Successful Treatment for Isolated Bone Marrow Hodgkin Lymphoma in an Human Immunodeficiency Virus (HIV)-Negative Patient

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Patient: Female, 36-year-old
Final Diagnosis: Diffuse large B cell lymphoma
Symptoms: Shortness of breath
Medication: —
Clinical Procedure: —
Specialty: Hematology

Objective: Rare disease
Background: Hodgkin lymphoma is a type of lymphoid neoplasm characterized by the presence of Reed-Sternberg cells in histopathology. It presents with swollen lymph nodes, and in advanced cases, it can involve bone marrow. Isolated and primary involvement of Hodgkin lymphoma in bone marrow is a very rare presentation, especially in an HIV-negative patient, and has a high mortality rate, even with appropriate management.

Case Report: A 36-year-old male patient presented with a 6-month history of chills, night sweats, and generalized weakness. Laboratory investigations showed pancytopenia. A peripheral blood smear was unremarkable. A bone marrow biopsy revealed Reed-Sternberg cells, consistent with Hodgkin lymphoma. Further imaging did not show any lymphadenopathy, and the spleen was normal. Therefore, primary bone marrow Hodgkin lymphoma was diagnosed at stage IV, with an International Prognostic Score of 5 potential unfavorable factors. He was started on conventional chemotherapy for Hodgkin lymphoma and received the first cycle of ABVD (adriamycin, bleomycin, vinblastine, and dacarbazine) during his hospitalization. Meanwhile, he had fever without focus, and was managed empirically by broad-spectrum antibiotic treatment (piperacillin-tazobactam). Hospitalization lasted for 2 weeks. He continued to receive other cycles as an outpatient, with good clinical response. The patient remained in complete remission after 2 years.

Conclusions: Isolated Hodgkin lymphoma of bone marrow is a very rare scenario, especially in HIV-negative patients, with no established management for patients. Here, we report a patient successfully treated with a conventional chemotherapy protocol for Hodgkin lymphoma.

Keywords: Hodgkin Disease • Human Immunodeficiency Virus (HIV) • Bone Marrow

Abbreviations: ABVD – adriamycin, bleomycin, vinblastine, dacarbazine; CD – cluster of differentiation; PET – positron emission tomography; EBV – Epstein-Barr virus

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Hodgkin lymphoma accounts for approximately 10% of all lymphoma cases [1] and characteristically presents with superficial lymphadenopathy [2]. Bone marrow involvement by Hodgkin lymphoma was reported in an average of 10% of cases, with a higher incidence in the advanced stage [3].

Isolated bone marrow involvement without nodal or extranodal manifestation is a very rare presentation, mainly in HIV-negative patients. Only 5 cases were reported as isolated bone marrow Hodgkin lymphoma in HIV-negative patients [4-8], and 2 of them were successfully treated [6,8]. In this report, we are presenting a case of a 36-year-old man who presented with a history of chills and pancytopenia, was diagnosed with isolated bone marrow Hodgkin lymphoma, and was successfully treated by conventional chemotherapy.

Case Report

A 36-year-old man with a 20-pack-year history of smoking and otherwise unremarkable past medical or family history of hematological disease presented with a 6-month history of generalized weakness, night sweats, and chills. He denied a history of weight loss, fever, itching, skin rash, bleeding tendency, and swelling. During this initial evaluation, he was found to have pancytopenia, according to the referral report, with the only available hemoglobin result of 4 g/dL. Other parameters of complete blood counts were not reported. He received 2 units of blood and was planned for further investigation at our hospital. There was a delay in referral due to barrier restrictions between Gaza and the West Bank.

Upon admission to our hospital, he was hemodynamically stable, afebrile, and looked pale. The examination was unremarkable, with no palpable lymph nodes. The liver and spleen were not palpable. A complete blood count showed pancytopenia (hemoglobin 7.4 g/dL, MCV 88 fL, WBC 2800 cells/μL, ANC 1660 cells/μL, platelets 102×10⁹/L, LDH 149 U/L, albumin 3.3 g/dL). Serological and microbiological tests did not show any pathogens, including HIV and Epstein-Barr virus (EBV). A peripheral blood smear showed only pancytopenia, with no abnormal cells. Accordingly, a bone marrow biopsy and aspiration were done, which showed 80% cellularity and no blast cells. There was an infiltrate of the fibrotic nodule with large atypical cells with binucleation and multinucleation with prominent red nucleoli, which were positive for cluster of differentiation (CD) 30 and focally faintly positive for PAX 5. They were negative for CD 20, CD 79a, CD 3, CD 15, CD 45, ALK-1, and EMA. These findings were suggestive of Hodgkin lymphoma. Chest, abdomen, and pelvis computed tomography scanning did not show lymphadenopathy, masses, or abnormal spleen. As we could not do positron emission tomography (PET) scan, another opinion for the result of bone marrow was taken from the King Hussein Hospital, who confirmed the diagnosis of isolated bone marrow Hodgkin lymphoma.

The following day, he developed a spike of fever up to 39°C, with high inflammatory markers. He was neutropenic, and there was no clinical focus for fever. We put him in an isolated room, blood and urine cultures were obtained, and then he was started on broad-spectrum antibiotics (piperacillin-tazobactam). Within a few days, he improved clinically. The cultures remained clear, but he still had spiking fever. We started him on ABVD (adriamycin, bleomycin, vinblastine, dacarbazine) chemotherapy. Over the following days, the fever subsided, and C-reactive protein levels returned to normal. He was discharged from the hospital and continued his chemotherapy treatment as an outpatient. The total duration of hospital admission was 14 days.

The patient received a total of 6 cycles of ABVD as an outpatient, with an excellent response. A PET scan at the end of treatment showed no active uptake at any site. A bone marrow biopsy was repeated showing no infiltration. He had complete remission and is currently on regular surveillance by laboratory and physical examination every 3 months. His last follow-up was 2 years after diagnosis, and his complete blood counts were as follows: hemoglobin 13.5 g/dL, MCV 85 fL, WBC 6500 cells/μL, ANC 4700 cells/μL, and platelets 160×10⁹/L.

Discussion

Typical presentations of Hodgkin lymphoma are asymptomatic lymphadenopathy or mass identified by physical examination or imaging investigations [9], which were absent in our case. B symptoms, including fever, night sweats, and weight loss present in about 30% of cases [10], and their presence usually indicates adverse outcomes [2]. Bone marrow involvement in Hodgkin lymphoma is uncommon, reported as a range of 5% to 16% [3,11-13]. Primary bone marrow lymphoma is diagnosed by pathologically confirmed bone marrow involvement; in addition to the absence of lymph node, liver, or spleen involvement by physical examination or imaging investigations, it also needs to exclude other leukemia/lymphomas that primarily involve bone marrow [9]. In our patient, Reed-Sternberg cells from the bone marrow sample were positive for CD 30, which was suggestive for Hodgkin lymphoma, but it was negative for CD 15. However, CD 15 is less frequently expressed [14]. Our patient had stage IV Hodgkin lymphoma with an International Prognostic Score (IPS) of 5, matching the criteria for primary bone marrow Hodgkin lymphoma.

There are very few reported cases of primary bone marrow Hodgkin lymphoma, and most reports were of HIV-positive
patients or were associated with EBV, which is found in all cases of HIV patients with Hodgkin lymphoma, indicating its role in pathogenesis [8]. Our case was negative for both, which was a very rare scenario.

Primary bone marrow Hodgkin lymphoma has a very poor prognosis, even with treatment. Conventional treatment for advanced Hodgkin lymphoma consists of combination chemotherapy with ABVD [15-17]. Prognosis is determined by IPS [18]. Our patient had 5 potential unfavorable factors, which means that with treatment, he had a predicted 5-year progression-free survival of approximately 42% and an over 5-year overall survival of 56%. However, this was not consistent with reported cases of patients with HIV-negative primary bone marrow Hodgkin lymphoma, as survival was very low in these cases [8]. Of the 4 reported patients treated with conventional ABVD chemotherapy, 2 survived, 1 survived for 15 months, and the remaining patient was subsequently treated with brentuximab vedotin-based chemotherapy [6,8]. Previous reports suggest that conventional chemotherapy using the CHOP or ABVD protocol can have a poor outcome [8]. However, we chose conventional ABVD chemotherapy because the risk of death due to sepsis was similar regardless of which chemotherapy was used, and because brentuximab vedotin-based therapy was only available for refractory Hodgkin lymphoma.

The main causes of death in previously reported cases were sepsis and multiorgan failure. We started broad-spectrum intravenous antibiotics for his documented fever in the hospital, despite there being no clinical or radiologic focus for the source of fever. After the first week of chemotherapy, his clinical condition markedly improved, his fever subsided, and he was discharged to continue his chemotherapy as an outpatient.

Conclusions

Isolated bone marrow Hodgkin lymphoma is very rare and has a high mortality rate, and treatment with conventional chemotherapy could be effective and can be associated with improved survival. Also, early treatment for possible sepsis with broad-spectrum antibiotics could be helpful.

Availability of Data and Materials

All data supporting the study are presented in the manuscript or available upon request from the corresponding author of this manuscript.

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