Clinical characteristics of Herpes Zoster – A retrospective clinical study –

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Abstract

Background
Herpes zoster also known as shingles or Zona and is caused by a neurotrophic DNA virus called Varicella Zoster, a member of the herpes viridae [1]. The incidence of herpes zoster ranges from 1.2 to 3.4 cases, reaching up to 3.9 –11.8 per 1,000 individuals among those older than 65 years [2].

Material & methods
Medical records from a period of 2013 – 2015 march were analyzed for the details regarding number and clinical presentation of patients diagnosed as herpes zoster. Twelve cases with complete clinical details were selected and analyzed.

Results
Twelve of the affected patients were aged between 21 to 62 years and eight of them were male. Maxillary nerve and left side was affected more. All the patients complained severe pain with severity of 10 in visual analog scale (VAS). Clusters of vesicles, ulcers, post infection hypo / hyper pigmentation and post herpetic neuralgia were reported. Two of the patients are serologically confirmed cases of HIV+ive.

Conclusion
1. Herpes zoster affecting maxillary nerve is more often seen in dental institution.
2. Left side nerve is more affected and oral lesions are seen only in cases of maxillary and mandibular nerve.
3. Post herpetic neuralgia is more seen in older patients above 50 years.
4. Post infection pigmentation could be attributed to poor hygiene and secondary bacterial infection.

Key words;- Herpes zoster, Varicella Zoster virus, pigmentation, Prodromal pain and Post Herpetic Neuralgia.

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الملخص : يعتبر فيروس الحماق النطاقى هو المسبب لمرض الهربس النطاقى، وتتراوح نسبة حدوث مرض الهربس النطاقى بين ٢,١ - ٤,٣ حالة، وقد تصل الى ٣,٩ - ١١,٨ حاله من بين كل ألف شخص يزيد عمرة عن ٦٥ عاما.

وبمراجعة الملفات الطبية للمراجعين خلال الفترة من ٢٠١٣ - ٢٠١٥ تم رصد ١٢ حالة هربس نطاقي بأعراض سريرية متكاملة، وتراوحت أعمارهم بين ٢١-٦٢ عاما وكان منهم ٨ ذكور، وقد غلب وجود الأعراض المرضية في العصب الفكي العلوي والجانب الأيسر للوجه. وقد عانى كافة المرضى من ألم شديد مقداره ١٠ درجات وفقا لمقياس النظير البصري، وقد لوحظ وجود حوصلات وقرح كذلك فرط ونقص التصبغ التالي للعدوى البكتيرية الثانوية والألم العصبي التالي للإصابة الهربسية.

وقد خلصت الدراسة الى الاتي:

* زيادة حدوث مرض الهربس النطاقى في العصب الفكي العلوي لدى مرضى كليات طب الأسنان.
* زيادة حدوث مرض الهربس النطاقى في الجانب الأيسر للوجه، مع ملاحظة وجود التقرحات الفموية حال اصابة العصبين الفكي العلوي والفكي السفلى.
* زيادة حدوث الألم العصبي التالي للإصابة الهربسية في المرضى الذين تزيد أعمارهم عن ٥٠ عاما.
* التصبغ التالي للعدوى البكتيرية قد يكون سببه عدم العناية و الاهتمام بالصحة العامة للجسم، أو وجود عدوى بكتيرية ثانوية.

Introduction

Herpes zoster (HZ) is a condition characterized by localized eruption of vesicular lesions along the trajectory of a sensory nerve as well as pain and inflammation of the affected nerve root [3]. The word Herpes Zoster is derived from the Greek word Herpein meaning "creep" referring to the latent and recurring infections and Zoster meaning "belt" or "girdle named after the characteristic belt-like dermatomal rash [4]. Zoster sine herpete is a condition where a patient has all symptoms of herpes zoster except the characteristic rash.

Herpes zoster may have additional symptoms depending on the dermatome involved. Herpes zoster ophthalmicus involves the eye and occurs in approximately 10–25% of cases. It is caused by the reactivation of virus in the ophthalmic division of the trigeminal nerve causing symptoms that may include conjunctivitis, keratitis, uveitis, retinal damage, chronic ocular inflammation, loss of vision, and debilitating pain. Herpes zoster oticus, also known as Ramsay Hunt syndrome involves the ear and is thought to result from the virus spreading from the facial nerve to the vestibulocochlear nerve. Symptoms include hearing loss and vertigo (rotational dizziness) [5]. Only in the beginning of the 20th century the first indications, that chickenpox and herpes zoster were caused by the same virus was noticed. This was eventually proved by the first isolation of the virus in cell cultures by the Nobel laureate Thomas Huckle Weller in 1953[6].

Pathophysiology

Herpes zoster results from the reactivation of varicella-zoster virus that

has been dormant in dorsal root ganglion or Gasserian ganglion in the base of the skull following primary infection known as "varicella" or chickenpox which generally occurs in children and young adults[7]. Years or decades after a primary infection, the reactivated VZV are liberated from the trigeminal ganglion and travels downwards along the axons of the affected nerve root to reach the nerve endings to cause characteristic cutaneous rash and vesicular eruptions[8]. Typically the viral particles take 3-4 days to reach the nerve endings, as the virus travel down the axons, it provokes perineural and intraneural inflammation experienced as prodromal symptoms that are often described as stinging, tingling, itching, aching, hyperesthesia, paresthesia, throbbing and even agonizing pain sometimes[9]. The prodromal pain may range from mild to severe. The vesicles eventually crusts, falls and heals within seven to ten days. Reactivation of the virus can be triggered by trivial trauma, physical and mental stress, radiotherapy, surgery etc. The most common sensory nerve affected are $C_{2,}$ $C_{3,}$ $T_{5,}$ $L_{1,}L_{2}$ and ophthalmic branch of trigeminal nerve [10] and the distribution of the vesicular lesions follows the distribution of the involved nerve root.

The most frequent, debilitating complication of HZ and which is often difficult to manage is post herpetic neuralgia (PHN) a form of neuropathic pain in the dermatomes affected by the VZV infection. PHN may develop in one out of five patients and the incidence increases significantly with age[11]. The pain associated with PHN is intense and disabling affecting the patient's quality of life [12]. Early diagnosis and prompt institution of antiviral medication in the prodromal stage itself can considerably reduce the morbidity of the disease.

Material & methods

Medical records from a period of 2013 – 2015 march were analyzed for the details regarding number and clinical presentation of patients diagnosed as herpes zoster. Twelve cases with complete clinical details were selected. The details like age, sex, affected nerve and side are tabulated in Table 1 and post infection complications like postherpetic neuralgia, hypo / hyperpigmentation and scar are tabulated in (Table-2).

Results:

The tabulated data was analyzed and out of twelve patients with herpes zoster, five (42%) were in the group-I and two (17%) were in group II and 4 (33%) of them in group IV and 1 (8%) in group V, no patient were in the group III (Table1). Eight (67%) of the documented cases were males and four (33%) were females. Eight (67%) patients had lesion on the left side of body. Regarding the nerve affected, two cases (17%) were in ophthalmic nerve, five (42%) cases were in maxillary nerve, two (17%) in mandibular nerve and three (25%) in spinal nerves (Table 1). Regarding the post infection pigmentation, four (33%) cases showed hypo pigmented scars and four (33%) case showed

Table 1.

No	Age	Sex	Nerve Affected	Prodromal Pain	R Or L Side	Stage Of Lesion	Post herpetic Neuralgia	Any Other
1	53	M	Opthalmic Branch Of V -CN	Yes	L	Hypo And Hyper Pigmented Scars	Yes	Conjuctivitis And Difficulty To Open Eye
2	36	F	Opthalmic Branch Of V –CN	Yes	L	Hyper Pigmented Pitting Scars	Yes	Residual Conjuctivitis
3	23	F	Maxillary Branch Of V - CN	Yes	L	Hyper Pigmented Pitting Scars	No	5 (21-25) Teeth Were Extracted And Missing.
4	21	M	Maxilary Branch Of V-CN	Yes	L	Hyper Pigmented Pitting Scars In Infra Orbital,Nose And Zygomatico Temporal Region	No	Nil
5	55	M	Maxilary Branch Of V-CN	Yes	R	Erythematous Area With Vesicles, Black Crustations Infra Orbital,Nose And Zygomatico Temporal Region	No	Unilateralpalatal Ulcers In R Side
6	58	M	Maxilary Branch Of V-CN	Yes	L	Vesicles, Black Crustations And Hypopimented Healed Areas Infra Orbital,Nose And Zygomatico Temporal Region	No	Unilateral palatal Ulcers In L Side
7	62	F	Maxilary Branch Of V-CN	Yes	R	Vesicles With Golden Yellow Color In Infra Orbital Region	Yes	Unilateral palatal Ulcers In R Side
8	33	M	Mandibular Branch Of V -CN	Yes	L	Clusters Of Vesicles In Face And Ipilateral Oral Mucosa	No	Unilateral Ulcers In L Side Buccal Mucosa, Lingual Mucosa And Labial Mucosa
9	51	F	Mandibular & Maxillary Branch Of V –CN	Yes	L	Ulcers In Angle Of Mouth,Half Of Tongue,Palate	Yes	Upper Labial Mucosal Ulcers
10	23	M	Cutaneous Branches Of Cervical Plexes	Yes	R	Hypopigmented Scars In Supraclsviculsr,Greater Auricular And Transverse Cervical	No	Hiv +Ive
11	21	M	T6 Spinal Nerve	Yes	R	Hypopigmented Scars In Skin Below The Nipple	No	Hiv +Ive
12	25	M	T10 Spinal Nerve	Yes	L	Erythmatous Area Above Umbilicus With Clusters Of Intact Vesicles	No	Nil

hyper pigmented scars and in five (41%) cases had no pigmented scar. The pain that persists even after the resolution of acute infection is known as post herpetic neuralgia. In our study group four (33%) patients had post herpetic neuralgia, three out of this four cases occurred in patients above fifty years of age in the group IV and V (Table 2).

Discussion

Herpes zoster is a sporadic disease with an estimated life time incidence of 10-20% [13]. The incidence of HZ increases dramatically with age peaking in the seventh decade of life as the key risk factor for the development of HZ is waning of the cell-mediated immune system associated with the normal aging [14]. Our patients were aged between 21 to 62 years. Eight patients are males and five of them are above 50 years.

A well documented risk factor for HZ is acquired inhibition of the cell-mediated immune response, such as treatment with immunosuppressive drugs or infection with human immunodeficiency virus (HIV) [15]. The relative risk of HZ is 15 times greater in HIV positive individuals and the recurrence rate of HZ in AIDS patients is as high as 25%, compared to less than 4% in immunocompetent individuals [16]. Ten of our cases are immunocompetent individuals and two were HIV 1+ive.

Although herpes zoster typically resolves within 2 weeks neuralgic pain may persist weeks or even years after the resolution of the rash. Postherpetic neuralgia is more common in patients older than 50 years [17]. All our patients complained severe pain with severity of 10 in visual analog scale. Four patients developed post herpetic neuralgia and three of them were above 50 years of age. According to the Literatures 50 % of patients with herpes zoster opthalmicus exhibits complications [18]. Two of our cases involving ophthalmic nerve showed eye changes like conjunctivitis, swelling of eyelids and difficulty in opening of eyes and were immediately referred to Ophthalmologist for management [Fig-1]. Seven cases exhibited hyper/hypo pigmented scar. Six of our cases were in early stage and exhibited clusters of intact vesicles in skin [Fig-2,4]. Oral mucosal ulcers are seen in five cases involving maxillary and mandibular nerves [Fig-3, 5]. In one case five teeth of upper jaw from 21- 25 (central and lateral incisor, canine and first and second pre molar) were unnecessarily removed by a general dental practitioner for the relief of pain. The most common oral complications in imunocompromised individuals are Neuralgia induced cavitational necrosis (NICO) and exfoliation of tooth which is most common, however the cases we report here did not show any complications except hyper pigmented scars. Three of our cases involved spinal nerves like cervical plexus, T6 and T10 spinal nerves [Fig-6].



Figure 1 HZ of ophthalmic nerve showing healed lesion and hyperpigmented scars distributed over the left half of forehead, eyelids and nose.



Figure 2 HZ of maxillary nerve showing clusters of yellowish blisters on the right middle one third of the face.



Figure 3 Intra oral view showing multiple small ulcers present on the right half of hard and soft palate.



Figure 4 HZ of left mandibular nerve showing unilateral clusters of vesicles distributed along buccal, mental nerve branches.



Figure 5Intra oral picture showing unilateral distribution of erythema and pin headed sized ulcers in left half of lower labial mucosa.



Figure 6HZ of T6 spinal nerve showing healing ulcerative lesions with area of hyper and hypo pigmentation and scarring.

Antiviral therapy is the main stay in the treatment of HZ, inhibiting VZV replication and shortening the duration of signs and symptoms of the disease. However the effectiveness and the potential capacity to reduce the occurrence of complications, specifically postherpetic neuralgia is still a controversy. Acyclovir has been the standard drug in treatment of HZ however new drugs like Valaciclovir (1000 mg three times a day for7 days) and Famciclovir (500 mg three times a day for 7 days) demonstrate superior efficacy, good safety and tolerability and a better patient compliance in terms of dosing regimen of 3 times a day compared with acyclovir's 800 mg 5 times a day dosing[19]. It is been reported that Acyclovir appears to benefit patients the most when therapy is initiated within 72 hours of onset of the skin lesions and higher rate of complications occurred among patients whose treatment was delayed[20]. The incidence of PHN in our cases could be due to the delay in reporting to hospital and delay in initiation of the treatment.

Treatment of PHN is complex and a multifaceted patient-specific approach is important. Clinical trials have shown that opioids, tricyclic antidepressants, and anticonvulsants and topical application of lidocaine patches or capsaicin may reduce the severity or duration of postherpetic neuralgia, either as single agents or in combination.

Pavan-Langston has outlined the following protocol for treatment of postherpetic neuralgia [21].

Anticonvulsants

Carbamazepine 100 mg orally at bedtime; increase dosage by 100 mg every 3 days until dosage is 200 mg three times daily, response is adequate or blood drug level is 6 to12 µg per mL (25.4 to 50.8 µmol per L).

Gabapentin 100 to 300 mg orally at bedtime; increase dosage by 100 to 300 mg every 3 days until dosage is 300 to 900 mg three times daily or response is adequate

Tricyclic Antidepressants

Nortriptyline, Amitriptyline, or Desipramine 25 mg up to 75 mg at bedtime

Topical application of capsaicin ointment daily 4 times/day or lidocaine patches

Transcutaneous electric nerve stimulation and, if necessary, neurosurgery (eg, Thermocoagulation of substantia gelatinosa Rolandi) have been found to be helpful in exceptional cases [21]. More serious complications, such as retinal involvement, may require days of intravenous therapy and months of oral antiviral therapy.

Conclusion

1. Cases of herpes zoster affecting maxillary nerve are more often seen in dental institution.
2. Left side nerve is more affected than right in this study
3. Oral lesions are seen in herpes zoster infection affecting maxillary and mandibular nerve.
4. The complication of postherpetic neuralgia is more often seen in older patients above 50 years.
5. Unnecessary dental treatment should be avoided during Prodromal pain and in post herpetic neuralgia.
6. The pain associated with herpes zoster is excruciating and all the patients grade it as 10 in the visual analog scale(VAS)
7. Post infection inflammatory hyper and hypo pigmentation is common and can be attributed to the poor hygiene and secondary bacterial infection.

Whilst HZ is rarely life-threatening, the incidence of long term morbidity such as visual disturbances and post herpetic neuralgia associated with the disease can be devastating [22]. The morbidity can be reduced by prompt institution of antiviral therapy as early as possible in the course of the illness. Hence an early diagnosis is mandatory for assuring greater quality of life for these patients.

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