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The analysis of risk factors for developing shingles

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ABSTRACT

Shingles (herpes zoster) is caused by the reactivation of human herpes virus type 3 (HHV-3) that has been latent in the cranial nerves ganglion and dorsal root ganglion. The purpose of this study was to assess the risk factors for the reactivation of HHV-3, present instructions for the treatment of shingles and describe preventive measures, namely vaccination. The study is based on the analysis of the shingles incidence in patients treated in the Dermatology Department and Dermatology Clinic at The 1st Clinical Military Hospital with Policlinic in years 2007-2011 in Lublin. The conclusion of the study is that the most important risk factors for herpes zoster are age, co-existing chronic diseases (including cancer) and immunosuppressive therapy. The course of disease in older patients is more severe and requires intensive treatment and hospitalization. In the face of increasing incidence of shingles, the introduction of vaccination against HHV-3 in patients over 50 years of age should be given due consideration in the next 20 years.

Keywords: shingles, treatment, risk factors, incidence

INTRODUCTION

Shingles is caused by the reactivation of latent human herpes virus 3 (HHV-3) previously called varicella-zoster virus (VZV). During the latent phase the virus resides in the cranial nerves ganglion and dorsal root ganglion [10]. It is estimated that shingles occurs sporadically: it constitutes 1% of all viral skin infections [4] and affects 10-20% of the population [6]. The purpose of this work is to assess risk factors for the reactivation of HHV-3, present instructions for the treatment of shingles and describe preventive measures, namely vaccination. The study is based on the analysis of the shingles incidence in patients treated in the Dermatology Department and Dermatology Clinic at The 1st Clinical Military Hospital with Policlinic in years 2007-2011.

METHODS

The studied group consisted of 39 shingles Caucasian patients who underwent medical treatment from January 2007 to December 2011. Of these patients, 7 were inpatients and 32 were outpatients at The 1st Clinical Military Hospital with Policlinic in Lublin. The conducted analysis of shingles incidence draws on data documented in medical records and includes the following information: sex, age, location of lesions, co-existing diseases, the administration of antiviral drugs, analgesics and topical treatment.

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RESULTS

The mean age of the subjects was 66 years (range, 25-89 years). The highest incidence rate of shingles was noted in patients between 70 and 79 years of age (Table 1). The incidence rate increased 3 times in patients between 50-59 years of age (Table 1, Fig. 1, 2). The most common site for a shingles outbreak was thoracic dermatome (Table 2). The result of the study indicated that shingles incidence in men and women does not vary significantly (Table 3, Fig. 3). Cardiovascular diseases (especially hypertension) were the most common co-existng diseases in patients infected with HHV-3 (Table 4). Ninety-five per cent of patients were administered aciclovir (5x800 mg/d p.o.). Twenty-three per cent of patients required additional analgesics treatment (Table 5). Shingles developed in 5 patients with impaired immune system due to pharmacotherapy (1 RA patient treated with methotrexate and 311-nm narrowband UVB phototherapy in a patient with erythrodermia psoriatica) and in 2 patients with co-existing diseases (1 neoplastic patient and 1 patient with hepatitis B) (Table 4). An acute shingles developed in 2 patients from age group 70-79 and caused hospitalization. One patient was diagnosed with cancer (renal cell carcinoma) within 2 years after developing shingles.

Table 1. Shingles incidence and the age of patients.

Age group	Number of cases	%	Population according to age Poland 2010*	Ratio rate**
20-29	2	5.13	6 140 509	1.00
30-39	2	5.13	5 808 782	1.06
40-49	2	5.13	4 792 211	1.28
50-59	7	17.95	5 770 823	3.72
60-69	6	15.38	3 682 048	5.00
70-79	12	30.77	2 502 346	14.72
80-89	8	20.51	1 201 493	20.44
Total:	39	100.00		

*Source – Central Statistical Office
**The incidence ratio of each age group to controls (age group 20-29 as frequency 1)

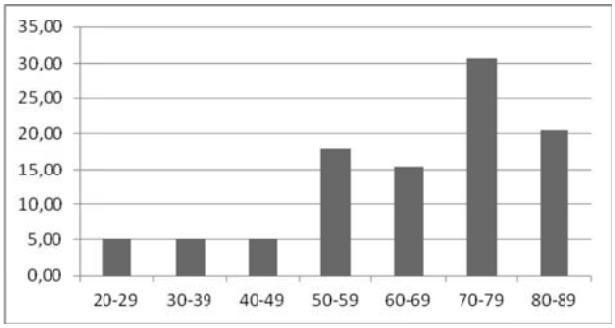


Fig. 1. Shingles incidence and the age of patients

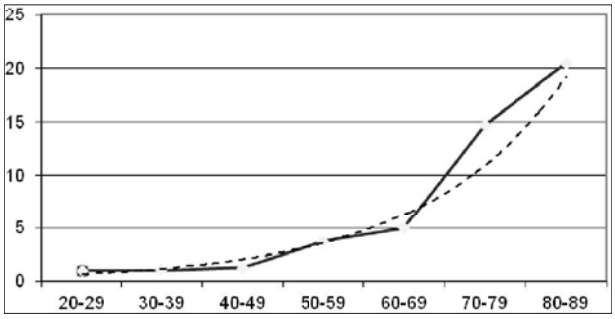


Fig. 2. Index of shingles incidence in analized group of patients

Table 2. Location of skin lesions

Location	Number of Cases	%
Chest	19	48.7
Upper extremity	4	10.3
Lower extremity	1	2.6
Face	2	5.1
Eye	2	5.1
Ear	2	5.1
Back	5	12.8
Perineum	2	5.1
Generalized shingles	2	5.1
Total	39	100.0

Table 3. Shingles incidence with sex distribution

Year	Number of Women	Number of Men	Total
2007	2	1	3
2008	6	8	14
2009	4	6	10
2010	5	4	9
2011	3	0	3
Total	20	19	39

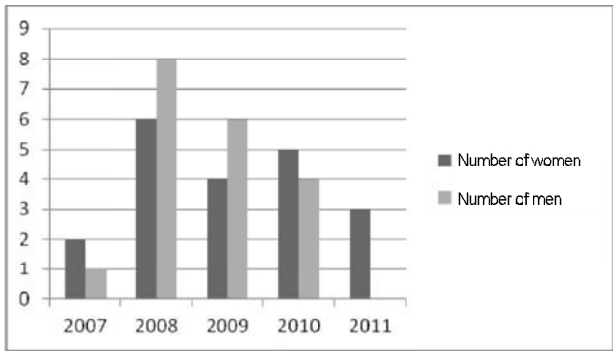


Fig. 3. Shingles incidence with sex distribution

Table 4. Co-existing diseases in patients with shingles

Co-existing diseases	Number of cases	%
Cardiovascular diseases	16	41
Respiratory diseases	4	10
Diabets	3	7
Thyroid diseases	4	10
Prostatic diseases	3	7
Digestive diseases	5	12
Others*	4	10

*Hepatitis B, kidney cancer, psoriasis vulgaris, RA

Table 5. Types of treatment in the studied group

Type of Treatment	Number of cases	%
Acyclovir 5 x 800mg/d p.o.	37	95
Non-steroidal anti-inflammatory drugs	9	23
Antibiotic therapy	7	18
Topical treatment	35	90
Carbamazepine	4	10

DISCUSSION

Primal infection with HHV-3 is manifested as chicken pox – an acute infectious disease [3]. Following active infection, virus becomes inactive (period of latency) and resides in the cranial nerves ganglion and dorsal root ganglion. Herpes zoster occurs when HHV-3 reactivates, migrates down nerve axons and causes viral infection in the dermatome involved. The symptoms that follow dermatome infection are severe pain, hypersensitivity and shingles rash with patches of red bumps and clusters of vesicles on erythemic base [1]. Within about 2-3 weeks blisters form crust and heal. In some cases, however, after the healing of the rash severe pain may persist for a few weeks or years (post herpetic neuralgia) and may not respond to analgesic treatment. The risk of post herpetic neuralgia increases with age [14].

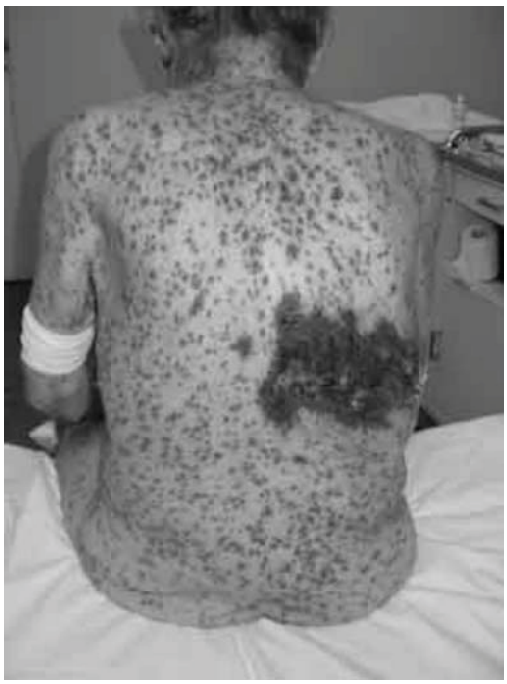
Shingles incidence depends on various factors whose mechanism suppresses cellular immunity: impaired T cells response leads to HHV-3 reactivation, replication, ganglionitis, inflammation and destruction of neurons and supporting cells, which causes skin eruption.

One of the most important factors that put at risk for shingles is the patient's age. The outcome of the study shows that shingles incidence among patients of Dermatology Unit aged 50-59 increases 3 times. Highest incidence was noted in the group aged 70-79. The latest research

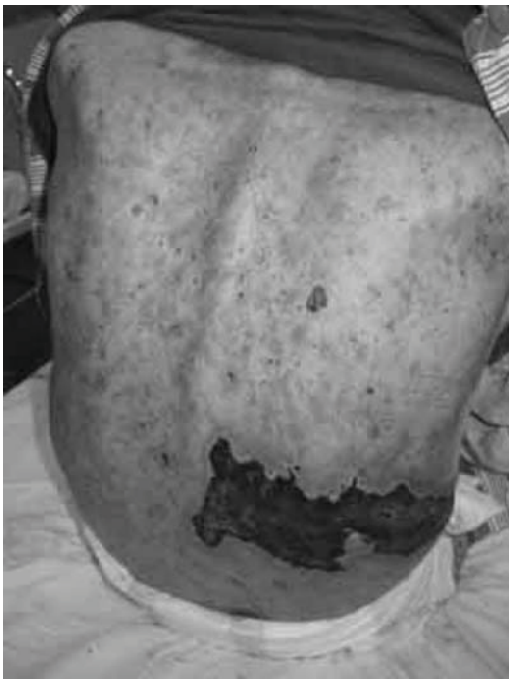
shows that the incidence rate in children under 10 years is 0.74 per 1000, while in older adults aged 80-89 the incidence rate is 10.1 per 1000. It is estimated that approximately 50% of adults aged 85 years will develop shingles [15].

Reactivation of VZV is a result of waning of VZV-specific cell-mediated immunity (CMI) and is associated with aging of the immune system and the age of primal infection with HHV-3. The factor that stimulates immunity against reactivation of the virus is the exposure to VZV antigen – the effect that resembles contact with a chicken pox patient or a patient with subclinical infection (with shingles). Decreased shingles incidence is observed in adults that were exposed to chicken pox [6] and individuals vaccinated with live attenuated vaccine versus placebo (treatment) [12]. One of the most important risk factors associated with shingles is the age of primal infection with HHV-3. The risk of developing shingles in children under 12 years of age is even 35 times higher if the mother was infected with HHV-3 during pregnancy [15].

The relationship between sex and the reactivation of HHV-3 is not explicit. The analysis of shingles incidence in patients at The 1st Clinical Military Hospital with Policlinic does not imply correlation between shingles incidence and the patient's sex. According to other research [11], the female gender is an independent risk factor for shingles incidence in individuals between 25-64 years of age. But treating women as a higher risk group implies a contradiction: women being mothers are more frequently exposed to HHV-3 due to contact with children infected with chicken pox. Owing to this women have a higher level of VZV antibodies and develop shingles less frequently.



a) Patient before treatment



b) Patient after treatment

Fig. 4. Effects of treatment in a patient with generalized gangrenous and haemorrhagic shingles

The risk of shingles and its life-threatening complications increases several times in patients with malfunction of the immune system, especially with impaired T-cells response in patients with cancer during immunosuppressive therapy [2, 15], including BMT recipients and the recipients of parenchymal organs [13]. The risk of shingles increases 5 times in neoplastic patients and is highest in patients with leukaemia and lymphoma [2, 6].

The latest epidemiological research indicates that shingles incidence will increase in the next 20 years due to the introduction of vaccination against chicken pox in children: decreasing chicken pox incidence and reducing exposure to HHV-3 lowers the frequency of occurrence of the effect similar to contact with virus of persons that once had chicken pox. It is possible that introduction of vaccination against HHV-3 in older patients will reverse the above-mentioned tendency [11].

The goal of shingles treatment in immuno-competent patients is reducing pain, while in the case of patients with a damaged immune system drugs are used to prevent viral replication [4]. The recommended treatment options include antiviral drugs: acyclovir, famciclovir, brivudine, valaciclovir (Table 5, 6). The above-mentioned drugs (administered orally) shorten the duration of rash, accelerate the healing of lesions, reduce severe pain [4] and prevent post herpetic neuralgia.

The results of the latest clinical trials [7, 9] show evidence that the efficiency of valaciclovir and famciclovir is comparable and very high (Fig. 4a, b). Antiviral drugs should be given together with analgesics and corticosteroids in order to alleviate the pain [4]. The selection of analgesics

should be in compliance with generally accepted pain manage- ment standards: following assessment principles, regular dosing, evaluation of the response to treatment in order to adjust dozing to the patients' needs [4].

Table 6. Antiviral drugs (p.o.) used in treatment

Medication	Dosage	Duration
Valaciclovir	1000 mg 3 x daily	7 days
Famciclovir	500 mg 3 x daily	7 days
Acyclovir	800 mg 5 x daily	7-10 days
Brivudine	125 mg 1 x daily	7 days

CONCLUSION

The factors that put at higher risk for developing shingles include: the aging process, co-existing chronic diseases (inclusive cancer), immunosuppressive therapy. Older adults are at highest risk of developing shingles and they require intensive treatment and hospitalization. The treatment of herpes zoster should include antiviral drugs, corticosteroids and analgesics. In the face of increasing incidence of shingles, the introduction of vaccination against HHV-3 in patients over 50 years of age should be given due consideration in the next 20 years.

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