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Pediatric Herpes Zoster: A Study of 64 Cases

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Abstract

Herpes zoster (HZ), a reactivation of virus after initial chickenpox infection was earlier believed to be rare in children and a marker for immunodeficiency and malignancy. Data regarding epidemiology of HZ in Indian children is lacking; we report here a series of 64 cases of paediatric HZ seen over a year. Fourteen patients had one or more systemic disease; most of these were more than 7 years of age. Complications such as keratitis, secondary skin infection, scarring, dyspigmentation and associated psychological effects are a major concern in children. Universal varicella vaccination is likely to aid in reduction in paediatric HZ.

Keywords: Pediatric Herpes Zoster; Varicella.

Introduction

Herpes zoster (HZ) or shingles is a dermatomal viral infection caused by reactivation of latent varicella zoster virus (VZV). Initial infection with VZV presents with disseminated vesicles (commonly known as chickenpox) following which, the virus lies dormant in dorsal nerve root ganglion and can reactivate at a later time appearing as vesicles in a unilateral dermatomal distribution. It usually affects patients with waning cellular immunity such as HIV, solid organ transplant, cancer or in elderly. The estimated lifetime risk of developing HZ in those exposed to varicella is 30% implying one in every three cases of varicella will develop zoster [1]. Childhood herpes zoster though considered uncommon is now increasingly occurring in otherwise normal children. The cause of reactivation of VZV in the latter remains obscure.

Material and Methods

A retrospective analysis of all patients who presented to the dermatology OPD of a pediatric hospital from July 2012 to June 2013 and were clinically confirmed to have herpes zoster were done from the hospital records. Demographic profile of the patient, age of presentation, history of previous varicella, varicella immunization, any underlying systemic disease or immune-suppression, clinical presentation, dermatome involved, course of the disease, complications and laboratory investigations carried out were tabulated and analyzed. Complete blood count, erythrocyte sedimentation rate (ESR) and serology for HIV were done in all children presenting with HZ to rule out malignancy or immune-suppression. The aim was to review clinical and laboratory profile of all cases of childhood shingles and to look for any possible relationship between the demographic and laboratory profile and clinical outcome in these patients.

Inclusion Criteria

Clinically confirmed cases of Herpes Zoster who followed up till resolution of symptoms.

Exclusion Criteria

Patients lost to follow-up after the initial visit and patients presenting as zosteriform herpes simplex.

Results

We analysed 64 cases of clinically confirmed HZ in children below 12 years of age accounting for 0.42% of all new cases seen in the dermatology department of a paediatric hospital over a year. Out of 64 cases, 50% (32) were female and 50% (32) were male children showing no sex preponderance. 30% (19) children were between the age group of 2 to 6 years and 70% (45) were the age of 7 to 12 years. None of the 64 children were vaccinated for varicella. In 54.6% (35) children, there was a history of varicella infection and in one case mother had history of varicella at 4 months of gestation. HZ was seen earliest at the age of 2 years in two children with varicella-HZ interval being 6 months and longest interval 8 years in 11 year old child with mean varicella-HZ interval being 3.5 years. There was at least one constitutional symptoms such as zoster associated pain, fever and regional lymphadenopathy in 54% (35) cases. Among 64 cases, 23.4% (15) patients were having either some systemic illness (HIV-1, coeliac disease-2, tuberculosis- 4, bronchial asthma-1, hypothyroidism- 1, hepatitis-1, cholera- 1, neurocysticercosis-1, hemolytic uremic syndrome-1) or were on immunosuppressive therapy (3 patients). There was no case of associated malignancies in any child. Patient having cholera had disseminated zoster while in rest the lesions were multiple, grouped vesicles on erythematous base involving unilateral, single or two contiguous dermatomes. Zoster associated pain and burning sensation were observed in 5 patients. Thoracic dermatome involvement was observed in 62.5% (40) patients. In remaining 24 cases, trigeminal and lumbar was involved in 14% (9) each, cervical 6% (4) and sacral in one patient. Tzanck smear revealed multinucleated giant cells and HSV serology for IgM was negative in all cases. ESR was raised in 37.5% (24) patients while blood counts were not significantly altered in any. All confirmed cases of HZ who presented within 72 hours of onset were treated with acyclovir 20 mg/kg/qid for 7 days and rest were managed symptomatically with antipyretics and calamine lotion. There was complete resolution of the lesions without any sequelae in 55 patients; however in 9 patients, lesions healed with hypopigmentation and scarring. Post herpetic neuralgia was not observed in any child during follow up.

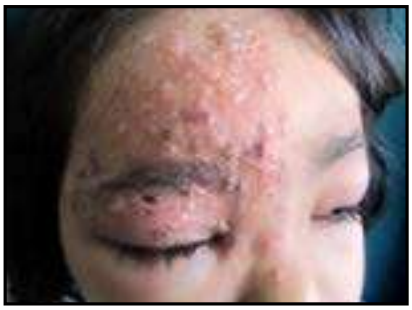

Fig. 1: HZ ophthalmicus affecting the ophthalmic division of trigeminal nerve in a 7 year old girl

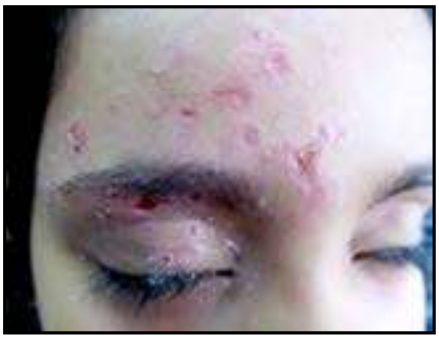

Fig. 2: Scarring following herpes HZ in the same patient

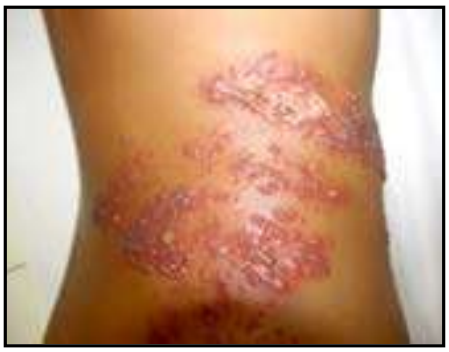

Fig. 3: HZ with secondary infection and ulceration affecting lower thoracic dermatomes in an 8-year old girl

Table 1: Age wise clinical and demographic profile of patients with HZ

	<7 years	>7years	Total
Number of cases	19	45	64
Sex distribution	M=10 F=9	M=22 F=23	M=32 F=32
Mean age of developing HZ	4.68 years	9.51 years	8.07 years
History of chickenpox			
• Mother during pregnancy	1	0	1
• Self	9	26	35
Age at development of chickenpox			
• Intrauterine	1	0	1
• < 2 years	4	1	5
• 2 years	5	25	30

Dermatome involved			
• Trigeminal	3	6	9
• Cervical	2	2	4
• Thoracic	6	34	40
• Lumbar	6	3	9
• Sacral	1	0	1
• Disseminated	1	0	1

Discussion

Usually, primary varicella is a disease of childhood, whereas herpes zoster is encountered in the aged. Herpes zoster (HZ) also known as shingles is a dermatomal viral infection caused by reactivation of latent varicella zoster virus (VZV). It usually affects patients with waning cellular immunity such as HIV, solid organ transplant, cancer or in elderly. Childhood HZ was initially considered rare with an incidence of 0.74 per 1000 in children less than 9 years and a marker for immunodeficiency and malignancy especially leukaemia, however recently few studies have shown increased incidence in immune-competent children too [2,3]. Due to lack of uniform system of reporting VZV infections and absence of any series or studies on paediatric HZ from India, epidemiology of paediatric HZ in India is not known. Our study suggests increasing incidence of HZ in children.

Our 64 cases of childhood HZ during one year period is one of the largest series of childhood HZ till date. Bhumesh et al and Takayama et al have reported case series of 26 and 92 patients diagnosed over a period of 2 and 17 years respectively [4,5]. Prabhu et al reported 10 cases of childhood HZ under the age of 14 years; 7 of whom were seen within six months [6].

In the present series, almost 45% of children had no prior history of varicella. Absence of history of varicella in 28 patients can be due to inability to recall or possibility of subclinical varicella infection. Nikkels et al have reported sub-clinical varicella or varicella with few lesions to be a risk factor for developing childhood HZ [3]. It is also likely that due to lack of awareness and poor access to healthcare, some patients with mild and indolent varicella infection may remain undiagnosed or disregarded as bacterial infections or insect bite reaction by the parents. Rising incidence of HZ in healthy children may be due to acquiring primary varicella infection *in utero*, or in infancy, wherein the immunity is not fully developed, as seen in our study where HZ occurred at the age of 2 years in two cases and in 19 cases up to 6 years. Tereda *et al*. stated that the immunological status at the time of acquiring the primary infection is the most important factor in childhood HZ. A low level of lymphocytes, natural killer (NK) cells and cytokines are seen in infants along with virus-specific immunoglobulins that may result in an inability to maintain the virus in a latent state. As a result the VZV reactivates during early childhood even in the absence of definite immunocompromise, leading to early appearance of zoster in children [7]. None of 64 children in our study were vaccinated for varicella.

Few authors have proposed that most cases of childhood HZ occur in otherwise healthy children and do not warrant investigation to look for definite immune-suppression [2,8]. In the present series, 19 cases of HZ below 7 years of age were recorded; one of them was positive for HIV and was immunocompromised along with one three year old male child with cholera having disseminated zoster. Some opine that varicella during pregnancy and first year of life especially in first 2 months represent risk factors for developing childhood shingles usually before 7 years of age as the level of protective antibodies at that time is low resulting in blunted immunological response and the VZV reactivates during early childhood even in the absence of definite immune-compromise [2]. Interestingly, an acute insult such as cholera probably led to development of disseminated zoster in that patient. Twelve out of 45 (27%) children above 7 years of age had either immune-deficiency or acute or chronic systemic disease that possibly led to reactivation of VZV infection. It is possible that infection with VZV beyond infancy is normally contained and reactivation may occur later in childhood following acute or chronic systemic compromise as it occurs later in life. Historically, childhood herpes zoster was thought to be an indicator for an underlying malignancy, especially acute lymphatic leukemia. However recent studies have shown no increase in the incidence of malignancy in children with herpes zoster [1,2]. Approximately 5% of the paediatric zoster cases occur in children with malignancies [9]. In our study there was no case of associated malignancies in any child, however we identified 23.4% (15) cases who were either on immunosuppressive therapy (patients) or were suffering from some acute or chronic systemic illness (12 patients) that possibly led to reactivation of VZV infection. Associations between the incidence of HZ and lymphoma, human immunodeficiency virus (HIV)

disease, cancer, autoimmune disease, systemic lupus erythematosus (SLE), rheumatoid arthritis (RA), diabetes mellitus (DM), hypertension, congestive heart failure, psychological disease and major depression have been well recognized and documented [10,11]. Recently bronchial asthma has been also reported as a risk factor for HZ implicating use of inhalational steroids as a predisposing factor [12]. We had only one case of bronchial asthma in our study. However, self-use and abuse of inhalational and oral steroids on and off for minor coughs, breathing difficulties and skin rashes is rampant in our country. Our observation of co-existence of underlying systemic illness such as coeliac disease(2), tuberculosis(4) and one case each of bronchial asthma, cholera, neurocysticercosis, hepatitis, haemolytic uremic syndrome and hypothyroidism may suggest an independent risk factor for HZ if acquired early in life. Nevertheless, it remains unknown whether the risk of developing HZ increases in patients with common underlying diseases that might alter immune functions. In addition, mal-nutrition prevalent amongst the children in lower socioeconomic strata may also be contributory towards the incidence of herpes zoster though we did not specifically assess for it.

Most of the complications of HZ in children do not depend on presence or absence of defective immunity and immunocompetent children are equally at risk of complications [13]. Besides, children more frequently develop HZ in the distribution of trigeminal nerve as compared to adults (32% in children vs 15% across all ages) [13,14]. One of the most long lasting complications seen in adult herpes zoster that is post herpetic neuralgia is not seen in children. However, secondary infection, scarring and ophthalmic complications occur in children and may have more devastating consequences on the physical and mental well being. In our study though we did not have any ophthalmic complications, hypo-pigmentation and scarring were noted in 9 patients; five of these were female with facial lesions. The resultant poor self-esteem and deep negative psychological impact because of cutaneous scarring especially in facial HZ in children cannot be undermined.

So far, almost all the reported series and isolated case reports have stressed upon the fact that childhood zoster is a relatively mild disease with negligible prodromal symptoms, post herpetic neuralgia or other significant complications and healthy children with HZ does not necessitate acyclovir treatment. However several studies linked VZV to arterial ischaemic stroke (AIS) by infecting the trigeminal nerve, which provides innervation to the cerebral vasculature. The virus may directly invade vessel walls and cause a focal arteriopathy ("post-varicella arteriopathy") leading to ischaemic stroke and acyclovir may have a role in prevention [15,16]. Complications can also occur because of secondary bacterial infection and eye involvement leading to cutaneous scarring, blindness and keratitis.

Live vaccine for varicella is available and there is some evidence that children vaccinated for varicella have lower risk of developing HZ than those with history of varicella [17, 18]. Immunization for chicken pox is currently not part of the Universal immunization programme in many countries including India and vaccination is available only to affording patients in private hospitals or clinics. Venkitaraman et al. found a progressive increase in sero-prevalence of varicella zoster virus with age in India [19]. As increasing proportion of children get vaccinated, unvaccinated children remain protected during childhood by herd immunity and reach adulthood without any immunity. Varicella infection in adults is known to be more severe and post herpetic neuralgia is a major persistent problem associated with HZ occurring later in life. Thus in the long course, the immunised children will put unvaccinated children at greater risk of morbidity and mortality due to VZV infections than in a completely unimmunised population. Verma et al in 2011 recommended inclusion of varicella vaccination in the universal immunisation programme of India and we propose that it will also help in reducing the incidence of herpes zoster also in children [20]. Incidence of HZ in vaccinated children was reported to be 79% lower than in unvaccinated children and half of HZ cases in vaccinated group were due to wild-type VZV in one study [17]. Besides, HZ developing after varicella vaccination is known to be milder as compared to after sporadic varicella infection [21].

Conclusion

To conclude, childhood HZ is not as uncommon as was previously thought but probably often under recognized and under-reported and its incidence seems to be increasing. Child's immunological status at the time of acquiring primary varicella infection is the most important

factor in childhood HZ. It may occur even in immune-competent children and is not necessarily associated with malignancy though presence of immune-suppression or systemic disease might further predispose. Therefore screening for acute or chronic systemic compromise is recommended. Universal vaccination for varicella is likely to reduce the incidence and severity of HZ in children and aid in preventing the negative impact of scarring and complications in this population.

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Key Message

What this study adds:

- Paediatric herpes zoster is not uncommon; but often under recognised and under reported.
- Indian studies on paediatric HZ are lacking.
- Incidence of paediatric HZ appears to be increasing.
- It can affect immunocompetent children as well; though likelihood of finding an underlying systemic disease is higher.
- Cutaneous scarring, keratitis, dyspigmentation and consequent psychological effects are important complications.
- In the absence of universal varicella vaccination, most Indian children remain predisposed to ill effects of chickenpox as well as future reactivation as herpes zoster and their complications.

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