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Case Report

Tailored therapy and bloodless supportive care measures for a Jehovah's witness with metastatic Ewing sarcoma

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ABSTRACT

A seventeen-year-old Jehovah's witness with metastatic Ewing sarcoma initially declined cancer therapy due to the risk of life-threatening bone marrow suppression. He then subsequently agreed to other treatment options with bloodless supportive care measures in order to achieve quality of life and long-term control of his disease. This case report adds to the collective knowledge of providing treatment options including bloodless supportive care measures for Jehovah's witness patients with cancer.

Keywords: Jehovah's witness, Bloodless cancer treatment, Ewing Sarcoma

INTRODUCTION

Jehovah's witnesses (JW) are members of a Christian movement who object to receiving infusions of any blood products based on their literal interpretation of the Bible. Consequently, management of cancer in JW patients presents unique challenges since chemotherapy often results in bone marrow suppression causing life threatening anemia and thrombocytopenia.

JW patients may be offered a wide variety of treatment options which can ultimately affect their survival outcomes. Some oncologists may refuse treatment of JW patients knowing that they will have a poor clinical outcome without the support of blood products.[1] Some JW patients are offered modified chemotherapy regimens which may involve dose reductions or alternative medications to avoid the possibility of life-threatening anemia and thrombocytopenia.[1] Other JW are offered standard chemotherapy regimens with the bloodless supportive care measures such as erythropoietin and thrombopoietin analogs.[2]

Our case report below shows an example of a JW patient with metastatic Ewing sarcoma treated with multiple chemotherapy regimens supported with bloodless supportive care measures in order to achieve long term control of his disease.

CASE REPORT

17-year-old previously healthy male Jehovah's witness presented to an outside emergency department (ED) in March 2016 with respiratory distress. He was found to have multiple pulmonary lung nodules and was discharged with follow up with pediatric pulmonology. He was followed by pulmonology for 4 months after being diagnosed with Valley Fever. He began to have increased pain in his left hip which prompted a repeat CT Chest that showed increasing size of the lung nodules. He was then sent for a biopsy of one of the lung nodules which showed Ewing sarcoma. PET CT revealed a primary lesion in the left femur, left hemipelvis, and multiple lung nodules (Figure 1). While awaiting referral to pediatric oncology, he presented back to the ED a month later with left lower extremity pain, fever, night sweats, 25-pound weight loss over the past 6-7 months.

He had a CT chest which showed multiple lung nodules, the largest in the left upper lobe and pleural based, 8.7×4.8×9.1 cm and CT pelvis which showed a destructive lesion in the left pubis with large soft tissue extension into the pelvis as well as adenopathy in the pelvic walls. He was admitted to the hospital where pediatric oncology was consulted. Pediatric oncology discussed the treatment plan including supportive care with blood transfusions, but the patient and the family objected to any blood transfusions. The oncology team expressed that they are not able to provide him with systemic chemotherapy for his Ewing sarcoma if they did not consent to blood transfusions. He was placed on hospice and referred to our center for a second opinion and possible palliative radiation.

He presented to our pediatric oncology clinic 10 months after his initial presentation. He was sitting in a wheelchair and quite sleepy since he was on large amounts of narcotics to manage his pain. His vital signs were stable, and his exam was remarkable for a large tissue swelling over his left inguinal and femoral area.

The patient and the parents confirmed that they will continue to object to any blood transfusions, but they were interested in other chemotherapy options that would not require any transfusion support. He was offered vincristine, irinotecan, and temozolomide (VIT) which is considered a reduced intensity chemotherapy regimen for Ewing sarcoma. This was presented as palliative chemotherapy with the intent of decreasing his pain and providing him with some quality of life. The patient and the parents agreed to the treatment plan and understood that chemotherapy will be held if his hemoglobin and platelet count became dangerously low.

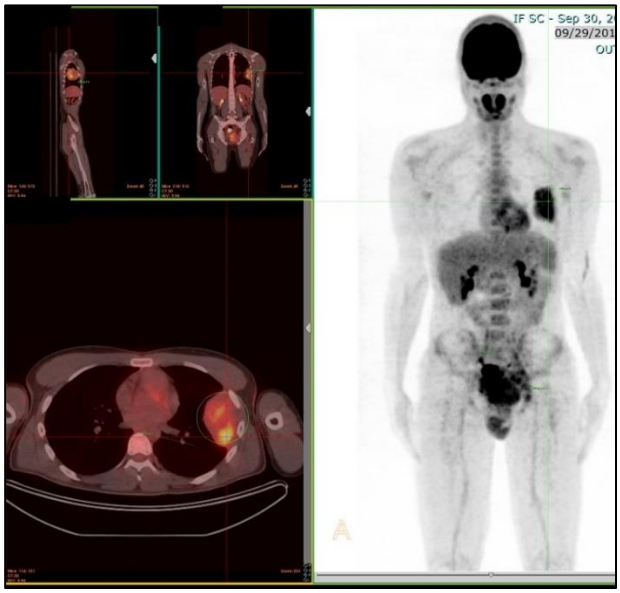

Figure 1: PET CT scan prior to treatment demonstrating the primary tumor in the left hemipelvis and femur (not shown) and multiple lung metastases.

After two cycles of chemo, he had a good response showing significant decrease in the size of pleural based and primary tumor in the pelvis area (Figure 2). In addition, he was quickly weaned off pain medications and was able to ambulate. Surgery was consulted, but the family declined any surgery as major abdominal surgery and debulking would likely require transfusion support. He continued chemotherapy given he had an excellent response without significant myelosuppression. Repeat scans after 5 months of VIT revealed overall decrease in the size of his primary tumor and the metastatic lung nodules, but not as significant response as seen initially. The family agreed to proceed with IMRT to lung and pelvis over seven weeks while receiving the same chemotherapy concurrently. He received a total of 10 cycles of VIT and did not develop severe anemia or thrombocytopenia.

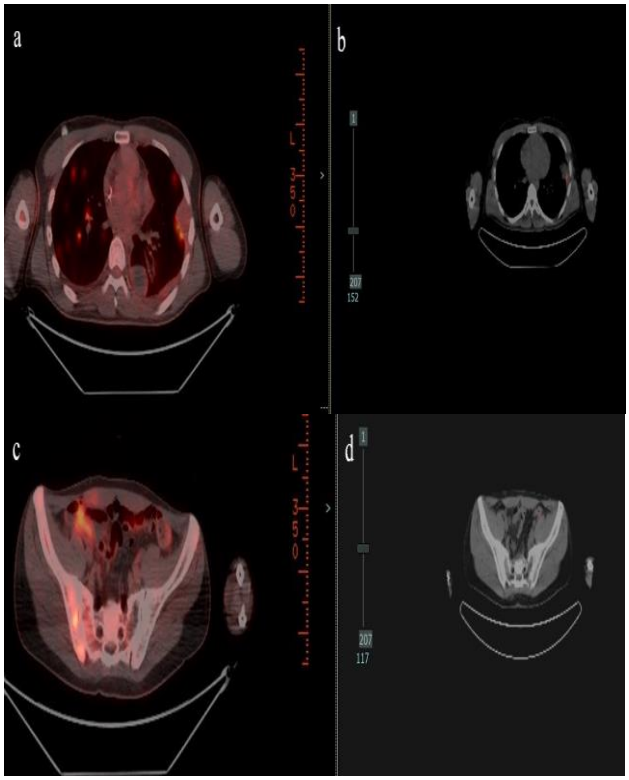

Figure 2 (A-D): PET CT of FDG avid multiple lung nodules prior to VIT chemotherapy. PET CT of resolution of FDG avid lung nodules after VIT chemotherapy. PET CT of FDG avid tumor in the hemipelvis prior to VIT chemotherapy and PET CT of resolution of FDG avid tumor in the hemipelvis after VIT chemotherapy.

With chemotherapy and radiation, the patient had a great quality of life and wanted the chance for longer control of his disease. We proposed the standard of care chemotherapy for Ewing sarcoma with compressed regimen of vincristine/ doxorubicin/ cyclophosphamide alternating with ifosfamide/ etoposde (VDC/IE per COG protocol AEWS0031) with support with Epogen (3500 units 2-3× per week), Promacta (25-50 mg daily), and

Neupogen. He was on Epogen 3500 units 2-3x per week to keep Hgb >7, Promacta 25-50 mg daily to keep platelet count >50 K, and neupogen after each course of chemotherapy as per standard of care. He completed VDC/IE with minimal delays supported with Epogen, Promacta, and Neupogen. The patient did not develop any thrombosis while on Epogen and Promacta. Disease evaluation scans after 12 weeks of VDC/IE showed inconsistent findings with the dominant lesion in the pelvis diminishing in size significantly, but with some osseous lesions increasing in size. Consequently, he had another course of palliative radiation for a total of 24 gy. He completed alternating cycles of VDC/IE without any severe anemia or thrombocytopenia and without side effects from Epogen, Promacta, or Neupogen.

PET CT showed increased FDG activity in the lungs with stable disease in the pelvis without any evidence of recurrence. The patient decided to restart VIT due to these findings. His disease progressed 9 months later with new and worsening lesions in the lungs and new osseous metastasis. He started on pazopanib but progressed while on pazopanib after a month. Patient was enrolled on a clinical trial and started on Olaparib. A month later, he was found to have intracranial metastases and died shortly after.

DISCUSSSION

The management of cancer in JW patients presents a unique challenge to oncologists. Their preferences and beliefs are stringent and must be respected when making treatment decisions. According to Lee's case series of 63 JW patients with solid malignancies and lymphoma, all patients declined blood transfusions and their preference did not change during treatment. Despite all patients declining transfusion support, most of the patients accepted the proposed treatment with 86% with full acceptance, 8% with partial acceptance, and only 6% with complete refusal of any treatment. Patients who refused all treatment options at baseline were concerned of reaching the threshold of when anemia may be life threatening.[1]

Despite the treatment challenges in JW cancer patients, most can be successfully cured of their disease with the use of bloodless supportive care measures. These have been well documented in the literature and include erythropoietin stimulating factor, iron replacement, granulocyte stimulating factors, thrombopoietin stimulating factor, and stem cells. In the Lee series, 11 patients in the early-stage group received erythropoiesis stimulating agents (Epogen Alfa), iron replacement, and pegfilgrastim and were able to complete full dose chemotherapy regimen.[1] Arora et al presented a 21-year-old JW with Philadelphia positive B-cell acute lymphoblastic leukemia who was successfully treated with chemotherapy using darbepoietin alfa and romiplostim as support for her disease/chemotherapy associated anemia and thrombocytopenia.[2] Romiplostim was used for an 11-year-old JW patient with large B-cell lymphoma on myelosuppressive chemotherapy to reduce the exposure of prophylactic blood products.[3] Lastly, Tenenbaum and colleagues presented a case series of 14 children of JW with pediatric cancer who was supported with iron, human erythropoietin, interleukin 11, granulocyte colony-stimulating factor, and autologous or allogeneic stem cell rescue during the duration of their chemotherapy treatment.[4] A case series by Oh and colleagues analyzed 77 JW adult patients with cancer who were supported with GCSF and erythropoietin during surgery and chemotherapy. Three and five-year survival rates were 80% and 70%, respectively. In addition, bloodless cancer surgery and chemotherapy were not accompanied by serious complications.[5]

Bloodless hematopoietic stem cell transplant has also been shown to be successful in many cases. The first case of a transfusion-free allogeneic stem cell transplant (SCT) in a Jehovah's witness with CML who underwent a successful HLA-identical peripheral blood SCT after reduced-intensity conditioning with total body irradiation and fludarabine.[6] A Mexican case series involving 132 peripheral blood stem cell transplants (73 allografts and 59 autografts) was also published in 2005 and concluded that, by using certain preparative regimens, both allo and auto hematopoietic stem cell transplants can be conducted without the transfusion of blood products.[7] A review by Sloan and colleagues proposed supportive care measures such as optimal stimulation of erythropoiesis and thrombopoiesis as well as the prevention and management of bleeding during extreme thrombocytopenia in a transplant patient.[8]

Despite the availability of bloodless supportive care measures, some JW cancer patients may choose reduced intensity regimens to avoid the risk of life threatening anemia.[1] Unfortunately, suboptimal treatment may result in short term response without durable long-term remission.[9] During instances when a JW patient has chosen a reduced intensity chemotherapy for palliative care, the regimen can be modified to avoid myelosuppression. This can include dose reduction of chemotherapy and/or dose delay until the desired hemoglobin level and platelet count have been achieved prior to proceeding to the next cycle. It can also include the use of molecular targeted therapy agents or alternative chemotherapy regimens that are not as myelosuppressive. Lastly, palliative radiation can also be considered in lieu of surgery for large tumors. These suboptimal treatment options may not lead to cure but can provide short term control of the disease which may lead to decreased pain and improved quality of life.

CONCLUSION

JW patients are often limited by their treatment by choices given their objection to receive blood transfusions. There are approximately 8.7 million JW worldwide and we, as physicians, should respect their

autonomy and religious beliefs when making treatment decisions. This case report highlights the importance of exploring treatment options for JW cancer patients including reduced intensity chemotherapy, targeted therapies, and bloodless supportive care measures to achieve their treatment goal whether the goal is cure or palliative care.

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