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Case report / Приказ болесника

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Herpes zoster in an immunocompetent infant with a history of varicella in early infancy and after a minor injury – case report and literature review

Херпес зостер код имунокомпетентног одојчета након лаке повреде са анамнезом овчијих богиња у раном одојеначком узрасту – приказ случаја и преглед литературе

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Herpes zoster in an immunocompetent infant with a history of varicella in early infancy and after a minor injury – case report and literature review

Херпес зостер код имунокомпетентног одојчета након лаке повреде са анамнезом овчијих богиња у раном одојеначком узрасту – приказ случаја и преглед литературе

SUMMARY

Introduction Chickenpox is a common pediatric disease, while herpes zoster (HZ) is rare among children, especially among infants. HZ in infancy may appear after intrauterine or postnatal infection with varicella-zoster virus (VZV). We report on a case of HZ in an immunocompetent infant who had a history of chickenpox in early infancy.

Case outline A seven-month-old male infant was presented with skin changes in the left T1 and T2 dermatomes. Skin changes appeared eight days after the infant had a mild left-arm traction injury. The patient's medical history revealed that he had a mild form of chickenpox at the age of three and a half months. After the clinical diagnosis of HZ was made, he was treated with oral acyclovir 20 mg/kg every six hours for five days and had complete recovery without any sequelae.

Conclusion Risk factors for pediatric HZ are immunosuppression and chickenpox during the first year of life. Local trauma is a reported risk for VZV reactivation among adults. To our best knowledge, our case is the first reported pediatric case in which the injury of the left arm precedes HZ appearance. Routine vaccination against chickenpox may be an important preventive measure because herd immunity will protect infants and immunocompromised children from getting chickenpox and thus HZ.

Keywords: herpes zoster; infants; trauma

САЖЕТАК

Увод Овчије богиње су честа болест у педијатријском узрасту, док је херпес зостер (ХЗ) редак код деце, а изузетно редак код одојчади. У одојеначком периоду ХЗ се може јавити као последица интраутерине или постналне инфекције варицела-зостер вирусом (ВЗВ). Ми смо приказали случај ХЗ код имунокомпетентног одојчета које је прележало овчије богиње у раном одојеначком периоду.

Приказ случаја Мушко одојче узраста седам месеци прегледано је због кожних промена у регији Т1 и Т2 дерматома лево. Кожне промене које одговарају ХЗ су се појавиле осам дана након што је одојче имало мању тракциону повреду леве руке. Из личне анамнезе сазнали смо да је одојче имало овчије богиње у узрасту од три и по месеца. Након што је клинички постављена дијагноза ХЗ, одојче је лечено оралном применом ацикловира у дози 20 *mg/kg* на шест сати током пет дана и потпуно се опоравило, без икаквих последица.

Закључак Фактори ризика за појаву ХЗ код деце су стање имуносупресије и овчије богиње у првој години живота. Код одраслих се као један од факора ризика наводи претходна траума у регији ХЗ. Према нашим сазнањима ово је први описан случај ХЗ у одојеначком узрасту где је повреда леве руке претходила појави ХЗ и вероватно била окидач за реактивацију ВЗВ. Рутинска вакцинација против ВЗВ би била важна превентивна мера, јер би стицањем колективног имунитета имунокомпромитовани и одојчад били заштићени од обољевања од овчијих богиња, а самим тим и ХЗ.

Кључне речи: херпес зостер; одојчад; повреда

INTRODUCTION

Herpes zoster (HZ), also known as shingles, occurs as a result of reactivation of varicella-zoster virus (VZV) which persists in latent form within sensory ganglia after primary infection. HZ is rare in immunocompetent children. In the first year of life, HZ may

appear as a consequence of intrauterine infection or after birth due to postnatal infection with VZV. We report a case of HZ in an immunocompetent infant who had a history of chickenpox in early infancy. We also review the literature on risk factors for the development of HZ infection in children.

CASE REPORT

Parents provided written consent to report the case of their child. A seven-month-old male infant was presented to the outpatient clinic with a three-day history of skin changes in the left armpit and left upper arm. Skin changes appeared eight days after the child had a mild left-arm traction injury. The injury happened on the same day when the child received the vaccine against hepatitis B. Radial head subluxation was diagnosed by an orthopedic surgeon who performed a reduction maneuver in the outpatient settings after which the infant regained full mobility of the arm. The patient's medical history revealed that he had been a full-term normal delivery with a birth weight of 2.9 kg. At the neonatal ward, complete blood count (CBC) and routine blood biochemical analysis were performed and the results were as follows (normal range for age is shown in parentheses): leukocyte 18.9 × 10^9/L (5–21 × 10^9/L), hemoglobin 185 g/L (135–195 g/L), platelet 330 × 10^9/L (150–450 × 10^9/L). The differential leukocyte count showed 48% of neutrophils (19–49%), 3% of bands (0–15%), 35% of lymphocytes (26–36%), 14% of monocytes (7–18%), 0% of both basophils (0–1%) and eosinophils (0–1%). Blood levels of glucose, urea, creatinine, total protein, albumin, total and direct bilirubin, sodium, chloride, potassium, calcium, aspartate transaminase, alanine transaminase, and C-reactive protein were normal. The infant was breastfed for the first five months of life. He was fully vaccinated according to schedule (including BCG vaccine at the neonatal ward, which is part of a routine vaccination program in Serbia) and he did not experience any vaccines side effects. He had a mild form of chickenpox with around 50 skin

changes and with no accompanying fever at the age of three and a half months. As an epidemiological risk factor, parents reported indoor gatherings with friends and family two weeks before varicella eruption, but the definitive source of the infection remains unknown. The infant's mother had chickenpox at age of eight years. Also, the mother was tested for HIV and TORCH pathogens during the first trimester of pregnancy and all tests were negative. The rest of the past medical history was unremarkable.

On physical examination, the infant's weight was 8100 g (at the 40th percentile) and his length was 70 cm (at the 65th percentile). There was polymorphic rash (papules, vesicles, and crusts) in dermatomes T1 and T2 (Figure 1). The infant was slightly irritable while the rest of the examination was normal. At that time, his complete blood count (CBC) was as follows (normal range for age is shown in parentheses): leukocyte 14.25 × 10^9/L (6–17 × 10^9/L), hemoglobin 116 g/L (109–138 g/L), platelet 412 × 10^9/L (150–450 × 10^9/L). The differential leukocyte count was: neutrophils 18.7% (23–66%), lymphocytes 72.5% (18–60%), monocytes 5.03% (5–13%), basophils 0.37% (≤ 2%), eosinophils 3.4% (≤ 6%). We established the diagnosis of HZ based on clinical presentation and medical history.

The infant received treatment with oral acyclovir 20 mg/kg q6h for five days. Ten days after the start of treatment all skin changes became crusts (Figure 2). At the next follow-up visit, four weeks after diagnosis, complete resolution was noticed. In the six months follow-up time, there were no sequelae, his psychomotor development was normal and he did not suffer from any other infection during this period.

DISCUSSION

Primary infection with VZV causes varicella, also known as chickenpox. Chickenpox is a disease of childhood with > 90% of individuals tested being seropositive by 10 years of age in most countries [1]. In Serbia, where vaccine against VZV is not part of the routine

vaccination schedule, the percentage of seropositive results increases from 41.2% in the age group of 1–4 years to 92.7% in the age group of 15 to 19 years [2]. The seroprevalence among infants younger than one year is 75% which is higher than in the age group 1–4 years, probably due to the presence of passively transplacental transfer of maternal antibodies [2]. During the first year of life infection with VZV can be acquired transplacentally (if the mother was seronegative before pregnancy and acquire the infection during pregnancy) or after postnatal exposure. Regarding postnatal exposure, infants born from seropositive mothers are at lower risk to contract varicella in the first few months after birth. However, if an infant develops the disease, he/she will have a mild form of the disease or subclinical infection because of transplacentally transferred maternal VZV-specific antibodies [3], as was the case in our patient.

After primary infection settles down, the virus remains latent in sensory nerve ganglia. The reactivation of the latent virus manifests as HZ. The triggers for reactivation are still not well understood, but declining VZV-specific cell-mediated immunity plays an important role. The known risk factors for the appearance of HZ are immunocompromising states such as malignancy (especially leukemia and lymphoma), HIV infection, organ transplantation, use of immunosuppressive medications (e.g., chemotherapy agents, corticosteroids) [4], and chronic diseases [5].

The overall incidence of HZ among children younger than 18 years of age was estimated to be 74 per 100,000 person-years [6]. The incidence among unvaccinated children younger than five years is 20 per 100,000 person-years [7]. The incidence of HZ among vaccinated children is 78% lower than among unvaccinated children and the incidence among immunocompetent children was 5–6 times lower than in immunocompromised children [6]. A higher risk for HZ was found in children who had chickenpox during their first year of life [6]. The probable cause is that immature adaptive T-cell response is less able to withhold

VZV in the latent state [8]. In countries where vaccine against chickenpox is a part of the routine vaccination schedule, the trend of decreasing HZ incidence among unvaccinated children was noted. It is likely due to a lack of primary VZV infection resulting from herd immunity in a highly vaccinated population [6]. In children who had chickenpox during the first year of life, the duration of latency ranges from 8 to 142 months [9], which is significantly longer than 3.5 months of latency as it was in our case. The probable cause of this early virus reactivation was a minor injury to the left arm. Studies on adults showed the association between HZ and trauma at the HZ site [10, 11] and the effect was rapid peaking in the first week after trauma [11], which is consistent with our case. Although injury-induced VZV reactivation is not well understood, the probable mechanism is excessive stimulation of the sensory nerve which triggers reactivation of the latent virus in the sensory ganglion. Another possible mechanism may be local immunity impairment by direct trauma and subsequent immune escape of latent virus [10]. Reactivations of VZV after different types of vaccines (vaccine against influenza, hepatitis A, rabies, Japanese encephalitis, and COVID-19) were described in adult patients [12, 13, 14], but to the best of our knowledge HZ after hepatitis B vaccine was not reported yet. Immunomodulation after hepatitis B vaccine was observed [15], but there is weak evidence that hepatitis B vaccine contributed to VZV reactivation in our case.

HZ can be a manifestation of cellular or combined immunodeficiency. Our patient didn't fulfill any of the clinical criteria [16], which would indicate the need for diagnostic evaluation for primary immunodeficiency. Also, he didn't have risk factors for acquired immunodeficiency (e.g., immunosuppressive therapy, malignancy).

The most frequent skin localization of HZ in children is thoracic dermatomes [17, 18, 19], as it was in our patient. Classical clinical presentation of HZ in an immunocompetent child includes the appearance of papules and vesicles within one, rarely two adjacent

dermatomes. Later on, crusts develop from papules and vesicles. Pain and/or pruritus in the involved area may precede rash. Systemic manifestations such as fever, lymphadenopathy, and headache may occur. The differential diagnosis of HZ includes impetigo, poison ivy rash, strophulus infantum, and miliaria rubra. Our patient had a typical clinical presentation, therefore careful history taking, physical examination, and observation of skin changes evolution were sufficient to establish the diagnosis of HZ. In cases with atypical lesions, the diagnosis may be confirmed by detection of multinucleated giant cells in the Tzanck smear of scrapings from the floor of vesicles or by positive VZV PCR in vesicle fluid. Pediatric HZ has a good prognosis. The most common complication among immunocompetent children is a bacterial skin infection, while postherpetic neuralgia, the most common complication in adults, is less frequent in children [20].

Considering that HZ has a mild course in most children with a lower incidence of complications than in adults, antiviral therapy is usually reserved for immunocompromised patients and patients with disseminated disease. We decided to treat our patient with oral acyclovir because it was reported that antiviral therapy shortens the disease course and period of contagiousness, antiviral therapy should be considered in immunocompetent patients of any age with HZ to accelerate healing [19] and prevent further spread among susceptible individuals. The benefit is the most obvious if the therapy is started in the first 72 hours of illness [21].

Children who get chickenpox during the first few months after birth can have a mild form or even clinically unrecognized disease if the mother had immunity to VZV before pregnancy. It could be challenging to diagnose HZ in such cases. Although an injury is a well-known risk factor of HZ in adults, to the best of our knowledge, our patient is the first described pediatric case of injury precipitated HZ. Routine vaccination against chickenpox

may be an important preventive measure because herd immunity will protect infants and immunocompromised children from getting chickenpox and thus HZ.

Conflict of interest: None declared.

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Figure 1. Initial clinical presentation of the patient with papules, vesicles, and crusts within left T1 and T2 dermatomes

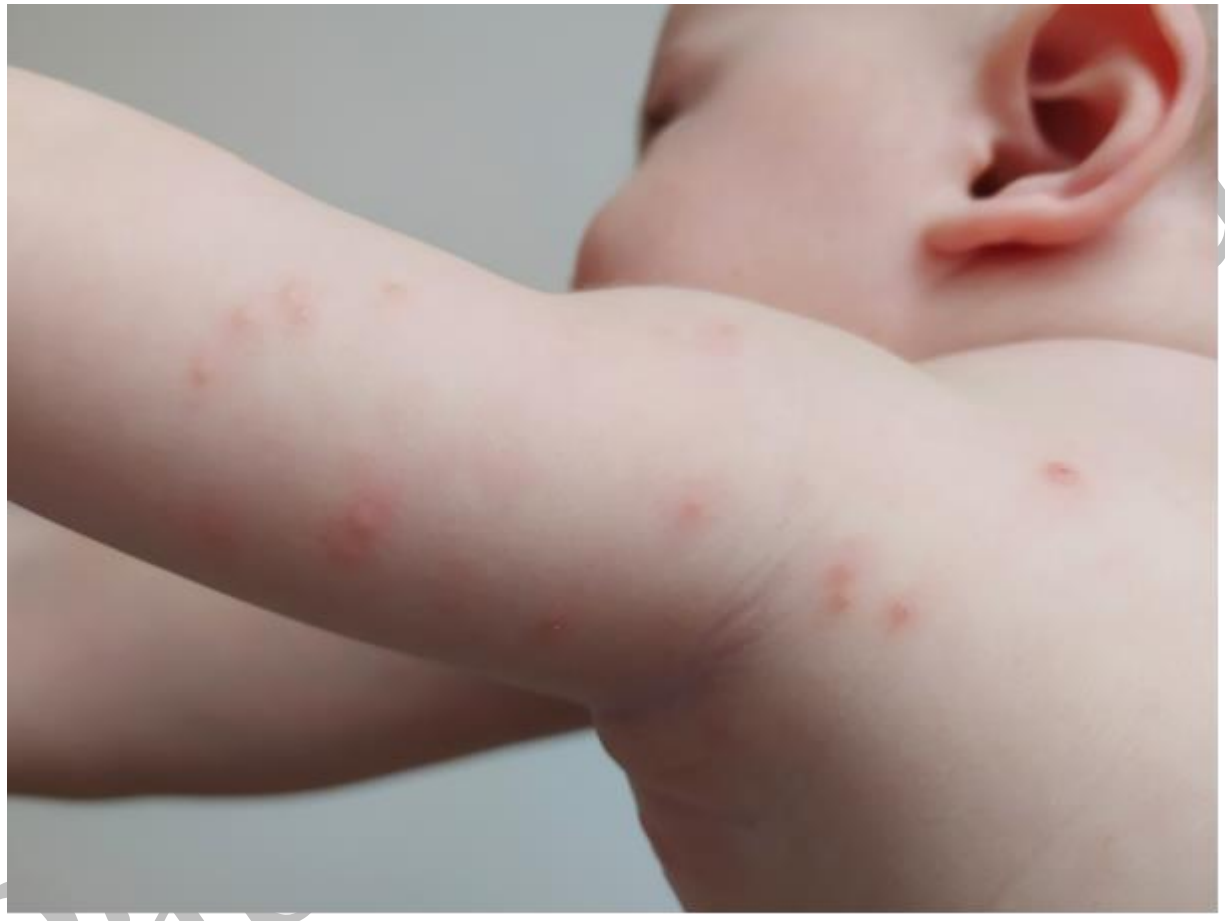

Figure 2. Clinical appearance at the follow-up visit 10 days after the start of treatment.