University of Novi Sad, Faculty of Medicine Novi Sad,
Department of Histology and Embryology, Novi Sad[1]
Clinical Center of Vojvodina Novi Sad, Pathology and Histology Center[2]
Institute for Pulmonary Diseases of Vojvodina, Sremska Kamenica
Clinic of Granulomatous and Interstitial Lung Diseases[3]
Clinical Center of Vojvodina Novi Sad, Emergency Center, COVID Hospital[4]
Otorhinolaryngology and Head and Neck Surgery Clinic[5]
Clinic of Gynecology and Obstetrics[6]

Case report
Prikaz slučaja
UDK 616.68-033.2-036.8
UDK 616-006.44-06
https://doi.org/10.2298/MPNS2208259I

BONE MARROW METASTASIS FROM TESTICULAR SEMINOMA IN A PATIENT WITH CONCOMITANT FOLLICULAR NON-HODGKIN LYMPHOMA – A CASE REPORT

METASTAZA SEMINOMA U KOŠTANU SRŽ PACIJENTA SA KONKOMITANTNIM FOLIKULARNIM NON-HOČKIN LIMFOMOM – PRIKAZ SLUČAJA

Jelena ILIĆ SABO[1, 2], Stefan IVIĆ[2], Ana MILENKOVIĆ[3], Milica TRKULJA[4], Vanja TOVILOVIĆ[5] and Borislav GOLIJAN[6]

Summary

Introduction. Seminomas are the most common testicular tumors. Initial therapy includes orchiectomy with resection of local lymph nodes, followed by adjuvant radiotherapy. Testicular tumors usually metastasize to retroperitoneal and mediastinal lymph nodes, lungs, liver, spleen, gastrointestinal tract, and adrenal glands. Bone metastases from testicular tumors are very rare, while seminoma metastasis to the bone marrow is a curiosity, without any references in the scientific literature. **Case Report.** A 66-year-old patient, previously treated for follicular non-Hodgkin lymphoma, was admitted due to complaints of malaise, abdominal and back pain, and hepatosplenomegaly. After examination and radiologically verified enlarged retroperitoneal lymph nodes, the patient was referred to a hematologist. Based on the patient's medical history, a relapse of lymphoma was suspected, and bone marrow biopsy was performed. The hematoxylin-eosin staining of the biopsy sample showed diffuse large cell infiltrates with bright cytoplasm, polygonal nuclei and prominent nucleoli. By immunohistochemical staining, the cells showed positivity for cluster of differentiation 10, cluster of differentiation 117, octamer binding transcription factor 3/4, placental alkaline phosphatase, and cytokeratin 8/18, after which the diagnosis of seminoma metastasis to the bone marrow was made. Shortly after the histopathological diagnosis was made, the patient died. **Conclusion.** A seminoma is a testicular tumor with a favorable prognosis. Due to suppression of hematopoiesis, bone marrow metastases generally lead to the worst prognosis. The outcome of our patient highlights the importance of timely diagnosis and therapy, which would increase the chances of survival.

Key words: Bone Marrow; Neoplasm Metastasis; Testicular Neoplasms; Seminoma; Lymphoma, Non-Hodgkin; Biopsy; Immunohistochemistry

Sažetak

Uvod. Seminomi su najčešći tumori testisa. Primarnu terapiju predstavlja orhiektomija sa resekcijom lokalnih limfnih nodusa, nakon čega sledi adjuvantna radioterapija. Tumori testisa najčešće metastaziraju u retroperitonealne, medijastinalne limfne noduse, pluća, jetru, slezinu, gastrointestinalni trakt i nadbubrežne žlezde. Retki su slučajevi koštanih metastaza tumora testisa, dok metastaza seminoma u koštanu srž predstavlja kuriozitet bez postojećih navoda u literaturi. **Prikaz slučaja.** Pacijent starosti 66 godina, ranije lečen od folikularnog nehočkinskog limfoma, javlja se na pregled zbog tegoba u vidu malaksalosti, bolova u stomaku i leđima i hepatosplenomegalije. Nakon pregleda i radiološki verifikovanih uvećanih retroperitonealnih limfnih čvorova, pacijent je upućen hematologu. Na osnovu anamnestičkih podataka, postavljena je sumnja na relaps limfoma, nakon čega je načinjena biopsija koštane srži. U bioptičkom uzorku, bojenom hematoksilin-eozin metodom, uočena je difuzna ćelijska infiltracija krupnim ćelijama, svetle citoplazme, poligonalnih jedara sa prominentnim jedarcima. Imunohistohemijskim bojenjem ćelije su pokazale pozitivnost na CD10, CD117, OCT3/4, PLAP, CK8/18 nakon čega je postavljena dijagnoza metastaze seminoma u koštatnoj srži. Ubrzo nakon postavljanja patohistološke dijagnoze, pacijent je preminuo. **Zaključak.** Seminom spada u prognostički povoljne tumore. Metastaze u koštanoj srži, zbog supresije hematopoeze, generalno dovode do lošije prognoze za pacijente. Ishod bolesti našeg prikazanog pacijenta upravo ukazuje na lošiju prognozu, kao i na važnost pravovremene dijagnostike i terapije, čime bi šanse za preživljavanjem bile veće.

Ključne reči: koštana srž; metastaze; neoplazme testisa; seminom; non-Hočkinov limfom; biopsija; imunohistohemija

Introduction

Seminomas are the most common testicular tumors. They usually occur in patients aged 40 to 50 years, presenting as painless testicular masses [1, 2].

Macroscopically, seminomas are soft, well-demarcated, grayish-white tumors that bulge from the cut surface of the affected testis. Large tumors may contain foci of necrosis, usually without hemorrhage. They are composed of large, uniform cells with dis-

Corresponding Author: Doc. dr Jelena Ilić Sabo, Medicinski fakultet Novi Sad, KCV - Centar za patologiju i histologiju, 21000 Novi Sad, Hajduk Veljkova 1-7, E-mail: jelena.ilic-sabo@mf.uns.ac.rs

Abbreviations

CD10 – cluster of differentiation 10
CD117 – cluster of differentiation 117
PLAP – placental alkaline phosphatase
OCT3/4 – octamer binding transcription factor 3/4
CK8/18 – cytokeratin 8/18
HE – hematoxylin and eosin

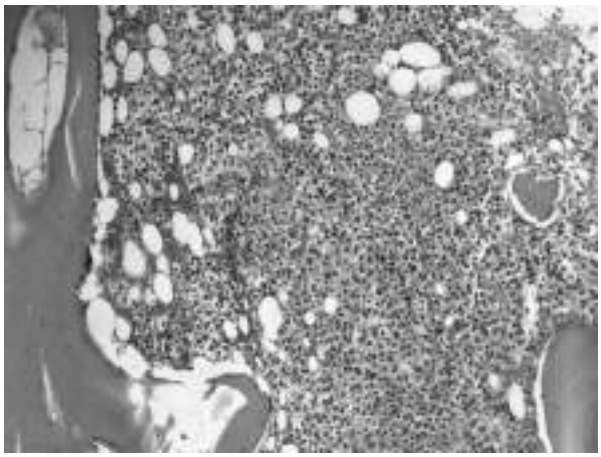

Figure 1. Bone marrow metastasis from a testicular seminoma (HE x 100); Diffuse large cell infiltrates with bright cytoplasm, polygonal nuclei and prominent nucleoli in the bone marrow
Slika 1. *Metastaza seminoma u koštanu srž, hematoksilin-eozin x 100 – Difuzna infiltracija koštane srži krupnim ćelijama, svetle citoplazme, poligonalnih jedara sa prominentnim jedarcima*

tinct cellular borders, clear, glycogen-rich cytoplasm, round nuclei with conspicuous nucleoli. The cells are often arranged in small lobules, separated by fibrous septa. Lymphocytic infiltrate is usually present and may overshadow the neoplastic cells [1, 2].

Initial therapy includes orchiectomy with resection of local lymph nodes, followed by adjuvant radiotherapy or chemotherapy [1, 2]. There are few techniques for fertility preservation, such as cryopreservation of gametes and embryos which proved to be efficient and safe, while there are also some experimental techniques like cryopreservation of gonadal tissue and cells that are not yet used in daily practice [3].

Testicular tumors most often metastasize to retroperitoneal and mediastinal lymph nodes, lungs, liver, spleen, gastrointestinal tract, and adrenal glands. Bone metastases from testicular tumors are very rare, while metastasis from seminoma to the bone marrow is a curiosity, not reported in scientific literature [4, 5].

Case Report

A 66-year-old patient, previously treated for follicular non-Hodgkin lymphoma, was admitted due to complaints of malaise, abdominal and back pain, and hepatosplenomegaly. After the initial physical examination and radiologically verified enlarged retroperitoneal lymph nodes, the patient was referred to a hematologist. Based on the patient's medical history, a relapse of lymphoma was suspected, and trephine bone marrow biopsy was performed.

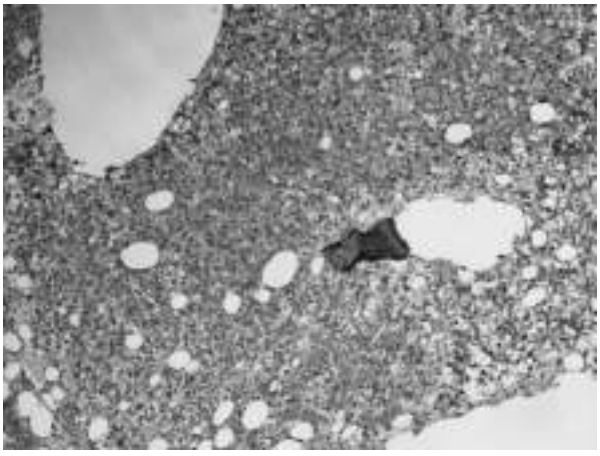

Figure 2. Seminoma tumor cells in the bone marrow express immunohistochemical positivity for CD 117 (HE x 100)
Slika 2. *Tumorske ćelije seminoma u koštanoj srži pokazuju imunohistohemijsku pozitivnost na CD 117, hematoksilin-eozin x 100*

The hematoxylin-eosin (HE) staining of the biopsy sample showed diffuse large cell infiltrates with bright cytoplasm, polygonal nuclei and prominent nucleoli **(Figure 1)**. The cells showed immunohistochemical positivity for cluster of differentiation 10 (CD10), cluster of differentiation 117 (CD117) **(Figure 2)**, placental alkaline phosphatase (PLAP) **(Figure 3)**, octamer binding transcription factor (OCT) 3/4 **(Figure 4)**, and cytokeratin (CK) 8/18, after which the diagnosis of seminoma metastasis to the bone marrow was made. Shortly after the histopathological diagnosis was made, the patient unfortunately died.

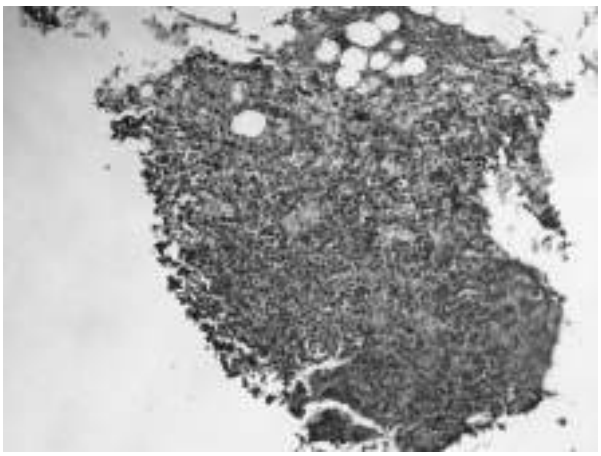

Figure 3. Seminoma tumor cells in the bone marrow express immunohistochemical positivity for PLAP (HE x 100)
Slika 3. *Tumorske ćelije seminoma u koštanoj srži pokazuju imunohistohemijsku pozitivnost na placentnu alkalnu fosfatazu, hematoksilin-eozin x100*

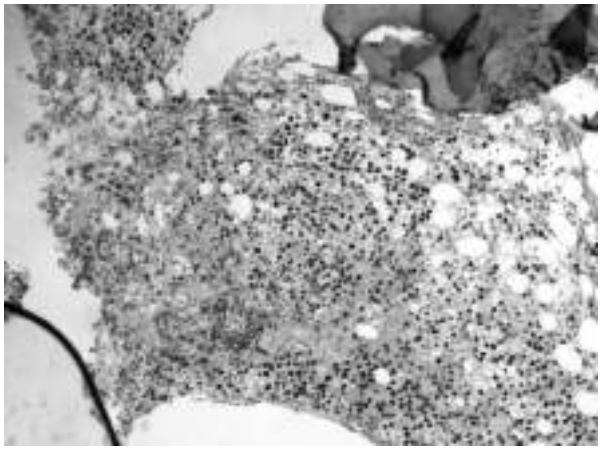

Figure 4. Seminoma tumor cells in the bone marrow express immunohistochemical positivity for OCT3/4 (HE x 100)
Slika 4. *Tumorske ćelije seminoma u koštanoj srži pokazuju imunohistohemijsku pozitivnost na OCT3/4, hematoksilin-eozin x 100*

Discussion

As mentioned above, seminomas are the most common testicular tumors, followed by mixed germ cell tumors, often including seminomas. In the majority of cases the disease is diagnosed in the early stage [1, 2]. Even though, subclinical metastases in the retroperitoneum occur in about 15 – 20% of patients with stage I seminoma. Since the risk of disease recurrence is considerably high, the initial therapy includes radical orchiectomy followed by adjuvant radiotherapy, sometimes combined with chemotherapy [1, 2]. Germ cell testicular tumors have worse prognosis than seminomas, with recurrence and distant metastases being much more common [6].

The common sites of testicular tumors metastases are retroperitoneal and mediastinal lymph nodes, lungs, liver, spleen, and suprarenal glands [1, 2]. Individual, retrospective studies of testicular tumors noted some unusual sites of metastasis such as: kidneys, inferior vena cava, muscles, pelvis, seminal vesicles, prostate and pericardial tissue [4].

The bone metastases from testicular tumors are very rare (3 – 9%). The majority are found in patients with mixed germ cell tumors (77%), while pure seminomas account only for 23% of cases [6, 7]. According to the study of 154 autopsies of patients with testicular tumors, bone metastases were found only in 40 patients (26% of cases), but none of the metastases were in the bone marrow [7]. An extremely extensive study dealing with the presence of solid tumor metastases in the bone marrow, showed that out of 73 cases, just one bone marrow metastasis was from a testicular tumor (1.4%) [8]. A study that specially focused on seminomas showed that there were no cases of bone marrow metastases [9]. A study which analyzed 2,550 patients with bone metastases of primary tumors showed that there were only 3 cases of seminoma metastases in the bones [10]. There were also a few cases of seminoma metastases detected in the spinal cord [11] and also concomitant metastases in the bones and central nervous system [12]. A rare case of a non-seminomatous germ cell testicular tumor with jaw metastasis was also reported [13].

After an extensive literature research, we found only one case of bone marrow infiltration with mixed germ cell testicular tumor [6], but still we did not find a single case of bone marrow metastasis from testicular seminoma.

Conclusion

A seminoma is a testicular tumor with a favorable prognosis. Due to suppression of hematopoiesis, bone marrow metastases generally lead to the worst prognosis. The outcome of our patient highlights the importance of timely diagnosis and therapy, which would increase the chances of survival.

References

1. Oldenburg J, Berney DM, Bokemeyer C, Climent MA, Daugaard G, Gietema JA, et al. Testicular seminoma and non-seminoma: ESMO-EURACAN Clinical Practice Guideline for diagnosis, treatment and follow-up. Ann Oncol. 2022;33(4):362-75.

2. Albers P, Albrecht W, Algaba F, Bokemeyer C, Cohn-Cedermark G, Fizazi K, et al. Guidelines on testicular cancer: 2015 update. Eur Urol. 2015;68(6):1054-68.

3. Nikoletić K, Mihailović J, Matovina E, Žeravica, R, Srbovan, D. Reliability of positron emission tomography-computed tomography in evaluation of testicular carcinoma patients. Med Pregl. 2015;68(3-4):109-15.

4. Degirmencioglu S, Degirmencioglu B. Isolated femoral muscle and bone metastases rarely encountered in testicular seminoma. Case Rep Oncol Med. 2013;2013:780493.

5. Kumar U, Ramteke P, Das P, Gogia A, Tanwar P. Isolated bone marrow metastasis of testicular tumor: a rare cause of thrombocytopenia. Urol Ann. 2017;9(1):96-8.

6. Oing C, Oechsle K, Necchi A, Loriot Y, De Giorgi U, Flechon A, et al. Impact of primary metastatic bone disease in germ cell tumors: results of an International Global Germ Cell Tumor Collaborative Group G3 Registry Study. Ann Oncol. 2017;28(3):576-82.

7. Bredael JJ, Vugrin D, Whitmore WF Jr. Autopsy findings in 154 patients with germ cell tumors of the testis. Cancer. 1982;50(3):548-51.

8. Kilickap S, Erman M, Dincer M, Aksoy S, Harputluoglu H, Yalcin S. Bone marrow metastasis of solid tumors: clinicopathological evaluation of 73 cases. Turkish Journal of Cancer. 2007;37(3):85-8.

9. Rick O, Siegert W, Schwella N, Dubiel M, Krusch A, Beyer J. Seminoma: high-dose chemotherapy as salvage treatment for seminoma. Bone Marrow Transplant. 2002;30(3):157-60.

10. Jamal-Hanjani M, Karpathakis A, Kwan A, Mazhar D, Ansell W, Shamash J, et al. Bone metastases in germ cell tumours: lessons learnt from a large retrospective study. BJU Int. 2013;112(2):176-81.

11. Fard-Esfahani A, Marzban M, Emami-Ardekani A, Hassanzadeh-Rad A, Fallahi B, Beiki D, et al. Spinal cord me-

tastasis from testicular seminoma detected by F-18 FDG PET/CT study prior to neurological symptoms: an unusual presentation. Iranian Journal of Nuclear Medicine. 2016;24(2):147-9.

12. Gómez FJ, Bánez IA, González RL, Jiménez-Granero P, Dorado IB. 18F-FDG PET/CT with unusual bone and CNS metastases from testicular seminoma. Int Braz J Urol. 2015;41(2):393-4.

13. Siverino RO, Uccello A, Giunta ML, Uccello M, Amadio P, Petrillo G. Non-seminomatous germ cell tumor metastasis to the jaw: an imaging case report. Iran J Radiol. 2016;13(3):e27812.

Rad je primljen 17. XI 2022.
Recenziran 7. XII 2022.
Prihvaćen za štampu 7. XII 2022.
BIBLID.0025-8105:(2022):LXXV:7-8:259-262.