Sudden onset of herpes zoster following chemotherapy for orbital lymphoma in a HIV positive patient

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ABSTRACT

We report a 38-year-old HIV positive female, who developed an acute attack of herpes zoster (HZ) involving the mandibular, C2, C3, C4, T1, and T2 dermatomes, 9 days after the commencement of the first cycle of chemotherapy regimen for non-Hodgkin's lymphoma (NHL). She had developed NHL of the ovary approximately 6 months earlier, followed by metastasis to the left orbit resulting in proptosis of the left eye. A combination of a positive HIV status, lymphoma, and chemotherapy can predispose a patient to an attack of HZ involving many dermatomes.

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The human immunodeficiency virus (HIV) epidemic, is a worldwide problem and the scale of infected numbers of people is vast.[1] Several studies have documented that 50-75% of adult patients with acquired immunodeficiency syndrome (AIDS) will experience ocular complications.[2] For the ophthalmologist in Africa, herpes zoster (HZ) infection is a common first presentation of HIV infected individuals and the ocular effects may be extremely severe. The correlation between severe HZ ophthalmicus in young adults and HIV seropositivity is well-established.[3] Herpes zoster is a marker for the HIV infection in Africa with a high positive predictive value.[4] The varicella zoster virus (VZV) causes varicella (chickenpox), remains dormant in dorsal root and cranial nerve ganglia and can be reactivated as a consequence of declining VZV-specific cellular immunity leading to HZ (shingles).[5] There is also an increased incidence of HZ in patients with Hodgkin's and non-Hodgkins Lymphoma (NHL).[6,7] It appears that NHL is increasing in prevalence among patients with AIDS.[8] Non-Hodgkin's lymphoma is also known to be one of the opportunistic events in patients infected with HIV during the first 6 months of Highly Active Antiretroviral therapy (HAART).[9] This is a report of an HIV positive patient on HAART who had NHL of the ovary with metastasis to the orbit who developed HZ after commencement of chemotherapy in Benin City, Nigeria.

Case Report. A 38-year-old female trader presented to the eye clinic of the University of Benin Teaching Hospital on June 6, 2005 with a history of swelling of the eye and visual loss in the left eye of 2 weeks duration. The swelling was rapidly progressive with associated pains especially on the movement of the eyeball, purulent discharge, and itching. There was no history of trauma to the left eye prior to the onset of symptoms. There was also no history suggestive of an upper respiratory tract infection. She had used several eyedrops without improvement. She was not a known hypertensive or diabetic. There was a positive history of weight loss. There was no associated fever, night sweats, bleeding diathesis, and bone pains. She is a known HIV positive patient diagnosed in May 2005, and had been started on the HAART regimen (Tabs lamivudine 150 mg bd, tabs Nevirapine 200 mg daily for 2/52, then 200 mg bd, caps Stavudine 40 mg bd). She had a total abdominal hysterectomy in January 2005 for an ovarian mass at a private hospital. At that time, she was not known to be HIV positive as the HIV screen was not carried out preoperatively. Histology of the ovary showed the features of a NHL. No specific therapy was given for NHL after the initial diagnosis. She was referred to the University of Benin Teaching Hospital, where the HIV screening was carried out. The HIV test was performed by enzyme-linked immunosorbent assay (ELISA) and confirmed by the Western blot technique. She was found to be positive for HIV-1. Her CD4+ T lymphocyte count was 192 cells/µl using the Partec IVD flow cytometer. The viral load was not determined due to lack of facilities. She was put in

clinical stage 4 based on a history of significant weight loss and presence of lymphoma. She is a widow and has one child. Her husband died in 1995 after a brief illness. She had multiple sexual partners since then. Visual acuity was light perception in the left eye and 6/9 in the right eye. There was proptosis, discharge, optic atrophy, and chemosis of the left eye (**Figure 1**). The right eye was normal. An impression of a secondary metastatic tumor to the left orbit was made. An ocular ultrasound scan showed a mixed echogenic mass in the left retrobulbar area arising from the optic nerve measuring 3.9 x 2.4 cm with anterosuperior compression of the globe. An incisional biopsy was performed, which showed ocular tissue with a diffusely disposed infiltrate of medium sized lymphocytes with ovoid dark staining nuclei, many of which were plasmacytoid. The features were suggestive of NHL. She was commenced on chemotherapy (CHOP) regimen (cyclophosphamide 650 mg intravenous [iv] on day one and 8, adriamycin 45 mg iv day one and 8, vincristine 1.5 mg day one and 8, prednisolone 20 mg orally, 3 times a day x 10/7) after the incisional biopsy and stable hematological values. Blood film showed a dimorphic picture and few target cells. On the ninth day of the first cycle, she suddenly developed the left sided multiple vesicular eruptions affecting the mandibular, C2, C3, C4, T1, and T2 dermatomes (**Figure 2**). An impression of HZ was made. She was then commenced on tabs Acyclovir 800 mg 5 times daily for 2 weeks. By this time, proptosis had resolved remarkably; however, the visual acuity in the left eye had reduced further to no perception of light. She was discharged on July 6, 2005 and given appointment for the second cycle of chemotherapy, but she was lost to follow up.

Figure 1 - An HIV positive patient with proptosis of the left eye.

Figure 2 - Multidermatomal involvement by herpes zoster in a HIV positive patient.

Discussion. The HIV positive female was diagnosed after she had a total abdominal hysterectomy for an ovarian mass that was found on histology to be NHL. The HIV screening was not carried out preoperatively, so it was not certain if this patient was HIV positive before she developed the NHL of the ovary. Thus, not certain if the NHL was related to opportunistic events of HIV infection. However, in view of the patients' history of multiple sexual partners for 10 years since the death of her husband, the fact that the exact cause of her husbands' death was not known, a history of weight loss and the short interval between the total abdominal hysterectomy and the diagnosis of HIV, it was presumed that she might have been HIV positive before the onset of lymphoma. Several possible predisposing factors to the attack of HZ in this patient can be recognized. These include the HIV infection,[3,4] lymphoma,[6,7] and chemotherapy,[10,11] or a combination of these. Herpes zoster during HAART has been shown to be an immunopathological consequence of the host immune response, correlating with the beginning of immune restoration.[12] The incidence of HZ is reported to be the highest in the first 6 months of enrollment in patients at the late stage of HIV infection, and thus, did not increase with the introduction of HAART.[13] The baseline CD4+ lymphocyte count was the most significant risk factor associated with the development of HZ. Herpes zoster was associated with the increased risk of the HIV progression, but not mortality.[13] These findings are agreeing with this report, where the HZ occurred <2 months after the commencement of HAART regimen with the low CD4+ lymphocyte count. Multidermatomal involvement has been shown to be more common in HZ in the presence of HIV infection.[14] This is agreeing with the finding in the patient in this report where 6 dermatomes were involved

by the HZ. Malignant lymphoma is associated with an increased risk of HZ even without HIV.[6,7] Lymphoma may modify the presentation of HZ in a variety of ways. Non-Hodgkin's lymphoma may be complicated by the recurrent intractable generalized HZ.[7] Lesions of disseminated HZ may also be infiltrated by NHL.[15] This may result in resistance of the lesions to antiviral therapy unless it is combined with chemotherapy. A combination of HIV infection and lymphoma is thus, more likely to be complicated by HZ. Chemotherapy for lymphoma may also be responsible for initiating the attack of HZ.[10,11] In this report, the vesicles of HZ were observed in 9 days after the onset of the first cycle of the CHOP regimen for lymphoma. Specific cellular-immune responsiveness to varicella-zoster virus can be markedly reduced during chemotherapy.[11] Reducing the immunosuppressive therapy to increase immune responses may initiate the resolution of HZ lesions and halt dissemination.

In conclusion, this report presents a case where several factors predisposed an HIV positive patient to a dramatic attack of multidermatomal HZ. The HIV infection, lymphoma, and commencement of chemotherapy might have combined to predispose this patient to an acute attack of HZ.

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