Clinical Profile of Herpes Zoster Ophthalmicus in Ethiopians

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We conducted a prospective study of 100 consecutive Ethiopian patients with herpes zoster ophthalmicus (HZO); this study revealed a high incidence of HZO among the young (mean age, 35 years). Eighty-one (95%) of 85 patients who underwent serological testing were seropositive for antibodies to human immunodeficiency virus (HIV). Unlike previous investigators, we found a marked increase in the incidence and severity of eyelid (25%) and ocular (78%) complications as well as postherpetic neuralgia (55%). Visual loss occurred in 56% of the cases. Lack of medication, delay in presentation, severity of HIV-related HZO, and application of herbal medications adversely affected the outcomes for these patients. We conclude that all patients with HZO, especially those younger than 45 years of age, should be screened for HIV infection. Because HZO is a vision-threatening problem, all health care workers should become aware of its management.

Herpes zoster ophthalmicus (HZO) is a maculopapular rash that becomes a vesicular rash and later leaves a scar on the dermatomal distribution of the ophthalmic division of the trigeminal nerve. Few cases of HZO that did not involve a cutaneous eruption have been reported in the literature [1]. HZO is most often due to reactivation of latent varicella-zoster virus from the gasserian ganglion, although exogenous exposure to the virus may occasionally be responsible for the rash [2]. HZO occurs in 10%–17.5% of patients with herpes zoster [3, 4]. Aging, malignancies, immunosuppressive therapy, chemotherapy, tuberculosis, malaria, syphilis, and trauma are predisposing factors [1, 5, 6]. Since the advent of the HIV pandemic, HZO has been recognized as an early clinical marker of HIV infection and as an ocular manifestation of AIDS [7–10].

Ophthalmic findings vary considerably. Ocular complications occur in 50%–89% of patients with HZO; these complications lead to substantial visual disability, severe postherpetic neuralgia, and, rarely, fatal cerebral complications [9, 11–13]. Systemic zoster encephalitis and pneumonitis may develop in immunocompromised patients [3, 5, 7, 11, 12].

In one Ethiopian study, HZO was found to be the second leading reason for seeking care at the neuro-ophthalmic clinic of a tertiary eye-care referral center [14]. Health care workers at two hospitals in Addis Ababa have reported cases of HZO in association with AIDS and HIV infection [15, 16].

Our objectives in conducting the present study were to describe the clinical features and complications of HZO in Ethiopian patients; to determine the demographics of patients with HZO (with special reference to age, sex, marital status, and occupation); and to determine the prevalence of HIV infection in Ethiopian patients with HZO.

Patients and Methods

From 1 October 1993 to 31 May 1995, we prospectively studied the cases of 100 consecutive Ethiopian patients with clinically diagnosed HZO who were seen at the Menelik II Hospital in Addis Ababa. Facilities for viral culture are not available in Ethiopia. Patients with presumptive diagnoses of zoster sine eruptione were excluded because of the rarity of this form of the disease and because an assay of serum CF antibody to varicella-zoster virus, needed for definitive diagnosis, could not be done in Ethiopia. All patients were examined within 30 days of onset of the rash.

An open-ended questionnaire was used to collect demographic data including age, sex, address, occupation, and marital status, as well as the following medical data: the date of onset of prodromal symptoms and rash; a history of weight loss or known systemic illnesses (i.e., tuberculosis, sexually transmitted diseases [STDs], and diabetes mellitus); a history of immunosuppressive drug intake, irradiation, blood transfusions, or repeated injections before the onset of HZO; a history of a similar previous attack of zoster in any other part of the body; recent exposure to persons with chickenpox; and use of herbal medication for treatment of the illness. The presence or absence of postherpetic neuralgia was recorded. Postherpetic neuralgia was defined as the presence of continuous or frequent pain for ≥6 months after the onset of disease [13].

The dermatomal distribution of the rash (75% of patients) or scars (25%) was evaluated, and an eyelid examination was performed, after which a thorough ocular examination that
The distributions of the patients by age and sex are shown in table 1. Ages ranged from 18 years to 70 years (mean age \[\pm SD\], 35.24 ± 10.2 years). The male-to-female ratio was 2:1. Eighty percent of the patients were aged \(\leq 45\) years. Eighty-four percent of the patients were from Addis Ababa or resided within a 100-km radius of the city, while the remaining patients (16%) came from different regions of the country. Forty-three of the patients were married, which was not a statistically significant factor \((P = 0.9)\). Fifty percent of the patients were government employees; taxi, bus, and truck drivers; or housewives.

Fourteen patients were found to have tuberculosis, for which they received treatment. Sixteen patients had histories of STDs. One patient developed HZO 1 month after undergoing surgical intervention (orbitotomy). He was seropositive for antibodies to HIV before the operation. None of the patients was diabetic or iatrogenically immunosuppressed (either as a result of chemotherapy or radiation therapy); none had a history of recent exposure to persons with chickenpox; none had bilateral involvement; and none had had a previous episode of HZO.

Because of the unavailability of acyclovir and its costliness when available, only 22 patients received the drug (18 received topical therapy for established ocular complications and four received oral therapy soon after the development of the disease). Fifteen patients fulfilled the criteria of the WHO clinical case definition of AIDS [18]. One patient with AIDS died of diarrheal disease. Thirty-four patients applied herbal medication to the rash soon after the onset of the disease.

The dermatomal distribution of HZO was localized in the ophthalmic division of the trigeminal nerve in 95% of cases. Three patients had mixed ophthalmic- and maxillary-division involvement, and two patients had involvement of all divisions of the trigeminal nerve. The right eye was affected in 49 patients, and the left was affected in 51.

Ocular complications were observed in 78% of the patients. We observed zoster corneal involvement in its protean manifestations in 65% of our patients. Anterior uveitis, which was observed in 50% of our patients, occurred with or without corneal involvement. (It is usually chronic, tends to recur, and requires topical corticosteroid therapy for a long period). Secondary glaucoma, which developed in 50% of the patients with anterior uveitis, was difficult to control. We detected cataracts, which occur secondary to the inflammatory process (uveitis) or long-term use of corticosteroids, in 14 of the patients. We also observed cases of scleritis, optic neuritis, hypopyon, retinal artery occlusion, and phthisis bulbi. The rates of the different ophthalmic complications in the present study, as compared with those in other studies, are shown in table 2. Frontal and/or corneal anesthesia occurred in 47% of the patients.

Surgical correction of the eyelid, temporary tarsorrhaphy, and evisceration were performed for six patients, four patients, and three patients, respectively. The follow-up period ranged from 6 months to 18 months, with an attrition rate of 15%. The visual acuity was <20/200 for 40% of the patients, and another 36.47% (31 of 85) went blind (visual acuity, <20/400) in the involved eye (on the basis of the WHO defini-
Table 2. Comparison of ophthalmic complications in patients with herpes zoster ophthalmicus who were from Ethiopia, the United States, the United Kingdom, and Rwanda.

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<td>Corneal involvement</td>
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<td>Postherpetic neuralgia</td>
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<td>17.4</td>
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NOTE. The study periods were as follows: Ethiopia, 1993–1994; United States, 1975–1980; United Kingdom, 1972–1988; and Rwanda, 1987. Data are percentages of patients; some patients had more than one complication.

* Of 85 patients who were followed for ≥6 months in our study.

tion of blindness). There was no statistically significant difference in the final visual acuity between patients who did or did not receive topical acyclovir after the development of ocular complications.

The results of baseline laboratory investigations were all normal. Nineteen (22.35%) of the 85 patients who volunteered to undergo VDRL and FTA-ABS testing had reactive tests. The double ELISA technique revealed HIV infection in 81 (95.3%) of the 85 patients. All of the patients aged <45 years were infected with HIV. Four patients >45 years of age were found to be seronegative for HIV, a finding that decreases the seropositivity rate to 76.47%.

Discussion

HZO was previously believed to be a disease of the elderly [3, 4, 11–13]: in a study from the United States that was published in 1983, the mean age of the patients was 65 years [12]. In a prospective study from the United Kingdom in 1977 that included 77 patients, the youngest patient was 46 years old [19]. Since the advent of the HIV pandemic, this pattern has changed. In our study, 83% of the patients were <45 years of age (mean age, 35 years). This finding is in agreement with that of Kestelyn et al. [9], who in 1977 described 19 patients from Rwanda for whom the mean age was 28 years. Although children are said to constitute 7% of patients with HZO [1], the youngest patient in our series was 18 years old.

Harding et al. [13] found a significant predominance of males among patients <60 years of age; this predominance was more pronounced among patients <40 years of age. Other studies haven’t shown a sexual predilection [1, 3, 4, 12]. The higher rate of HZO among our male patients is not due merely to a higher prevalence of this disease in males; as has been shown in other hospital-based studies in Ethiopia, our findings reflect the fact that males have better access to health care institutions [14].

Marital status didn’t appear to play a role in the development of HZO in our series of patients. In terms of occupation, most of the patients were government employees, drivers and their assistants, housewives, and soldiers, which parallels the findings of the recent report on Ethiopian patients with AIDS [20]. The fact that none of the patients had a history of recent exposure to chickenpox favors viral latency as a cause of herpes zoster.

HZO has been found to be one of the ocular manifestations of AIDS [10, 16] and an early clinical marker of HIV infection [8, 9]. Fifteen of the patients in this study were found to have AIDS; 14 of these patients had concomitant tuberculosis. The prevalence of HIV infection among our patients (95.3% of the total population and 100% of patients aged <45 years) is in agreement with that reported from Rwanda in 1987 [9] but differs from that reported in the United States in 1993, where only 21% of the total number of patients and 56% of the patients aged <45 years were HIV infected [10].

Nineteen (22.35%) of our 85 patients had positive serologies for syphilis. Recent studies among donors of blood to the blood bank and of pregnant women receiving antenatal care showed that 8%–13.1% had reactive VDRL tests and that the rate of positivity for antibodies to Treponema pallidum is higher among HIV-infected patients [21, 22]. Syphilis has been
incriminated as a predisposing factor for the development of HZO [6], and the strong association between syphilis and HIV infection is also a risk factor for acquiring HZO.

The dermatomal distribution of HZO is observed with equal frequency on the right and left sides [12]. Involvement of two or more branches of the trigeminal nerve, which is seen in 5% of cases, is said to be a sign of disseminated zoster in the immunocompromised patient [2]. The high degree of eyelid involvement that we observed among our patients (nearly twice that seen among patients in the United States study [12]) might have resulted from the common practice of using herbal medication and from the severity of HZO in the HIV-infected patients. The use of herbal medication was associated with both bacterial superinfection and chemical toxicity, resulting in more-severe eyelid disease.

The incidence of corneal involvement among our patients (65%) is higher than that observed in studies from the United States (54.6%) [12] and the United Kingdom (49%) [11] and close to that observed in a recent study of HIV-infected patients from Rwanda [9]. The combination of eyelid abnormalities and neurotropic keratopathy is likely to lead to permanent corneal damage [1]. Scleritis, optic neuritis, retinal artery occlusion, and phthisis bulbi have also been described in association with HZO [1, 2, 11, 12].

A prospective study of 61 patients in the United Kingdom showed that 31% had extraocular muscle palsy [19]; most of the patients developed this complication during the first 2 weeks of the rash. In our study, the rate of this complication was 12%, which is much higher than the rate of 3% in a study from the United States [12]. All of our patients with extraocular muscle palsy, except two with external ophthalmoplegia, recovered completely.

Postherpetic neuralgia, which is usually severe and intractable, occurred at an alarmingly high frequency in our study: in other reports, the rates ranged from 9% to 42% [3, 4, 9, 12, 13], whereas 55% of our patients developed this complication. Unlike Harding et al. [13], we did not find a statistically significant association between postherpetic neuralgia and increasing age in our patients. Although we didn't encounter any patient with systemic complications secondary to HZO, cases of hemiplegia, cerebral angiitis [12], and other cerebral complications leading to death [7, 11] have been reported.

There is a significant rate of visual loss following the development of HZO. Our finding is similar to that of a study from Malawi, in which 66% of patients had a final visual acuity of <20/60, and 40% had light perception only or no light perception [23]. In contrast, a study from the United States that was conducted before the AIDS era showed a visual acuity of <20/60 for only 24 (28%) of 86 patients [12].

In general, the incidence and severity of ocular complications and postherpetic neuralgia were higher for our patients than for patients described in studies from the developed world [3, 4, 10, 12, 13]; however, our findings are in agreement with those of other recent African studies on HIV-related HZO [9, 23].

Oral acyclovir, if given in the first 72 hours after the onset of HZO, protects against ocular complications [24] and reduces the severity and incidence of postherpetic pain [25]. Because an insufficient number of patients (eight) received this drug in our study, a valid comparison of outcomes with and without treatment cannot be made. For established ocular complications, a controlled coded trial [26] showed that topical acyclovir was significantly superior to topical steroids with respect to treatment duration, and there were no recurrences of HZO after the patients stopped receiving treatment with acyclovir. The reductions in treatment duration and recurrence rate would be expected to result in a reduced incidence of ocular damage and visual loss among acyclovir-treated patients [26]. Topical steroid therapy should be withheld in all but the most severe cases and should be supplemented with topical acyclovir therapy [26].

It has been claimed that systemic steroids prevent postherpetic neuralgia, but the studies from which this claim originates had many pitfalls in terms of meeting the necessary standard for drug trials [2]. Investigators who conducted a randomized placebo-controlled study of steroid therapy for HZO concluded that prednisolone does not prevent postherpetic neuralgia [27]; therefore, clinicians should be cautious in prescribing systemic steroids, as there is increased potential for the development of systemic zoster in immunocompromised patients [1, 5].

Late presentation, application of herbal medication, and the unavailability and cost of acyclovir were the possible causes of the increased incidence of ocular complications in our patients. Thus, the poor visual outcomes and high incidence of postherpetic neuralgia among these patients is much like the scenario that prevails in Malawi [23].

Seroprevalence studies in Ethiopia have shown that ~20% of urban antenatal-care recipients, 9% of blood donors, 32%–42% of patients, and 0–6% of the general rural population had become infected with HIV by the end of 1994 [20]. The prevalence of HIV infection in our series of patients with HZO was 95.3%, a finding indicative of the strong association with HIV infection. Thus, a randomized controlled study is needed. All patients with HZO, especially those aged ≤45 years, should be screened for HIV infection; if such patients are found to be seropositive, they should receive counseling to prevent the spread of this fatal disease.

With the presently increasing magnitude of HIV infection, there will be increasing numbers of patients with HZO, especially in the young, economically productive age group. Thus, in a country like Ethiopia where the number of trained ophthalmologists is limited, primary care physicians should be well versed in the management of HZO, which affects all structures of the eye and may lead to blindness.

References