CASE REPORT

Herpes-zoster virus ophthalmicus as presenting sign of HIV disease

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KEYWORDS
Chicken-pox;
Herpes zoster;
Varicella-Zoster;
 Opportunistic infection;
HZO;
Anti-viral;
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Abstract  After a childhood episode of chicken pox, a Varicella-Zoster infection, the viral DNA reside in a dormant state in the dorsal root ganglia. The viruses get reactivated when the individual is immuno-compromised, in adulthood to cause characteristic lesions of Herpes zoster on the skin and the eyes. This case reports a 32 year old female who presented with neuralgia and clinical features of crusting skin ulcers involving the ophthalmic division of the trigeminal nerve, corneal dendritis and anterior uveitis with circumlimbal injection of the right eye. Visual acuity was OD: 6/60 and OS: 6/9. These clinical signs and symptoms were consistent with Herpes Zoster Ophthalmicus (HZO). Further medical laboratory tests showed positive for HIV and patient had a CD4$^+$ count of 350 cells/μl of blood with a viral load of 100,000 copies/ml. Patient was subsequently treated of the Herpes zoster infection with Acyclovir (800 mg) prescribed five times daily for 7 days. While, at the HIV/ AIDS project facility she was placed on Hyper Active Antiretroviral therapy (HAART): Stavudine (30 mg) bid for 2/12, Zidovudine (300 mg) bid for 2/12 and Efavirenz (600mg) nocte for 2/12. There was complete resolution of the keratopathy, the visual acuity of OD improved to 6/12 by the 2nd month and the patient was without the experience of post herpetic neuralgia. At present (after 3 months) her CD4$^+$ has increased to 1000 cells/μl. HIV infection should always be considered in patients younger than 65 years with Herpes zoster ophthalmicus.

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PALABRAS CLAVE
Varicela;
Herpes zóster;
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 Infección oportunista;
HZO;
Antivírico;
VIH/ SIDA

Resumen  Después de un episodio de varicela en la infancia, una infección del virus varicela-zóster, el ADN vírico permanece en estado latente en los ganglios de la raíz dorsal. Los virus se reactivan cuando el sujeto está inmunodeprimido; en la edad adulta causa lesiones características del herpes zóster en la piel y en los ojos. Se reporta el caso de una mujer de 32 años con neuralgia y características clínicas de úlceras en la piel con costras implicando la división oftálmica del nervio trigémino, dendritis corneal y uveítis anterior con inyección circunlimbal del ojo derecho.

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Introduction

Chicken pox (varicella) is a highly contagious skin disease primarily in children 2 to 7 years of age. The causative agent is the Varicella-Zoster virus, a member of the family Herpesviridae, which is acquired by droplet inhalation into the respiratory system. Following an incubation period from 10 to 23 days, small vesicles erupt on the face or upper trunk. These get filled with pus, get broken and become covered by crusting with an intense sensation of itching. Individuals who recover from chickenpox are subsequently immune to this disease; however they are not free of the virus as viral DNA resides in a dormant (latent) state in the dorsal root ganglia.

Later in life when this primary infected person is immuno-compromised, the virus may become activated. The viruses migrate along afferent sensory nerves to the skin and eye where they replicate and cause the characteristic lesions. This reactivated form of chickenpox (Varicella) is termed Herpes Zoster. This report describes a HIV-2 positive patient who presented with Herpes zoster infection which affected the ophthalmic branch of the right trigeminal nerve.

Case report

A 32 year old female presented to the optometric facility of Central ophthalmic clinic in Eket, with complains of burning sensation and deep lancing pain on the surface of the right eye, upper lid, anterior scalp and forehead which followed soon after few days of fever, malaise and headache. Inspection showed skin lesions on the right half of the face, the frontal and the nasociliary i.e. the ophthalmic branch of the trigeminal nerve which have formed crusting ulcers.

The ocular signs were microdendritic ulcers on the right eye which were mostly peripheral with few central ones that abutted the visual axis. The microdendrites stained with Rose – Bengal. Another ocular sign on the OD was the presence of anterior uveitis with a circumlimbal injection. There was transient diplopia with restricted ocular movement when gaze was directed laterally and upward due to the involvement of the 3rd cranial nerve. Funduscopic examination revealed no retinal involvement. There was no abnormality detected (NAD) on the left eye. Visual acuity was OD: 6/60 and OS: 6/9. In addition the patient disclosed a previous childhood history of chickenpox during her primary school days, about 25 years ago. These signs and symptoms were consistent with Zoster.

Patient claimed to have enjoyed a general good health till this event, though agreed to have recently lost some weight. The patient was referred to the state owned Immanuel General Hospital, Eket for further medical laboratory tests. PCR test for Varicella – Zoster was positive. Genie II rapid HIV screening test was positive for HIV-2. The CD4+ count was 350 cells/µl blood and viral load was 100,000 copies/ml.

In the optometric facility, patient was treated for Herpes Zoster Ophthalmicus (HZO) with oral Acyclovir (800 mg) prescribed 5 times daily for 7 days and topical prednisolone acetate (1%) 2 drops instilled four times daily for 7 days. The pupil of the right eye was kept dilated with Atropine (1%) of which 1drop was instilled three times daily for one week.

After one month, on appointment she returned to Immanuel General Hospital, to the Global HIV/AIDS initiative of Nigeria (GHAIN) project facility for her counseling. She was categorized “ stage 2B” by the CDC clinical and immunological staging and placed on Hyper Active Antiretroviral Therapy (HAART): Stavudine (30 mg) bid × 2/12, Zidovudine (300 mg) bid × 2/12 and Efavirenz (600 mg) noct e × 2/12.

After 3 months on her HAART, her CD4+ count was increased to 1000 cells/µl and the viral load markedly reduced to less than 1,000 copies/ml.

Her ophthalmic and Acyclovir medications prevented synaechia and the chronic form of cornea ulcer. There was a total resolution of the keratopathy. The visual acuity (VA) on the right eye improved to 6/12 by the second month; and presently the VA stands at 6/6 on either eye. The patient also restored is a smooth ocular motility without the experience of diplopia. Patient has been also without the experience of a post-herpetic neuralgia.

Discussion

A Herpesviridae is a double stranded DNA virus, with the outstanding property of establishing a lifelong persistent infection in their hosts by undergoing reactivation; with the
reactivated infection being clinically quite different from
disease caused by primary infection.\(^3\)

Varicella (Chickenpox) and Herpes Zoster (Zoster) are
different conditions caused by the same herpesviridae
called Varicella–Zoster. While Varicella is common in
children, Herpes Zoster mainly affects the elders.\(^1,8,9\)

Throughout the world the incidence rate of herpes zoster
every year ranges from 1.2 to 3.4 cases per 100 healthy
individuals, increasing to 3.9–11.8 per 1,000 individuals
among those older than 65 years.\(^8\)

The current theory of etiology is that after an attack of
chicken pox and its attendant viraemia, some virus spread
along the sensory nerves from the skin lesions to be retained
in the ganglia adjacent to the spinal cord (dorsal root
ganglion) or the semilunar ganglion in the base of the
skull.\(^7,9\) Later, under the influence of trigger factors
particularly reduced immunity by such factors as
psychological, physiological stress, age or AIDS, the virus
reactivates and migrates along afferent sensory nerves to
the skin and eye where it causes the characteristic
facial lesions.\(^2–7\) This is directly the result of viral infection,
antigen-antibody reactions, delayed cell mediated
hypersensitivity reactions, denervation and ischaemia
induced by vasculitis.

Approximately 15% of all cases of Herpes Zoster affect the
frontal, lacrimal and nasociliary branches—that is the
ophthalmic division of the trigeminal nerve.\(^9\) The condition
is then referred to as Herpes Zoster ophthalmicus (HZO).
The HIV positive population have a 15–25 times greater
prevalence of zoster compared to the general popula
tion\(^10\) and the risk of developing HZO has been reported to
be 6.6 times higher than that of the general population.\(^11\)

As occurs with other opportunistic infections in HIV,
Herpes zoster can be more debilitating with greater skin
and ocular involvements. HZO is usually described by a
prodrome of fever, malaise and headache which typically
herald the neuralgia component which precedes the
cutaneous lesion of HZO. The neuralgia varies from itching,
burning sensation to severe deep boring or lancing pain
which is either persistent or intermittent. These may
totally resolve within the first 4 weeks. Trigeminal neuralgia
is caused by demyelination of trigeminal sensory fibres
resulting from compression by an overlying blood vessel or
in ltrations.

The skin lesions of Herpes zoster are histopathologically
identical to those of Varicella.\(^3\) The rashes may involve one
or all the three branches of the ophthalmic distribution
of the trigeminal nerve.\(^9\) Initially the lesion is maculopapular
and then becomes pustular. The pustules subsequently burst
to form crusting ulcers (figure 1). The involvement of the
nasociliary nerve (Hutchinson’s sign) which supplies the side
of the nose correlates significantly with the subsequent
development of ocular complications.\(^12\)

Conjunctivitis is common and always associated with
vesicles on the lid margins. This usually resolves within one
week. If chronic, a mucus-secreting conjunctivitis may be
accompanied with lipid-lined granulomata under the tarsal.

Episcleritis occurs in about 1/3 cases at the onset of
the rash but it is usually concealed by the overlying
conjunctivitis; scleritis is much less common. When present,
scleritis frequently becomes chronic and gives scleral
atrophy, while a neglected sclerokeratitis yields a
progressive scarring of the cornea.

Corneal complications occur in approximately 65% of
cases with HZO. Punctate epithelial Keratitis develops in
about 50% of patients within 2 days of the onset of the
rash.\(^10\) The foci consist of swollen epithelial cells containing
replicating virus. The lesions stain with Rose Bengal and are
usually peripheral, multiple, raised and occasionally
coated with mucous.

Microdendritic ulcers are also another mark of epithelial
disease and appear within 4-6 days. HZO microdendrites are
common and have no central ulceration or “terminal bulbs”
like dendritic ulcers. The ulcers are usually peripheral,
broader, more plaque like and more stellate shape than
dendritic (figure 2).

Nummular keratitis is seen beneath the Bowman’s
membrane in 33% of patients, 10 days after the onset of
rashes. The lesion is characterized by multiple fine granular
deposits which are surrounded by a halo of stromal haze.
Lesions may resolve without trace or become indolent with
chronic cellular and lipid in ltration that impair vision.

\[\text{Figure 1} \quad \text{Rashes distributed along the ophthalmic branches of}
\text{the right Trigeminal of the patient.}\]

\[\text{Figure 2} \quad \text{Microdendrites on patient’s right cornea that stain}
\text{with ourescein.}\]
Disciform keratitis: most at times follows nummular keratitis. It appears in 5% of cases 3 weeks after the onset of rashes and usually central in location. If neglected there will be scarring, vascularization and deposition of lipid.

Mucous plaque keratitis develops in about 5% of cases at any time from two weeks of onset rashes. It is marked with a sudden onset of ciliary injection and mucous plaque deposits on the surface of a diffusely swollen corneal epithelium. The white-grey plaque is adherent to the surface epithelium, with sharply demarcated margins and may be branched or linear. The plaques disappear after 3 months leaving a faint diffused corneal haze.

The neurological complications are cranial nerve palsy particularly of the 3rd cranial pair. Recovery occurs spontaneously within six months. Optic neuritis occurs in about 1 in 400 cases.

Many cases of acute retinal necrosis associated with Varicella-Zoster virus have without other clinical features of varicella or zoster infection elsewhere. Hence a laboratory diagnosis for VZV is recommended in acute retinal necrosis when there are no other ocular complication or skin lesions.

A rise is specific antibody titer can be detected in the patient's serum by tests like Complement Fixation, Neutralization Test (in cell culture), Indirect Immuno fluorescence and Enzyme immunoassay.

When vesicles are present, diagnoses in the laboratory can also be made by staining smears of scrapings or swabs of the base of vesicles and multinucleated giant cells are seen. These are absent in non-herpetic vesicles. Immuno fluorescence staining of smear can be used as well to detect intra cellular antigens.

In rapid diagnosis, in electron microscope examination, Varicella-zoster virus – specific antigens or viral DNA can be detected in vesicle uid, in extracts of crust or in biopsy material.

The virus can also be isolated from vesicle fluid using cultures of human cell in 3-7 days. This is inoculated promptly since the virus is very labile in vesicle uid.

The presence of HZV in a young otherwise healthy patient should provide pause for the consideration of underlying HIV.

The laboratory diagnosis for HIV can be by viral isolation and culture, or by using assays for viral reserve transcriptase activity or viral antigens. However, diagnosis is best through the detection of specific anti HIV antibodies in the blood. These antibodies may be detected by GENIE or HIV AG and be its first clinical presentation.

Antiviral drugs, mydriatics and topical corticosteroids. Early treatment with Acyclovir 800 mg 5 times a day; Famiclovir 500 mg or Valacyclovir 1 gram t.i.d for 7 days reduce ocular complications. Patients with keratitis or uveitis require topical corticosteroids e.g. prednisolone acetate 1%instilled q.i.d initially, lengthening the interval as symptoms improve. The pupil should be dilated with Atropine 1% or scopolamine 0.25% 1 drop t.i.d., intraocular pressure must be monitored and treated if it rises significantly above normal values. For the symptoms, the use of a brief course of high doses of corticosteroids to prevent post herpetic neuropahty in patients more than 60 years who are in good general health remains controversial.

In our optometric facility this case was treated for Herpes Zoster Ophthalmicus (HZO) with oral Acyclovir (800 mg) prescribed 5 times daily for 7 days and topical prednisolone acetate (1%) 2 drops instilled four times daily for 7 days. The pupil of the right eye was kept dilated with atropine (1%) of which 1 drop was instilled three times daily for one week. There was a total resolution of the keratopathy. The visual acuity (VA) on the right eye improved to 6/12 by the second month; and presently the VA stands at 6/6 on either eye. The patient also restored a smooth ocular motility.

The antivirals currently approved for use in HIV disease to increase the CD4 count and reduce the viral load are of three types.

1. Nucleoside reverse Transcriptase inhibitors (NRTIS). Examples are Zidovudine (AZT), Stavudine (d4t), Lamivudine (3TC), Didanosine (ddi), Abacavir (ABC), Zalcitabine (ddc) and Emtricitabine.

2. The Nonnucleoside Inhibitors of Reverse Transcriptase (NNRTIS). Examples are Neviripine (NVP), Efavirenz (EFV) and Delavirdine (DLV).

3. The protease inhibitors (PI) work by blocking the activity of the HIV protease and thus interfere with vision assembly. Examples are Saquinavir (SQV) indinavir (IDV), Ritonavir (RTV), Nelfinavir (NFV), Amprenavir (APV) and Lopinavir (LPV).
Therapy with combinations of antiretroviral, such as the combination of AZI, ZTC and RTV, at high dosages to prevent the development of resistance is referred to as Highly Active Antiretroviral Therapy (HAART). It suppresses viral replication to below limits of detection in plasma and decreases viral loads in lymphoid tissue, allowing the recovery of immune response to opportunistic pathogens.19,20

The patient was placed on Hyper Active Antiretroviral Therapy (HAART): stavudine (30 mg) bid × 2/12, Zidovudine (300 mg) bid × 2/12 and Efavirenz (600 mg) nocele × 2/12. After 3 months on her HAART the viral load was markedly reduced to less than 1,000 copies/ml and her CD4+ count increased to 1000 cell/μl.

If HIV treatment is started early enough the immune system (as monitored by the increased CD4+ count) will be recovered after HIV levels have fallen.21 This prevents the development of opportunistic infections. Hence the need for early detection of HIV. Recognition of potential opportunistic infections in selected patients will help achieve the goal of early detection of HIV.

HIV infection should always be considered in patients younger than 65 years with herpes zoster ophthalmicus.15,22

Conflict of interests

No conflict of interests.

References

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