevertheless, about 15% of plasmacytomas located in the upper portion of the respiratory tract can metastasize to the lymph nodes of the neck. Also, advanced-stage multiple myeloma can, in almost 40% of cases, metastasize to the lymph nodes. Two-thirds of plasmacytoma sufferers are men between the ages of 39 and 76 years, and plasmacytoma often affects the glands of the cervical region. Survival in patients with lymph node involvement is similar to other extramedullary plasmacytomas that have not progressed to multiple myeloma [9]. Primary lymph node plasmacytoma is a rare hematological neoplasm manifesting as an enlarged cervical lymph node, without other plasma cell dyscrasias [10].

CASE REPORT

A 58-year-old man came to the doctor because of an enlarged palpable tumefaction on the right side of the neck but without a lesion on the skin above the growth. The physical examination revealed a palpable swelling – a lymph gland, hard in consistency, painless, located behind the sternocleidomastoid muscle, in the upper third. The patient had no fever, sweating, or weight loss. A broad-spectrum antibiotic was prescribed to be taken orally for 10 days, but there was no change.

As the swelling did not decrease, laboratory analyses were performed. The complete blood count was within the reference range, as were the biochemical analyses. The patient tested negative for biohumoral

mm. Bolesnik je upućen na maksilofacijalnu hirurgiju, gde je žlezda ekstirpirana u celosti i poslata na histopatološku analizu. Patohistološki nalaz je opisao difuznu infiltraciju plazmocitoidnim tumorskim ćelijama jako pozitivnim na: OCT2, BOB1, CD38, MUM1, lambda, CD31, VIM, CD79 alfa, a negativnim na kapa, dok je Ki67 pozitivnost bila prisutna kod 30% ćelija. Patohistološki, morfološki i imunohistohemijski, postavljena je dijagnoza plazmocitoma lambda tipa.

Po hospitalizaciji na Klinici za hematologiju, pacijentu je uzorkovana krv i rezultati svih urađenih analiza su bili u referentnom opsegu (Tabela 1). Urađena je dodatna dijagnostika – snimanje multislajsnim skenerom (*MSCT*) grudnog koša, abdomena i male karlice, kojim nije utvrđeno postojanje organomegalije niti je detektovano uvećanje limfnih nodusa (Slika 1).

Elektroforeza proteina nije detektovala postojanje M komponente u serumu niti u urinu. Izmerena je vrednost beta 2 mikroglobulina od 1,8 g/l (normalna vrednost: do 2,4 g/l), što je u referentnom opsegu. Urađena biopsija kosti i aspiracija koštane srži utvrdila je prisustvo 4% plazmocita.

Virusološke analize su utvrdile postojanje hroničnog virusnog hepatitisa B; HBsAg pozitivan (78,58 S/CO), HBeAg negativan (0,587 S/CO), HBe At pozitivna (0,11 S/CO), HBc IgG pozitivan (11,82 S/CO), HBc IgM negativan (0,06 S/CO), HBs At negativna (1,13 S/CO), dok su HCV At (0,06 S/CO) i HIV At bila negativna (0,88 S/CO). Infektolog je uključio antivirusnu terapiju (teno-

inflammatory syndrome. An ultrasound examination of the neck showed an enlarged lymph gland, 30 mm x 15 mm in diameter. The patient was referred to maxillofacial surgery, where the gland was completely excised and sent for histopathological analysis. The pathohistological finding described a diffuse infiltration of plasmacytoid tumor cells strongly positive for the following: OCT2, BOB1, CD38, MUM1, lambda, CD31, VIM, CD79 alpha, and negative for kappa, while Ki67 positivity was present in 30% of cells. Pathohistologically, morphologically, and immunohistochemically, a diagnosis of lambda-type plasmacytoma was established.

Upon hospitalization at the Clinic for Hematology, the patient's blood was sampled and the results of all the tests were within the reference ranges (Table 1). Additional diagnostics was performed – multislice scan (MSCT) of the chest, abdomen, and pelvis, which did not establish the existence of organomegaly or detect enlarged lymph nodes (Figure 1).

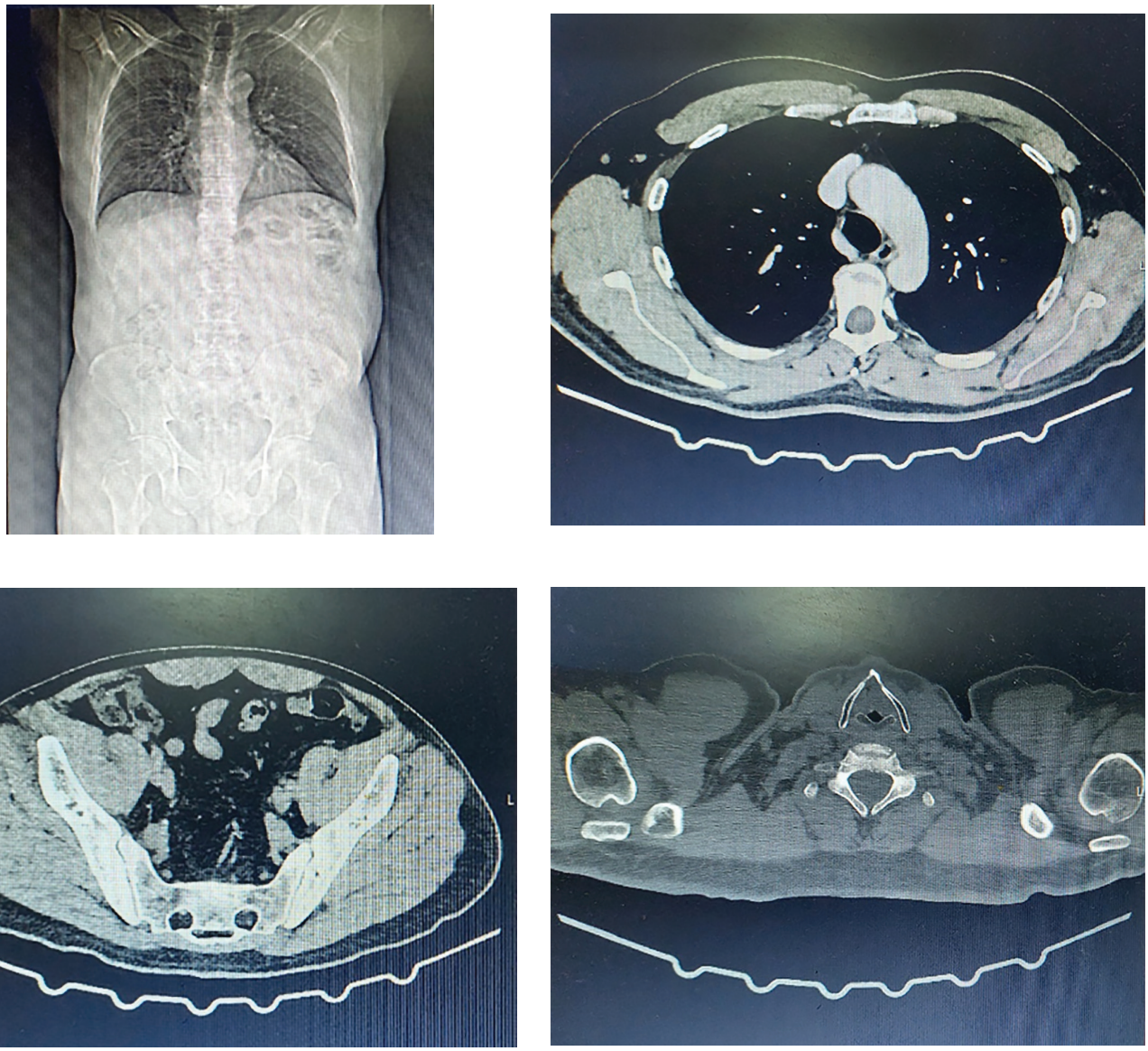
Protein electrophoresis did not detect the presence of the M protein in serum or urine. A beta 2 microglobulin level of 1.8 g/l (normal value: up to 2.4 g/l) was measured, which is within the reference range. Bone biopsy and bone marrow aspiration determined the presence of 4% plasma cells.

Virology tests established the existence of chronic viral hepatitis B; HBsAg positive (78.58 S/CO), HBeAg negative (0.587 S/CO), HBe At positive (0.11 S/CO), HBc IgG positive (11.82 S/CO), HBc IgM negative (0.06 S/CO),

Tabela 1. Analize krvi na prezentaciji

Table 1. Blood test results at presentation

Laboratorijske analize / *Laboratory analyses*	*Na prezentaciji / At presentation*	*Laboratorijske referentne vrednosti / Laboratory reference ranges*
Hemoglobin (g/l)	151	120.2 – 150.5
Hematocrit (%)	44	35 – 45
White blood cell count (10^{*9}/l)	6.0	4.0 – 10.0
Lymphocytes (10^{*9}/l)	0.60	1.2 – 3.4
Neutrophils (10^{*9}/l)	4.7	2.0 – 6.5
Monocytes (10^{*9}/l)	0.3	0.1 – 0.8
Platelet count (10^{*9}/l)	215	150 – 450
Urea (mmol/l)	3.6	3.0 – 8.0
Creatinine (umol/l)	79	49 – 106
LDH (U/l)	375	220 – 450
Ca (mmol/l)	2.47	2.02 – 2.65
Total protein (g/l)	65	64 – 83
Albumin (g/l)	45	35 – 52
Globulins (g/l)	20	20 – 31
CRP (mg/l)	2.0	0 – 5.0
Fibrinogen (g/l)	2.9	2.0 – 4.5
ESR (mm/h)	15	0 – 15



Slika 1. *MSCT* grudnog koša, abdomena i male karlice (nalaz uredan

Figure 1. MSCT of the chest, abdomen, and lesser pelvis (normal finding)

fovir) kako bi se sprečila reaktivacija infekcije.

Urađeni rentgen celokupnog koštanog sistema nije utvrdio postojanje osteoliznih lezija. Postavljena je konačna dijagnoza: solitarni plazmocitom limfnog čvora cervikalne regije. Prepisana je *IF* radioterapija (engl. *involved-field radiotrherapy – IFRT*) cervikalne regije desno, uz aktivno lečenje od strane infektologa.

DISKUSIJA

Ekstramedularni plazmocitom je retka forma plazmocitne diskrazije i čini 1,6% do 4% svih tumora plazma ćelija [11,12]. Ekstramedularna lokalizacija plazmocitoma se može inicijalno utvrditi na bilo kom organu, kao primarni tumor ili sistemska metastaza multiplog mijeloma. Najučestalija lokalizacija je u kostima, i čini oko 40% svih ekstramedularnih lokalizacija, a pri tom su odsutni *CRAB* kriterijumi za dijagnozu multiplog

HBs At negative (1.13 S/CO), while HCV At (0.06 S/CO) and HIV At were negative (0.88 S/CO). The infectious disease specialist started the patient on antiviral therapy (tenofovir) to prevent the reactivation of the infection.

An X-ray of the entire skeleton did not establish the presence of osteolytic lesions. A definitive diagnosis was established – solitary plasmacytoma of a lymph node in the cervical region. Involved-field radiotherapy (IFRT) of the right cervical region was prescribed along with active treatment by an infectious disease specialist.

DISCUSSION

Extramedullary plasmacytoma is a rare form of plasmacytic dyscrasia that accounts for 1.6% to 4% of all plasma cell tumors [11,12]. Extramedullary localization of plasmacytoma can be initially identified in any organ, as a

mijeloma, infiltracija u koštanoj srži je manja od 10% monoklonskih plazmocita, nema osteoliznih lezija na koštanom sistemu, nema monoklonskih lakih lanaca u serumu i urinu [13]. Kao solidni tumor, ekstramedularni plazmocitom najčešće zahvata gornji respiratorni trakt, uključujući nazalnu regiju, sinuse, orofarinks, pljuvačne žlezde i larinks – čak 80% prikazanih slučajeva plazmocitoma pripada ovoj regiji. Slede gastrointestinalni i urogenitalni trakt, koža i pluća [14–17].

Primarni plazmocitom u limfnom čvoru je posebno redak. On je primarno lokalizovan samo u limfnom čvoru a bez evidentne proliferacije plazmocita na bilo kojoj drugoj lokalizaciji i bez postojanja bilo kakve limfomske komponente u obolelog [18].

Prikazani bolesnik je imao uvećan solitarni limfni čvor, sa imunohistohemijski dokazanim monoklonskim plazmocitima u čvoru, bez izmene u skeletnom sistemu, bez infiltracije koštane srži patološkim monoklonskim plazmocitima, bez limfadenopatije na drugim lokalizacijama i bez izmene na drugim organima. Nije evidentirana nikakva limfomska komponenta bolesti.

Solitarni ekstramedularni plazmocitom je visoko radiosenzitivan tumor. Uspeh lečenja lokalnom radioterapijom (RT) ogleda se u dobrom odgovoru u 80% – 100% slučajeva. Optimalna doza je 40-50 Gy u 20 frakcija.

Hirurška biopsija je odgovorna za dijagnozu, ali radikalna hirurgija nije uobičajeno indikovana za lečenje, jer je tumor radiosenzativan i radioterapija je kurativna kod najvećeg broja obolelih [8,18]. Kod našeg bolesnika, limfni čvor je bio promera 30 mm x 15 mm i kompletno je hiruški ekstirpiran.

Plazmocitom, primarno u limfnom čvoru, može se prezentovati i diseminovanom limfadenopatijom, ali retko prelazi u multipli mijelom. Preživljavanje u bolesnika sa plazmocitomom je značajno duže nego onih obolelih od multiplog mijeloma [9]. Svakako, kod prikazanog bolesnika izolovano je bila bolesna jedna žlezda – solitarni plazmocitom, koja je hiruški odstranjena a potom je sprovedena i lokalna radioterapija. U daljem toku se podrazumeva redovno praćenje.

ZAKLJUČAK

Svaka limfadenopatija zahteva ozbiljan pristup kliničara, a da li je HBV infekcija bila okidač za nastanak plazmocitoma, ostaje za razmišljanje.

Sukob interesa: Nije prijavljen.

primary tumor or a systemic metastasis of multiple myeloma. The most common localization is in the bones, and it accounts for about 40% of all extramedullary localizations, while the CRAB criteria for the diagnosis of multiple myeloma are absent; infiltration in the bone marrow is less than 10% of monoclonal plasma cells, there are no osteolytic lesions in the skeleton, there are no monoclonal light chains in the serum and urine [13]. As a solid tumor, extramedullary plasmacytoma most often affects the upper respiratory tract, including the nasal region, sinuses, oropharynx, salivary glands, and larynx – as many as 80% of plasmacytoma cases presented in literature belong to this region, followed by the gastrointestinal and urogenital tracts, the skin, and lungs [14–17].

Primary plasmacytoma in a lymph node is particularly rare. It is primarily localized only in the lymph node, without evident proliferation of plasma cells in any other location and without the presence of any lymphoma component in the patient [18].

The patient presented in our article had an enlarged solitary lymph node, with immunohistochemically proven monoclonal plasma cells in the node, no lesions in the skeletal system, no bone marrow infiltration by pathological monoclonal plasma cells, no lymphadenopathy in other locations, and no lesions in other organs. No lymphoma component of the disease was recorded.

Solitary extramedullary plasmacytoma is a highly radiosensitive tumor. The success of treatment with local radiotherapy (RT) is reflected in a good response in 80% – 100% of cases. The optimal dose is 40-50 Gy in 20 fractions.

Surgical biopsy is used for diagnosis, but radical surgery is not usually indicated for treatment, because the tumor is radiosensitive and radiotherapy is curative in the majority of patients [8,18]. In our patient, the lymph node was 30 mm x 15 mm in diameter and was completely surgically excised.

Plasmacytoma, primarily in the lymph node, may also present with disseminated lymphadenopathy, but it rarely progresses to multiple myeloma. Survival in patients with plasmacytoma is significantly longer than in patients with multiple myeloma [9]. Certainly, in the presented patient, one gland was diseased in isolation – a solitary plasmacytoma, which was surgically removed, after which local radiotherapy was applied. Future regular follow-up of the patient is required.

CONCLUSION

Every case of lymphadenopathy requires a serious approach on the part of the physician, and whether HBV infection was the trigger for the formation of plasmacytoma remains to be considered.

Conflict of interest: None declared.

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