ORIGINAL CONTRIBUTIONS

NATURAL HISTORY OF HERPES ZOSTER IN THE ERA OF AIDS

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Seventy- four consecutive patients with herpes zoster (HZ) in Mumbai were recruited into the study to determine its natural history. Thirty- five (47.3%) with HZ were infected with HIV-1/2. HZ+HIV+ and HZ+HIV- were demographically similar but HZ+HIV+ were clinically different; the latter were characterised by multidermatomal involvement of thoracic dermatomes below T6 or that of trigeminal nerve, recurrent episodes, bullous lesions and 17/35 had associated illnesses such as severe weight loss,recurrent fever, chronic cough, active tuberculosis and oral candidiasis. Significant difference in the course of healing, incidence of secondary bacterial infection and scarring emerged between the two groups after day-10. HZ+HIV+ individuals had vesicles and ulcers persisting for significantly longer time with frequent sequelae of post inflammatory pigmentation and post herpetic neuralgia. In areas where resources are limited for health information, such clinical differences between HZ+HIV+ and HZ+HIV- will serve to identify individuals with HIV infection in dermatologic clinic. These findings will also be helpful for early diagnosis of HIV infection, associated opportunistic infections and prevent their secondary transmission through appropriate interventions.

Key words : HIV, Herpes zoster, AIDS

Introduction

Herpes zoster (HZ) is an acute vesiculobullous eruption along a dermatomal distribution. It is characterised by unilateral involvement associated with shooting pain in the dermatome. HZ is reported to be an early and readily detectable manifestation of HIV- induced immune suppression.[1,2] Recurrent HZ is listed as one of the AIDS-defining illnesses.[3,4] In HIV-infected individuals, many atypical manifestations such as ulcerations,[5] necrosis,[4] and ecthymatic hyperkeratotic papules [6,7] are reported. Neurological [8,9] cutaneous [1-9] and ophthalmic [10] complications have been described.

With the onset of HIV epidemic in India,[11] the number of young individuals presenting with typical and atypical forms of HZ have increased in recent years. The numbers of HZ are likely to continue increasing because UNAIDS estimates that by year 2000, India will have between 5 and 8 million infected individuals. Hence this study was designed to describe differences in clinical presentations, morphology, severity, and time taken to heal between HIV-infected and noninfected individuals.

Patients and Methods

A cohort of 74 consecutive patients was established among patients attending the AIDS Research and Control Centre (ARCON)

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and Skin/STD department at Sir J J Hospital in Mumbai. Criteria for inclusion in the study were: first time attenders with HZ, willingness to attend for follow up visits every week till tissue healing occurred, and domicile of Mumbai. After detailed demographic history and history of AIDS-defining illnesses, thorough physical examination included site of involvement, morphology of lesions (papular, vesicular, ulcerative or necrotic), number of dermatomes involved and dissemination.

Laboratory investigations included complete blood count, LFT, RPR, ELISA for HIV-1/2 (Sanofi, France and Qualigen, Glaxo) and Tzanck smears from the base of vesicles. CD4/CD8 counts were performed using TRAx Elisa (T Cell Diagnostics, USA). Due to restrictive funding for this study, 5 random HZ+HIV+ and 5 HZ+HIV- patients had CD4/CD8 counts performed.

All patients irrespective of their HIV status were managed for HZ symptomatically with analgesics and local/systemic antibiotics. Later decision was based on presence of secondary bacterial infection. Acyclovir 200 mg five times a day for 5-10 days was prescribed for 6 patients with ophthalmic HZ (4 were HIV infected) and 1 patient with disseminated HZ (HIV infected). Healing of vesicles and ulcers was graded as profuse, reduced or absent. Ulcers healed with pigmentary changes or with scarring.

Assessment of complications included post-herpetic neuralgia, corneal ulcers, blindness, tinnitus, secondary bacterial infections or encephalitis.

Results

Of 74 patients with HZ recruited into the study, 35 (47.3%) were HIV+ on two tests. There was no significant difference in demographic features including mean age and marital status between the two groups ($p>0.05$). The clinical presentation among HIV-infected individuals was significant involvement of thoracic dermatomes below T6 or involvement of the trigeminal nerve, bullous lesions, or recurrent episodes of HZ. The associated illnesses at the time of occurrence of HZ were severe weight loss, recurrent fever, chronic cough, active clinical tuberculosis, and oral candidiasis among 17/35 (48.6 %) HIV- infected individuals (Table.I).Significant difference in the course of healing emerged between the two groups after day 10. HIV-infected individuals had vesicles and ulcers persist for a signifi-

Table I. Clinical presentation of herpes zoster among patients with and without HIV infection

	HIV+ve n=35	HIV-ve n=39	Odd's ratio CI 0.95
I. Dermatomal Distribution			
Trigeminal	12	04	OR 4.6 CI 1.16, 19.38
Ophthalmic	04	02	
Mandibular	03	00	
Maxillary	05	02	
Cervical	11	11	
Thorasic	19	20	
T1-T5	06	15	
T6 - T12	13	05	OR 6.5 CI 1.33, 34.7
Lumbosacral	08	08	
II. Morphology			
Vesicular	33	34	
Papular	32	34	
Bullae	18	01	OR 40.2 CI 4.9, 875.2
Haemorrhagic	02	00	
III Pain		29	31
IV Recurrent HZ	06	00	
V. Multidermatomal	31	29	
VI. Disseminated	01	00	
VII. Associated illness	17	04	OR 9.3 CI 2.15, 34.49
Weight loss	15	03	
Recurrent fever	09	00	
Chronic cough	07	00	
Tuberculosis	10	01	
Oral candidiasis	06	00	

Table II. Natural history of herpes zoster among patients with or without HIV infection

	Vesicles		Ulcerations		Pigmentation		Scarring	
	HIV+	HIV-	HIV+	HIV-	HIV+	HIV-	HIV+	HIV-
Day 5	29	30	08	08	00	00	00	00
Day 10	32	09	20	09	00	00	00	00
	OR 35.5 CI 7.7, 190.9		OR 4.4 CI1.5, 13.8					
Day 15	16	00	29	06	01	00	00	00
	OR 32 CI 3.9, 696		OR 26.6 CI 6.7,115.2					
Day 20	04	00	23	01	04	03	01	02
			OR 72.8 CI1.7,1605.3					
Day 30	00	00	06	01	25	03	19	03
				OR30.CI6.59,158.2		OR14.3 CI 3.3, 17.2		

cantly longer time with frequent sequelae of postinflammatory pigmentation and scarring (Table 11).Complications such as post-herpetic neuralgia in 6/35 and secondary bacterial infections in 12/35 occurred among HIV-infected individuals. By comparison, 2/39 had postherpetic neuralgia and 2/39 had secondary bacterial infections among HIV-negative individuals. The mean CD4 cell counts were 860 and 1000 for selected HIV-infected and non-infected individuals, respectively.

Discussion

With 50% of individuals with HZ infected with HIV and absence of differences in prevalent demographic characteristics between individuals with HZ+HIV+, the subtle clinical differences between the two groups could help identify individuals with HIV infection. This identification could help us to intervene early during the infection to reduce transmission of HIV and occurrence of opportunistic infections.

HZ+HIV+ individuals are likely to have the following clinical features: multidermatomal, recurrent (2.3 times the risk), trigeminal or thoracic below T6, with occurrence of bullous lesions. Ulcers occur frequently (29/35 vs 9/39) as a result of rupture of vesicles. These lesions take significantly longer to heal with sequelae such as scarring and pigmentation. Associated illnesses such as weight loss, chronic fever, chronic cough, tuberculosis (15 times more common) and candidiasis are significantly associated with HZ+HIV+. Although mean CD4 counts were not significantly reduced, there is clinical evidence to suggest that occurrence of HZ is associated with mid-level progression of HIV disease. Among 13 individuals who had AIDS, the lesions of HZ were mild, possibly due to severe immune suppression. These healed without scarring or pigmentation.

The complications such as post-herpetic neuralgia occurred in 6/35 HZ+HIV+ and 2/39 HZ+HIV-. Post-herpetic neuralgia is pain that persists for more than one month after healing of zoster lesions. Thus, individuals with underlying HIV infection are at 4 times the risk of post-herpetic neuralgia. Secondary bacterial infection of lesions occurred in 12/35 HZ+HIV+ and 2/39 HZ+HIV-.Thus, individuals with HIV infection are at 9 times the risk of secondary bacterial infections.

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