A Rare Coexistence of Seminoma and Hodgkin’s Lymphoma in Hawai‘i

Zhaohui Liao Arter MD; Sanket Meghpara MD; Salvatore Mignano DO; and Jeffrey Berenberg MD

Abstract

Both Hodgkin’s lymphoma and testicular cancers can present in young men; however, concurrent Hodgkin’s lymphoma with seminoma is very rare. When they do coexist, careful consideration must be made to avoid missing new cancer by assuming the presence of primary metastatic disease when lymphadenopathy presents. Here we present a rare case of coexistence of seminoma and Hodgkin’s lymphoma and the staging and treatment challenges associated with a 2-cancer diagnosis.

Keywords

Hodgkin’s lymphoma, testicular cancer, seminoma, coexisting malignancies

Abbreviations and Acronyms

HL = Hodgkin’s lymphoma
CT = computerized tomography
PET = positron emission tomography
FNA = fine needle aspiration
BEP = bleomycin, etoposide, cisplatin
BV+AVD = brentuximab, vedotin, doxorubicin, vinblastine, and dacarbazine
TNMS = tumor, nodes, metastasis, serum biomarkers
ABVD = dexamethasone, bleomycin, vinblastine, and dacarbazine
EP = etoposide and cisplatin
LDH = lactate dehydrogenase
hCG = human chorionic gonadotropin
AFP = alpha-fetoprotein

Introduction

Testicular cancers are the most common solid tumor among young men aged 15 years to 34 years, estimating 5.6 cases per 100,000 persons per year. Among testicular cancer, germ cell tumors, including seminomas, make up 95% of all the cases. In the United States, Hodgkin’s lymphoma (HL) accounts for approximately 10% of all lymphomas and 0.6% of all cancers. HL has a bimodal age distribution, with a peak in late adolescence or young adulthood and a second peak in older adults.

Although both HL and germ cell tumors can present in young men, concurrent HL with seminoma is very rare. In the literature, there have been only a few reported cases. The clinical presentation for both malignancies is variable. This case demonstrates the diagnostic challenges posed and the clinical acumen and a full pathologic evaluation required to avoid a diagnostic error. Although both malignancies are chemotherapy-sensitive, the choice of regimens is different. Without any current guidelines, the therapeutic strategy can also be challenging.

Case Report

A 39-year-old active-duty man presented with new onset of right testicular discomfort for the past week after lifting weights. He denied any dysuria, penile discharge, fever, fatigue, weight loss, night sweats, or loss of appetite. His physical exam showed no palpable lymphadenopathy but was significant for a large, hard, tender right testicular mass. Scrotal ultrasound was positive for a hypervascular testicular mass. Orchiectomy revealed a 4.2-cm well-circumscribed testicular mass. Pathology showed a fibrous pseudocapsule; cells were arranged in diffuse, solid growth patterns with abundant intratumoral lymphocytes (Figure 1A). At high-power magnification, the tumor showed many large tumor cells with abundant clear to amphophilic cytoplasm, enlarged nuclei, and prominent macronucleoli (Figure 1B). These findings were diagnostic of pure seminoma. Lactate dehydrogenase (LDH), human chorionic gonadotropin (hCG), and alpha-fetoprotein (AFP) were within normal limits. Computed tomography (CT) of the neck, chest, abdomen, and pelvis revealed both an enlarged right external iliac and a left supraclavicular lymph node. Fine needle aspiration (FNA) of the left supraclavicular lymph node showed atypical cells suspicious for malignancy (Figure 1C and 1D) felt to be consistent with the diagnosis of seminoma (IIIA). Chemotherapy with bleomycin, etoposide, cisplatin (BEP) was initiated. An excisional biopsy of the supraclavicular lymph node was performed 9 days later. The final supraclavicular lymph node biopsy revealed classical Hodgkin lymphoma, lymphocyte rich subtype (Figure 1E and 1F). Immunohistochemical stains were performed. The neoplastic cells were positive for CD15, CD30, and weakly positive with PAX5 (Figure 1G). These cells were negative for CD3 (Figure 1H), CD20, and CD45, a characteristic but nonspecific feature of Hodgkin’s lymphomas. Staging positron emission tomography (PET)/CT showed lymphadenopathy in multiple locations, including supraclavicular, subcarinal, right external iliac, and right iliac bone lytic lesion (Figure 1I). Biopsy of the right iliac bone lesion was negative for malignancy. The patient continued therapy to complete a total of 3 cycles of BEP and repeat CT chest/abdomen/pelvis showed resolution of lymphadenopathy only at the right external iliac location.
Figure 1. A. Low-power view of seminoma. Large cells with clear to amphophilic cytoplasm, enlarged nuclei, and macronucleoli arranged in a solid growth pattern. There are abundant benign, small mature lymphocytes (x400, hematoxylin & eosin [H&E]). B. High-power view of seminoma, highlighting the cytologic features of the malignant cells with delicate, vacuolated chromatin, enlarged nuclei, and macronucleoli. Occasional binucleation is noted. Characteristic, abundant background lymphocytes and other leukocytes are seen (x4000, H&E). C. Low-power view of supraclavicular lymph node cytologic preparations (Pap-stained smear) revealed many lymphoid tangles. D. High-power view of supraclavicular lymph node aspiration (DiffQuik-stained smear). A few scattered single atypical cells in a background of polymorphous lymphocytes and histiocytes. These atypical cells display large irregular hyperchromatic nuclei, irregular nucleoli, and scant to moderate cytoplasm. E. Low-power view of supraclavicular lymph node excisional biopsy. An enlarged lymph node effaced by a vaguely nodular proliferation of small mature lymphocytes and scattered larger, neoplastic cells (x200, H&E). F. High-power of supraclavicular lymph node excisional biopsy. Neoplastic, binucleate cells, consistent with Reed-Sternberg (or Hodgkin) cells, rimmed by mature small lymphocytes (x4000, H&E). G. The scattered neoplastic cells are weakly positive for PAX5 (x4000, histochemistry, PAX5). H. The neoplastic cells are negative for CD3, CD20, and CD45. Nevertheless, benign background lymphocytes highlight these stains, showing a characteristic rimming pattern around the neoplastic cells, as pictured here (x4000, immunohistochemistry, CD3). I. Positron emission tomography and computed tomography revealed hypermetabolic activity in the left supraclavicular lymph node (Deauville score 2), subcarinal lymph node of 2.4 cm x 1.6 cm (Deauville score 3), right external iliac lymph node (Deauville score 4), and right iliac bone lytic lesion (Deauville score 3).

Given the distribution of the lymphadenopathy and resolution of the adenopathy below the diaphragm following BEP treatment, the diagnosis of stage IIA seminoma coexistent with stage II Hodgkin’s lymphoma was confirmed. The patient was started on brentuximab vedotin in combination with doxorubicin, vinblastine, and dacarbazone (BV+AVD) for Hodgkin’s lymphoma with complete metabolic response on PET/CT after 4 cycles.

Discussion

Testicular cancer is usually staged using the TNMS system (tumor, nodes, metastasis, serum biomarkers) for an appropriate therapy regimen. Most patients with seminoma present with stage I disease, which is defined as local disease with no lymph node or distant metastases.7,8 Stage II disease is defined by retroperitoneal lymph node metastasis. In contrast, stage III disease is defined by distant metastasis. The incidence of neck metastases ranges from 2.6% to 4.5% for testicular primary germ cell tumors.9 Wood et al reported 31 patients with supradiaphragmatic nodal metastases from testicular primary germ cell tumors and found neck lymphadenopathy in 10 of 11 patients with seminoma (91%).10 The European Association of Urology recommends Radiation Therapy for IIA/IIIB seminoma, with chemotherapy as an alternative. For stage IIC or III, chemotherapy with 3 cycles of BEP or 4 cycles of etoposide and cisplatin (EP) is recommended.11 Lymphadenopathy in a patient with known testicular cancer can be inappropriately assumed to represent metastatic disease since the coexistence of testicular cancer and lymphoma is very rare. Lymph node excisional biopsies are crucial for correct diagnosis, staging, and treatment in patients with coexistent seminoma with lymphoma, as illustrated in our case.

Selection of initial treatment for HL is usually based on presenting stage and prognostic factors. Both HL and germ cell tumors commonly involve lymph nodes, making staging more challenging, such as in our patient. Stage II HL involves 2 or more lymph node regions or lymph node structures on the same side of the diaphragm, while stage III HL involves lymph node regions or lymphoid structures on both sides of the diaphragm. Our patient’s right external iliac adenopathy resolved following BEP treatment, making the diagnosis of stage II HL more likely. Multiple clinical trials have studied the treatment strategy of combined modality therapy versus chemotherapy alone for HL.12-17 For patients with early-stage, favorable prognosis HL, combination chemotherapy with radiation therapy results in higher disease-free survival compared with chemotherapy alone. However, the overall survival is similar.18,19
ABVD (adriamycin, bleomycin, vinblastine, and dacarbazine) remains the “gold standard” chemotherapy for stage I and stage II HL patients. In our case, the patient had already received 3 cycles of bleomycin-based chemotherapy for seminoma; hence, BV+AVD was chosen for HL instead of ABVD. In 1 case with the coexistence of seminoma and HL, the patient received orchectomy for the seminoma followed by 6 cycles of ABVD for HL. Interim PET/CT showed complete response after 2 cycles.6

Even though both seminoma and HL are chemotherapy-sensitive, the choice of regimen is different, as discussed above. The sequence of chemotherapy for coexistent seminoma and HL depends on the individual malignancy’s staging and aggressiveness. In our patient, the atypical lymph node FNA result and the rarity of malignancy coexistence led to the missed diagnosis of HL. If HL was discovered earlier, we would have opted for ABVD for HL and radiation therapy for his seminoma instead of 3 cycles of BEP for seminoma followed by BV+AVD for HL.

In conclusion, we present a rare coexistence of seminoma and HL. Further research is needed to guide treatment for synchronous malignancies.

The views expressed in this case report are those of the authors and do not reflect the official policy of the Department of the Army, Department of Defense, or the US Government.

Conflict of Interest

None of the authors identify a conflict of interest.

Authors’ Affiliation:
- Tripler Army Medical Center, Medicine Department, Honolulu, HI (ZLA, S.Meghpara, S. Mignano)
- University of Hawai’i Cancer Center, Honolulu, HI (JB)

Correspondence to:
Zhaozhi Liao Arter MD, Tripler Army Medical Center (TAMC), MCHK-DMM, 1 Jarrett White Road, TAMC, HI 96859; Email: annarter2012@gmail.com

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