Iatrogenic Immunodeficiency Lymphoproliferative Disorder with Hepatic Impairment Treated with Salvage Gemcitabine

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ABSTRACT

Other iatrogenic immunodeficiency-associated lymphoproliferative disorders, classic Hodgkin lymphoma-type, is a subclassification of lymphoproliferative disorders typically seen in patients taking immunosuppressive medications in the setting of autoimmune diseases. Standard of care is currently Adriamycin, Bleomycin, Vinblastine, and Dacarbazine (ABVD) as it is for typical Hodgkin lymphoma, however, the side effect profile of these drugs include transaminase elevations which restrict their use in patients with underlying liver dysfunction. In patients in this clinical scenario gemcitabine has been infrequently used in the literature as salvage therapy as well as other alternative strategies. We report a case of classic hodgkin lymphoma-type other iatrogenic immunodeficiency disorder with impaired liver function who was treated empirically with salvage therapy of gemcitabine who developed symptomatic thrombocytopenia without recovery.

Key words: Gemcitabine; Hodgkin’s lymphoma; Other iatrogenic immunodeficiency-associated lymphoproliferative disorder; Chemotherapy

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List of abbreviations

classical Hodgkin lymphoma type (CHL-type), Adriamycin, Bleomycin, Vinblastine, and Dacarbazine (ABVD), classical Hodgkin lymphoma type, other iatrogenic immunodeficiency-associated lymphoproliferative disorders (CHL-type Oii-LPD), cyclophosphamide, etoposide, procarbazine, and prednisone (CEPP), N-acetylcysteine (NAC), Hodgkin’s lymphoma (HL)

INTRODUCTION

Other iatrogenic immunodeficiency-associated lymphoproliferative disorders (Oii-LPDs) are classified as tumors of hematopoietic and lymphoid tissues occurring in those receiving immunosuppressive therapy or those with autoimmune diseases. Among this category of lymphoproliferative disorders are classical Hodgkin lymphoma type (CHL-type) which is a rare entity with very few cases reported in literature[1]. The standard of care for Hodgkin lymphoma (HL) in the United States is currently a combination therapy of Adriamycin, Bleomycin, Vinblastine, and Dacarbazine (ABVD). However, there is a lack of data for patients who present with HL with impaired liver function and coagulopathy, as the side effect profile of traditional therapy has been reported to cause further transaminase elevations[2,3].
Few case reports have reported utilizing bridging therapy with Gemcitabine as salvage therapy in patients with refractory HL with only mild drug related toxicities. Although several experimental alternative regimens exist, this therapy was utilized in patients who are unable to receive ABVD and have reported some success with this regimen[1-2,4].

The best regimen of CHL-type Oii-LPD with liver impairment is yet to be established, although many regimens have been attempted with variable success[5]. We present an unusual case of CHL-type Oii-LPD with significantly impaired liver function who was initially treated with gemcitabine, steroids, and N-acetylcysteine (NAC) as salvage therapy who developed hemodynamic instability due to symptomatic thrombocytopenia without recovery.

CASE REPORT

A 39-year-old female with a history of Systemic Lupus Erythematosus, Rheumatoid Arthritis on hydroxychloroquine, Raynaud’s syndrome and alcohol abuse presented to the hospital with generalized fatigue. On arrival at the emergency department, she was found to be tachycardic and febrile with physical examination findings significant for jaundice and cervical lymphadenopathy. She received three units of packed red blood cells for worsening anemia after laboratory data revealed pancytopenia with a hemoglobin of 4.5g/dL (Hgb 12 to 16 g/dL), white blood cell (WBC) count of 2,400 B/L (3,700 to 10,500 B/L), and platelet count of 17,000 B/L (150,000 B/L to 400,000 B/L). Peripheral smear revealed pancytopenia with rare immature granulocytes, mild polychromasia and occasional nucleated RBCs with large platelets (Figure 1). Bone marrow biopsy was performed and revealed 50% of the marrow space was replaced by histiocytic infiltrate mixed with lymphocytes, plasma cells, and scattered eosinophils (Figure 2). A large area of necrosis was estimated to be 20% (Figure 3). Pax-5 stains show scattered small B cells and rare dimly positive large cells. Findings were consistent with extensive involvement by other iatrogenic immunodeficiency-associated lymphoproliferative disorders.

Lab values included elevations of her liver function test (LFT) with a total bilirubin of 5.3 mg/dL (0-1 mg/dL), direct bilirubin of 2.8 mg/dL (0-0.3 mg/dL), alkaline phosphatase of 1,270 u/L (39-117 u/L), and aspartate aminotransferase (AST) 57 u/L (normal value of < 31 u/L), alanine aminotransferase (ALT) 39 u/L (normal value of 0-31 u/L). Gamma glutamyl transpeptidase (GGT) was 116 u/L (0-30 u/L) and lactate dehydrogenase was 220 u/L (100-200 u/L). An MRI of her abdomen was performed to evaluate her transaminitis which was significant for hepatomegaly and steatosis. Due to the significant elevation of the LFTs on arrival, it was believed that the transaminitis was from a combination of patients underlying systemic lupus erythematosus, medication use of hydroxychloroquine use, and alcohol use. Due to the complexity of the patient’s condition and concern of underlying liver failure she was transferred to a tertiary care center for further management.

During her hospital stay at tertiary care center the patient obtained a computerized tomography (CT) scan of her chest which revealed large bilateral axillary lymph nodes with smaller mediastinal and hilar lymph nodes. Axillary lymph node biopsy revealed atypical lymphoid infiltrate scattered large atypical cells in the background of mixed inflammatory cells (Figure 4). Large cells with single to multiple nuclei. Atypical cells were positive for CD15, CD30, and PAX-5 with overall findings consistent with classical Hodgkin lymphoma and classified as Other iatrogenic immunodeficiency associated lymphoproliferative disorders (Figure 5). The patient was discharged home at this time and was scheduled to have a follow up appointment with hematology and oncology.

A week later, the patient was readmitted to the hospital for now concerns of worsening abdominal pain, ascites, and jaundice. She had...
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difficult

Figure 4 Right axillary lymph node fine needle cores show thin cores of lymphoid tissue with scattered large Hodgkin cells in a background of mixed inflammatory cells (100x magnification).

Figure 5 Immunohistochemical stain that is positive for CD30 (Fig. 5, 200x) suggesting Hodgkin lymphoma.

DISCUSSION

Other iatrogenic immunodeficiency-associated lymphoproliferative disorder, classic Hodgkin lymphoma-type, is a subclassification of lymphoproliferative disorders typically seen in patients taking immunsuppressive medications in the setting of autoimmune diseases[12]. The World Health Organization (WHO) classification not only recognizes the occurrence of ILD in patients post transplant, but also in patients that are undergoing prolonged immunosuppression therapy 1. Immunosuppression has a high correlation and is a strong risk factor for Hodgkin’ lymphoma incidence. Histologically, this disease subtype is characterized by scattered mononuclear and multinucleated giant cells surrounded by infiltrated non-neoplastic inflammatory cells. Immunohistochemical findings are similar to patterns seen in Classic Hodgkin lymphoma with expression of CD15, CD20, CD30, and PAX5, making the differentiation of these two disease entities difficult[13].

Malignant infiltration of the liver with Hodgkin’s disease causing acute liver failure is uncommon, but when concomitant carries a grave prognosis[6]. There are very few case reports of patients with Hodgkin’s lymphoma with acute liver failure at presentation[14]. Due to the small percentage of patients with aggressive lymphoma and hepatic involvement the treatment options are limited[15]. CHL is a particularly chemosensitive malignancy with high cure rates in patients treated with ABVD alone or followed by radiotherapy[6]. This therapy has been accepted as the standard of care for decades with response rates greater than 70% even in patients with poor prognosis[16]. Included in the standard treatment options for HL are doxorubicin and vinblastine which are metabolized in the liver complicating the treatment for patients who present with hepatic function impairment. Inferior results are typically seen with nonstandard first line chemotherapy to include dexamethasone, high dose cytarabine, and cisplatin (DHAP)[17]. Few therapies in the literature have been shown to be effective in patients with hepatic impairment which include cyclophosphamide, etoposide, procarbazine, and prednisone (CEPP) and gemcitabine[18,19].

Gemcitabine is a chemotherapeutic agent used widely in the treatment of cancers considered to have a good safety profile. There are very few cases of gemcitabine causing serious hepatotoxicity[14]. Gemcitabine has been shown to potentially be effective as salvage therapy in patients with refractory/relapsed Hodgkin’ lymphoma and pharmacokinetic trials have expressed that dose adjustments are not required in patients with hepatic or renal dysfunction[20]. Due to this reason, gemcitabine was chosen as an attempted salvage therapy in our patient.

The diagnosis of acute liver failure alone increases mortality and has complications to include coagulopathy and encephalopathy. 6. Liver biopsy was not obtained in our patient as she was significantly thrombocytopenic and the additional information obtained from a liver biopsy would not change subsequent management. In much of the literature surrounding HL with acute liver failure, biopsy of the liver is inconclusive[19]. Our patient developed symptomatic thrombocytopenia with epistaxis requiring intensive care monitoring of hemodynamic stability complicating the treatment course of her chemotherapy. Data is lacking in the literature regarding treatment of HL and acute liver failure specifically when treatment is complicated by coagulopathy as in this patient[22]. Ultimately this aggressive disease without adequate treatment left her inundated by the disease process and she ultimately transitioned to hospice care.

CONCLUSION

CHL-type Oii-LPD is a rare clinical entity with few cases reported in the literature. There are even fewer cases reported with associated liver failure. Due to concomitant disease, as demonstrated in this patient, treatment options are limited. It is our hope that the mortality of this patient will bring awareness for further research into treatment options for this rare patient population.

3458
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REFERENCES


