

Chemotherapy In HIV Associated Systemic Lymphoma With CNS Involvement- Experience With A Case.

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ABSTRACT

We report the case of a 49 year old health worker, HIV positive, who presented with a 2 months history of a rapidly enlarging cervical lymphadenopathy, right breast lump, hearing loss and weight loss. Disease progressed to a right facial nerve palsy, upper motor neurone type with right hemiparesis. CD 4 count was at 80/mm³ and Brain CT showed a left temporal lobe mass. She had a reversal of neurologic deficit within 72 hours with administration of doxorubicin. She continued cyclical chemotherapy with doxorubicin, vincristine, cyclophosphamide and later etoposide with intrathecal methotrexate, making a full recovery with complete resolution of the temporal lobe mass and neurologic symptoms. Granulocyte colony stimulating factor support, repeated blood transfusion and substitution of zidovudine containing HAART emerged effective strategies in achieving success.

Keywords: Chemotherapy, HIV, Lymphoma.

INTRODUCTION

Advances in the management of HIV patients have resulted in significant improvement in long term prognosis and incidence of opportunistic infections in HIV patients. Although HIV patients are reported to be at risk for AIDS defining cancers (Kaposi sarcoma, non-Hodgkin's lymphoma and invasive cervical cancers), studies show a marked reduction in incidence of systemic lymphomas from 13.6 to 1.8 per 1000 with the introduction of HAART.^[1] AIDS defining non-hodgkins lymphoma are reported to be aggressive, with central nervous system involvement on diagnosis at 20%.^[2] Given this aggressive tendency, chemotherapy is imperative in the management of this cancer. However, characteristic low CD4 counts at less than 100cells/mm³ coupled with higher viral loads in AIDS, reported as risk factors for B cell lymphoma,^[3] could contribute to making management of this subset of patients challenging.

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The risk-benefit of administering chemotherapy in this subset of patients has been a subject of debate given their myelosuppressant action in a background setting of an immunocompromised state. Thus

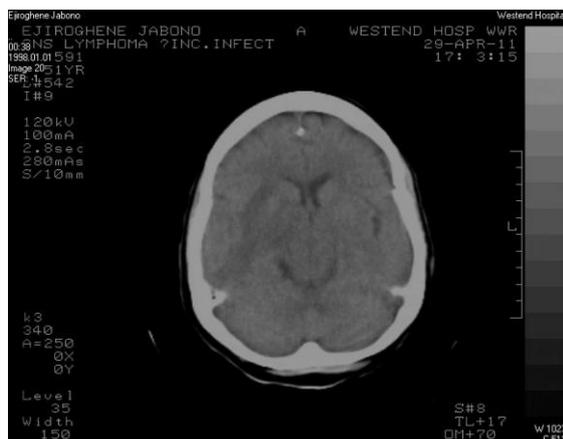
anecdotal concerns have been raised locally over safety of their use in HIV patients considering CD4 count depletion more so those in AIDS. Chemotherapy tends to be delayed or even omitted in these patients due to severe immune deficiency, stage IV disease, by many physicians.

CASE REPORT

A 49 year old health worker presented with a 1 year history of left cervical lymphadenopathy with rapid enlargement in two months prior to presentation and right breast lump. There was associated weight loss and hearing loss. There was however no history of diarrhea or cough. She was retroviral positive and had lost her spouse to the disease seven years earlier. She denied any history of sexual activity or blood transfusion since the loss of her spouse. Although testing positive to the virus much earlier, she was not on antiretroviral drugs; CD4 count said to be high. Examination showed a middle aged lady with evidence of weight loss (63kg as against a prior 75 kg), pale, anicteric, a left sided cervical lymphadenopathy with firm and matted lymph nodes. There was a right breast lump, 2cm in diameter which was firm and mobile. Bilateral axillary lymph node enlargement was demonstrable. Abdominal examination showed an enlarged liver at 4cm below the costal margin. CD 4 count was 80, hepatitis B was negative, PCV check was 28% and WBC count was 5,400/cm³. Cervical lymph node

and breast lump biopsy revealed a non-Hodgkins lymphoma. The patient was diagnosed to have stage IV retroviral disease, AIDS with systemic lymphoma.

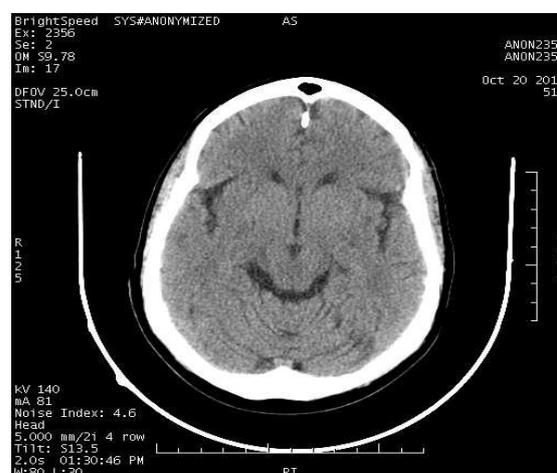
Antiretroviral drugs were commenced and soon after, chemotherapy with cyclophosphamide and vincristine were also commenced. There was progressive shrinkage in the cervical swelling. She developed right facial nerve palsy, upper motor neurone type with right hemiparesis, and Medical Research Council (MRC) power of 3/5 on the right upper and lower limbs. Brain CT showed a mass in the left temporal lobe [Figure 1]. She had doxorubicin commenced immediately. She responded with much improvement in muscle power (MRC 4+/5) by 72 hours and was able to walk unaided. She had 5 cycles of CHOP regimen. Additionally, prolonged periods of anaemia ensuing during chemotherapy from myelosuppression was managed with regular blood transfusions with cumulative amounts of 14 pints of blood over a 12 month period in achieving an average PCV of 25%. Granulocyte colony stimulating factor was also employed in boosting the white cell counts in between chemotherapy cycles. However with recurring cervical lymphadenopathy three weeks after CHOP regimen ceased, 5 cycles of etoposide and intrathecal methotrexate were administered. Subsequent brain CT showed no evidence of the tumour [Figure 2]. Currently, her weight is impressive at 73kg, BSA 25.3. CD 4 count is at 280. She has resumed normal work hours and no recurrences have been noted at three years post HIV-associated systemic lymphoma diagnosis.



DISCUSSION & CONCLUSION

Our case was diagnosed with advanced stage non-Hodgkin lymphoma involving the temporal lobe, associated hearing loss, left hemiparesis and severe immune deficiency (CD4 count of 80cells/mm³) requiring chemotherapy. Earlier schools of thought held that chemotherapy with HAART was not practicable for HIV associated cancers given the bone marrow suppressant effects of chemotherapy.

However, reports from several trials have shown significant increases in CD 4 counts and decrease in viral load despite concurrent use of chemotherapy with HAART.^[4] In the same vein, Vaccher et al reported superior outcome for cases treated with HAART combined with CHOP chemotherapy than those on chemotherapy only.^[5] Lesser AIDS opportunistic infections at 18% were recorded in cases treated with HAART/CHOP than chemotherapy alone at 52%.⁵ Kaplan et al have also showed evidence of complete response and survival following this combination as occurred in our case.^[6] The use of HAART has been shown to boost CD4 count restoring immunity, decrease the incidence of opportunistic infections and thus better tolerance to chemotherapy.^[7,8]



Although the tolerability of HAART with chemotherapy has been noted in several studies, our case developed neutropaenia up to 500 cells/mm³. This was due to the zidovudine component in the initial HAART combination of (zidovudine, lamivudine and nevirapine). Use of zidovudine has been reported with neutropaenia in 8% of AIDS patients thus being synergistic with chemotherapy induced myelosuppression seen in our case.^[9] Severe neutropaenia reversed following substitution of the older HAART with tenofovir, emtricitabine and efavirenz in our case. Out of concern for myelosuppression occurring in this subset of patients, earlier researchers had advocated for 'low dose chemotherapy'.^[2] One large study has used standard dose chemotherapy in patients with HIV associated lymphoma with complete regression observed in 63% of cases and 13% partial remissions. There were deaths in 14% during chemotherapy attributed to progressive disease in about half of this number.^[10]

Chemotherapy using doxorubicin produced a dramatic recovery of muscle power in hemiparetic limbs in this case within the early days of a first cycle administration. Doxorubicin, an anthracycline, has been rated as a potent chemotherapeutic agent. Chemotherapy induced myelosuppression in our case

who already was immunocompromised was managed with the use of granulocyte colony stimulating factor. Our case recorded good elevation of the white cell count with each administration when dealing with the nadir during chemotherapy. However cost still remains an issue in a developing economy.

Our experience with the use of chemotherapy in HIV associated lymphoma with support from granulocyte colony stimulating factor alongside HAART in this case was quite successful. More studies are required in the use of chemotherapy for patients with HIV associated lymphomas.

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