Synchronous mantle cell lymphoma and prostate adenocarcinoma – is it just a coincidence?

Istovremena pojava mantle čelijskog limfoma i adenokarcinoma prostate – samo slučajnost ili ne

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Abstract

Introduction. Synchronous occurrence of lymphomas and other cancers, mostly carcinomas are well established. The most of cases describe chronic lymphocytic leukemia as the leading lymphoproliferative disease with the tendency towards secondary malignancies development. Mantle cell lymphoma (MCL) has been described in only 2 cases to co-occur with prostate adenocarcinoma (PAC). There are scarce data about the connection between MCL and urology cancers. We presented the first case of synchronous occurrence of MCL and PAC in the same patient in Serbia.

Case report. A 64-year-old male initially presented with fatigue, splenomegaly, and bicytopenia. The bone marrow biopsy specimen revealed extensive infiltration with MCL. During lymphoma staging procedure prostate enlargement (57 mm) was accidentally found by multislice-computed tomography (MSCT). The serum prostate specific antigen (PSA) was elevated (52 ng/mL; normal values ≤ 4 ng/mL). Transrectal ultrasound biopsy revealed PAC. High Gleason score determined high-risk locally advanced PAC. The patient underwent treatment with chemotherapy and hormone therapy due to the existence of double malignancies. Cyclophosphamide, doxorubicin, vincristine, prednisone (CHOP) was applied for MCL, and luteinizing hormone-releasing hormone (LHRH) agonist, triptorelin, for PAC. Paradoxical remission was obtained for MCL, and stable disease for PAC. In a 1.5-year observation period the patient was still disease progression free for both of malignancies.

Conclusion. This case points out that elderly males are in need for careful observation during the staging procedure for lymphoma. The literature data suggest that MCL patients are in increased risk for urologic malignancies development. However, the etiologic connection between these two entities, except male gender and older age, remains unclear.

Key words: lymphoma, mantle-cell; prostatic neoplasms; adenocarcinoma; diagnosis; comorbidity; risk assessment.

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Apstrakt


Prikaz bolesnika. Muškarac, star 64 godine, najpre je doživio zbog pojave malaksalosti, splenomegalije i bicitopenije. Uzorak koštne srži pokazao je ekstenzivnu infiltraciju čelijskog limfoma. U toku procedure stadiranja limfoma slučajno je, primenom multislice-kompjuterizovane tomografije (MSCT) otkrivena prostate (57 mm). Prostata-specifični antigen (PSA) u serumu bio je povišen – 52 ng/mL (normalna vrednost ≤ 4 ng/mL). Transrektalna ultrazvučna biopsija pokazala je PAC. Visok Gleason skor ukazao je na visokorizični lokalno uznapređovali PAC. Bolesnik je lećen i hemoterapijom i hormonoterapijom zbog postojanja dualnog maligniteta. Protokol ciklofosfamid, dokorubicin, vinkristin i prednizuon (CHOP) primenjen je za MCL, uključujući hormon oslobađajući hormon (LH/RH) agonist, triptorelin za PAC. Paradijalna remisija postignuta je za MCL, a za PAC stabila bolest. U periodu od 1,5-godišnjeg praćenja bolesnik nije imao progresiju ovih bolesti. Ovaj prikaz ukazuje na to da stariji bolesnici zahtevaju pažljivije osparvanje u toku postupka stadiranja limfoma. Podaci iz literature sugerišu da bolesnici sa MCL imaju povišen rizik od razvoja uroloških maligniteta. Ipak, etiološka veza između ovih dva entiteta, osim muškog pola i starijeg životnog doba, ostaje nejasna.

Ključne reči: limfom, mantle-čelijski; prostata, neoplazme; adenokarcinom; dijagnoza; komorbiditet; rizik, procena.
Introduction

Mantle cell lymphoma (MCL) accounts for 2–10% of all non-Hodgkin lymphomas (NHL), with male predominance 2.3–2.5 : 1, and a median age at presentation close to 70 years. The stage is usually advanced, adenopathy typically non-bulky, with frequent extranodal involvement (bone marrow, leukemic presentation, liver, spleen, or Waldeyer ring). Gastrointestinal involvement in the form of multiple lymphomatous polyposis may be one of the possible presentation 2. The blastoid variant is rare but highly aggressive. MCL is characterized by the chromosomal translocation t(11; 14) (q13; q32), resulting in constitutinal overexpression of cyclin D1 and cell cycle dysregulation in virtually all cases 3. Cyclin D1 is detected by immunohistochemistry in 98% of MCL, although in remaining cases it may lack 4. The SOX11 is highly expressed in both Cyclin D1 negative and positive MCL suggesting this biomarker as an important factor in the pathogenesis of MCL 5.

Based on the results of Surveillance, Epidemiology, and End Results (SEER), for the period of 2008–2012 year, prostate cancer was fairly common with the incidence rate of 137.9/100,000 per year in all races. The same data source indicates a 5-year survival rate above 98% for the disease. The risk of clinically significant prostate cancer is related to age, ethnicity, family history, prostate specific antigen (PSA) level, free-total PSA ratio and findings on digital rectal examination (DRE) 7. PSA, although not highly specific, combined with DRE are the most commonly used clinical tools for prostate cancer early detection. The plasma PSA level, Gleason score and tumor-node-metastasis (TNM) classification are used for risk assessment of localized disease 8. The prostate cancer antigen 3 (PCA-3) has higher specificity, as well, positive and negative predictive values over PSA, although its sensitivity is slightly weaker. Therefore, it has stronger power in predicting patients who will benefit from prostate biopsy 9. Transrectal ultrasound (TRUS) biopsy of prostate with the minimum of 10–12 cores obtained is one of the diagnostic standards 8.

The association between MCL and urologic cancers was documented by some authors 10. Both malignancies are related to the patient age and gender. However, every other connection between these two conditions remains unknown or unexplored. We presented the first published case of synchronous occurrence of MCL and PAC in the same patient in Serbia.

Case report

A 64-year-old male had complaints of fatigue and feeling pressure under the left rib cage. Those were the only symptoms he had. Basic clinical examinations revealed splenomegaly and generalized lymphadenopathy. The routine blood picture showed marked bicytopenia [white blood cells – WBC 2.9 × 10^9/L, normal range (nr) 4–9 × 10^9/L; absolute neutrophil count (ANC) 0.6 × 10^9/L (nr 1.7–7.7 × 10^9/L); platelet (PLT) 55 × 10^9/L, (nr 120–380 × 10^9/L)]. The diagnostic trephine biopsy was performed and revealed extensive MCL infiltration of the bone marrow. Immunohistochemistry was typical: CD79a+, CD5+, CD20+, CyclinD1+, CD23−, CD43−/+ , CD3− (Figures 1a–d).

Discussion

MCL and PAC are diseases of predominantly elderly male population. However, co-occurrence of both diseases in the same patient at presentation has been rarely described in the literature. We found only 2 published cases of synchronous MCL and PAC co-existence. He et al. 11 described the cohort of 13 patients with indolent lymphomas, most of them with chronic lymphocytic leukemia and only 1 had MCL. Five of those patients underwent radical prostatectomy and developed lymphoma progression after the intervention. The patient with MCL received chemotherapy and had disease progression.
Rajput et al. described a case of both PAC and MCL in the prostate tissue of the same patient at the onset. A relation between those two entities is unknown and unexplored. Barista et al. found only a statistical significance in the number of additional neoplasms occurring in patients with MCL compared with the general population. In their cohort of MCL patients (n = 156), a higher number of cases with urologic cancer was reported, suggesting the possible association between those two malignancies. Proposed mechanisms may underlie genetic predisposition or some other common causes for both tumor groups. The detection of a concomitant neoplasm may be a consequence of early detection by procedure used in the diagnosis, staging and subsequent evaluation of response to treatment for the first malignancy. Moreover, elevated risks of dual malignancy may reflect the effects of host susceptibility or shared etiological factors.

Standardized treatment considering such a specific situation is undefined. Our strategy was to treat both coexisting malignancies. Rituximab (R) – CHOP is the mostly applied treatment for MCL, with proven benefit of R maintenance in elderly. R-bendamustine could be considered as rational alternative with less toxic effects and increased progression-free survival. Median overall survival for intermediate risk MCL is 51 months. Being incurable disease with inevitably relapse, salvage regimens are expected. New agents are in great expansion with promising results. In our circumstances only CHOP could be applied. PAC usually has a long-term evolution. The presented patient had locally advanced high-risk PAC which was asymptomatic. According to the ESMO 2015 guidelines recommendations, there are few different treatment strategies which could be applied in a concrete situation. Watchful waiting strategy with delayed hormone therapy is reserved for those who are not fit or unwilling to have treatment with curative intent. External beam radical radiotherapy plus hormone treatment could be another option. Radical prostatectomy with extended lymphadenectomy could be considered in highly selected cases. We decided to treat the presented patient with hormone LH/RH agonist only. This decision was made with respect to the presence of co-existing immunological cancer which could lead to increased risk of both cancers dissemination. While hormonally-sensitive PAC should be treated with dif-
ferent hormone blockers and upon the development of metastatic castration-resistant disease, chemotherapy on the basis of taxanes is recommended.

Nevertheless, the presented patient had two incurable diseases with relatively long-term survival rates. In this sense the main strategy should be to provide best supportive care with maximal duration of life quality, and not insisting on radical treatment methods.

**Conclusion**

This case report points out that elderly males need careful observation during the staging procedure for lymphoma. We can only assume that the only visible connections in synchronous MCL and PAC occurrence are older age at onset and male gender, or these findings remain just coincidental.

**REFERENCES**


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