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Case Report

Management of Hodgkin Lymphoma in a Sickle Cell Patient: A Case Report

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Keywords
Hodgkin lymphoma · Sickle cell disease · Chemotherapy

Abstract
Sickle cell disease (SCD) is an inherited disorder of hemoglobin mutation in red blood cells, with a patient population that is increasing in age in recent decades due to advances in modern medicine. Hodgkin's lymphoma (HL) is a cancer of white blood cells, and while concomitance of SCD and Hodgkin's has been reported, a discussion of treatment for HL in SCD is lacking from the literature. We present a case of effectively treated HL in SCD and put forth that the regimen used is a practical choice, and as it was completed fully as outpatient, it improved the patient's quality of life compared to an inpatient regimen.

Introduction

Sickle cell disease, an inherited disease of hemoglobin mutation, causes sickling of the red blood cells under certain circumstances, including hypoxia and acidemia, which creates vaso-occlusion that has many deleterious effects on a patient's body. As advances in medicine increase lifespan of these patients, they are increasingly susceptible to diseases of age including malignancy; the longer a person is alive the more opportunities for dividing cells to become cancer. The case we are presenting is Hodgkin's lymphoma in a sickle cell patient. Hodgkin's lymphoma typically has a few chemotherapy treatment options, including ABVD and

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BEACOPP, but in this case special consideration had to be made in the case of the patient's sickle cell disease. We present our choice of chemotherapy as an effective treatment for Hodgkin's lymphoma in a sickle cell disease patient.

Case Presentation

A 25-year-old male with past medical history of sickle cell disease with very few admissions for sickle cell pain crisis, low grade glioma that was resected 5 years ago presents to clinic with lump in his left neck for few months. A CT scan showed bilateral cervical adenopathy with a 7 cm predominant lymph node in the left cervical area. The pathology of excision biopsy was reviewed at Memorial Sloan Kettering Cancer Center as Epstein-Barr Virus positive Reed-Sternberg cells, and read as classical Hodgkin lymphoma, mixed cellularity type. The patient underwent PET scan showing confluent bulky lymph nodes centered in the posterior triangle of the entire left neck measuring up to 7.4 × 3.1 cm in total axial cross section, with maximum SUV range measuring up to 8. In the right neck, similar appearing hypermetabolic lymph nodes were seen individually measuring up to 1.5 cm with maximum SUV 4.9, much less extensive compared to the left side. No hypermetabolic nodes seen below the diaphragm.

The patient was followed up in clinic and started on treatment with ABVD regimen on day 1 and 15 of each cycle. On day 7 the patient followed up in clinic for labs and administration of IV fluids and blood transfusions as needed to keep hemoglobin above 7. He completed 4 cycles with significant decrease in size of neck lymph nodes with left internal jugular lymph node measuring 2.3 × 1.2 cm and standard uptake values ranged from 1.9–2.3. After completion of chemotherapy patient underwent consolidative radiation therapy with 30 Gy radiation to the involved site and additional 6-Gy boost sequentially administered to the PET- avid jugular nodes bilaterally. The patient was never admitted to the hospital during the entire course of treatment.

Discussion

Sickle cell anemia is an inherited disorder caused by homozygosity for the Hemoglobin S gene that results from a missense mutation in the B-globin gene of hemoglobin [1, 2]. This altered hemoglobin leads to destabilized red blood cell membranes that cause the cell to sickle under certain conditions, including hypoxia, acidemia, etc. The persistence of this mutation is accepted as a classic example of natural selection, in that the red blood cells serve as protection against Malaria, which is prominent in the African regions where sickle cell disorders originate from [1]. While benefiting the host by protecting against the Malaria parasite's ability to exist inside the cell, the sickled cells also cause widespread dysfunction via several mechanisms, in particular via vaso-occlusion. The consequences of vaso-occlusion are also numerous, including auto-splenectomy, pain crises, acute chest syndrome, and avascular necrosis [3]. Historically these complications lead to childhood death, however with advances in medicine, sickle cell patients are living longer [4]. For example, sickle cell patients undergo autosplenectomy at an early age secondary to vaso-occlusion, and without splenic function patients are predisposed to infection with encapsulated bacteria, including Pneumonia species, Neisseria species, Haemophilus influenza b, etc. Vaccines against these infections, newly available in the 1980's and reformulated since, have dramatically contributed to an increase of lifespan in sickle cell patients [5]. In the 1960s mortality of sickle cell patients was largely

before age 18, whereas in 2014 the average life expectancy was 58 years old [4]. Therefore, due to the increasing age of the sickle cell patient population, we are observing diseases not previously seen as comorbid diseases with sickle cell.

A study noting the incidence of cancers in sickle cell patients in California from the years of 1988–2014 noted that hematologic cancers comprised 26% of the total, whereas solid tumor cancers made up 66% [6]. Interestingly, compared to the general population, the study notes that women, adolescents, and young adult sickle cell patients had a three times higher incidence of leukemia. In a meta-analysis conducted of cancers in sickle cell studying 142 cases, hematologic malignancies were the higher trend, with 10% of cases being multiple myeloma, 10% myeloid leukemia, and 9% Non-Hodgkin lymphoma. Also notable were solid tumors of colon, prostate, and kidney, each comprising roughly 6% of cases. In that analysis, Hodgkin's lymphoma comprised 5.6% of cases [7].

Treatment of Hodgkin lymphoma is based on disease severity and involves combination chemotherapy and radiation. For favorable early-stage disease, which is defined by less than three sites of disease without bulk, extranodal extension, or elevated ESR, standard treatment is 2 cycles of ABVD-doxorubicin, bleomycin, vinblastine, and dacarbazine, followed by 20 Gy IFRT (involved-field radiotherapy). Early-stage unfavorable disease follows a similar protocol with 4 cycles of ABVD followed by 30 Gy IFRT [8]. Other chemotherapy regimens that have been used in conjunction with RT are MOPP-ABV-mechlorethamine, vincristine, procarbazine, prednisolone, doxorubicin, bleomycin, and vinblastine; and BEACOPP-bleomycin, etoposide, doxorubicin, cyclophosphamide, vincristine, procarbazine, and prednisolone [9]. However, treatments with these alternative regimens have shown no difference in disease outcomes, while creating higher toxicities, so ABVD remains the first line treatment [9].

As ABVD and BEACOPP regimens are associated with significant neutropenia, prophylactic granulocyte colony-stimulating factor is often used in conjunction. In fact it is a requirement for the BEACOPP protocol [10]. However, there is a risk of G-CSF association with sickle cell crises [11]. A case has been reported wherein a patient with sickle cell trait developed sickle cell crises after receiving Neulasta in conjunction with chemotherapy for breast cancer [12]. In an article reviewing the amount of cases of G-CSF used on sickle cell patients in 2009, 7 out of the 11 patients studied experienced severe complications including vaso-occlusive crisis, acute chest syndrome, multiorgan system failure, and death [13]. Relative to our case, one of those individuals was being treated for Hodgkin's lymphoma and developed bone pain crisis requiring hospitalization as a result of G-CSF administration [14]. Therefore, the regimen we selected for our patient excluded neupogen.

The increasing lifespan of patients with sickle cell disease yields the possibility of developing diseases that may present with age, including malignancy. The treatments recommended for non-sickle cell patients may be applied to sickle cell cases, with special consideration regarding the interactions of medications with this condition, as we put forth in our regimen used to treat a sickle cell patient with Hodgkin's lymphoma.

Statement of Ethics

The authors have no ethical conflicts to declare. The research does comply with guidelines for human studies and animal welfare regulations. Informed consent has been obtained from the patient. The study protocol was approved by human research at New York Presbyterian Brooklyn Methodist Hospital.

Disclosure Statement

The authors certify that they have no affiliations with or involvement in any organization or entity with any financial interest (such as honoraria; educational grants; participation in speakers' bureaus; membership, employment, consultancies, stock ownership, or other equity interest; and expert testimony or patent-licensing arrangements), or non-financial interest (such as personal or professional relationships, affiliations, knowledge or beliefs) in the subject matter or materials discussed in this manuscript. The authors do not have any conflicts of interest to disclose.

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