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Case Report Open Access

Primary Varicella Zoster Virus Infection in an Eritrean Male Refugee in Denmark

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Abstract

Primary infection with varicella zoster virus (VZV) in neonates, adults and in pregnancy may lead to severe disease and embryopathy. On the Northern hemisphere varicella is a mild childhood disease, but in tropical regions it typically occurs at later age and is more frequently observed among adolescents and adults. Disease presents with fever, malaise and a characteristic vesiculopapular rash (chickenpox) after an incubation period of 14 days on average. VZV is very contagious and transmission occurs mainly airborne. After infection, virus persists latent and prompts herpes zoster on reactivation. Severe complications include bacterial sepsis, pneumonia, encephalitis, haemorrhage, congenital varicella syndrome and others.

In our case report we present a 26-year-old Eritrean male refugee admitted to a Danish emergency unit, somnolent with a fever, unspecific generalized symptoms and a widespread vesicular exanthema. The patient was later assessed to have a severe systemic VZV infection and was treated with aciclovir. This case report questions whether routine VZV vaccination of pregnant refugees and families in reunification should be implemented in European countries to prevent severe disease. Further, it instigates discussion on whether Denmark and other countries should reconsider implementing national vaccination programs in childhood.

Keywords

Varicella infection, Vaccination, Seroprevalence, Global health, Immigrant health

Abbreviations

VZV: Varicella Zoster Virus; CNS: Central Nervous System; GCS: Glascow Coma Scale; CRP: C-reactive Protein; PCR: Polymerase Chain Reaction; HIV: Human Immunodeficiency Virus; IgM: Immunoglobulin M; IgG: Immunoglobulin G; HHV: Human Herpesvirus

Introduction

Primary infection with varicella zoster virus (VZV) is a very contagious infection. In the Northern hemisphere, it typically results in mild childhood disease manifesting with a distinctive rash [1-3]. Infection is frequent before primary school and at age 10 more than 90% are estimated immune [1]. However, in tropical regions the infection occurs at a later age, in adolescents and adults [3], with only 30-50% immunity among adults [4]. A Dutch study from 2012 found that 94% of the overall adult population was seropositive against 90-92% in first-generation immigrants [3]. Comparably, a German study on refugees found approximate 91% of subjects < 18 years seropositive [5]. In Scandinavia, varying immunity has been reported: 98% of 9-12 years old in Sweden, 91% of 10-year-old in Finland among only 78% in Norwegian 9-year-old [6]. Differences observed may be attributable to time of data collection, demography and others factors. Presumably, 98% of adults in Denmark have had the infection [4].

VZV is a herpes virus of the Herpesvidriae family, consisting of a double-stranded DNA genome [2]. The virus has tropism for T-lymphocytes, epithelial cells and sensory neurons and is highly communicable, spreading mainly by airborne route from airway and skin secretions [2]. After an incubation period of 10-21 days (on average 14), patients present with fever, malaise and the characteristic vesiculopapular rash, known as chickenpox. Infected individuals are contagious two days prior to the appearance of the rash and until all vesicles have scabbed [4]. After primary infection, the virus remains latent in sensory gangligas and prompts herpes zoster (shingles) on reactivation. A painful, vesicular rash confined to a dermatome, frequently seen in elderly and immunocompromised. Zoster can be complicated by postherpetic neuralgia, most commonly, and

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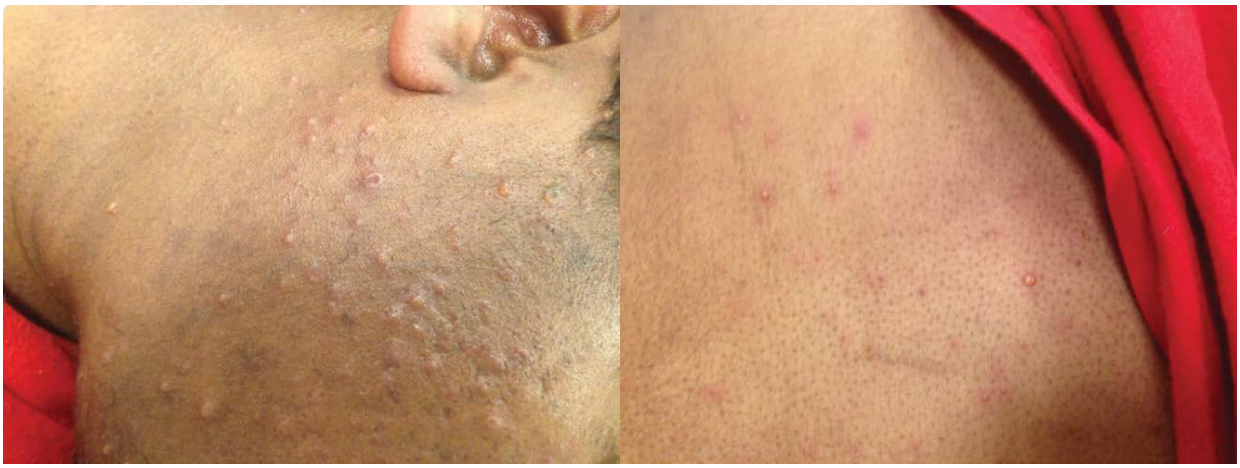

Figure 1: Varicella lesions on the face and on the back.

other neurological conditions [2]. Virus is susceptible to nucleoside analogues such as acyclovir, valacyclovir and famciclovir [2].

Primary infection with VZV is not always a mild childhood disease and complications occur in about 5% [4]. A recent review (Helmuth, et al.) has described the epidemiology in Europe and found reported hospitalization rate varying from 130-1.152/100.000 case of varicella [1]. The majority of hospitalized patients were previously healthy children under 5 years of age (77-92%). The majority of complications were bacterial super infections of the skin and soft tissue (21-47%) and less frequent neurological, respiratory tract and gastrointestinal manifestations.

Severe complications in VZV infection include bacterial sepsis, pneumonia, encephalitis and haemorrhage [1-3] and is often more severe and potentially fatal in certain individuals. Stroke in children is also associated with recent infection [1].

In particular, infants, adults, immunocompromised and non-immune pregnant women and their newborns are at risk of developing VZV infection associated complications, i.e. congenital varicella syndrome and neonatal varicella [1-3]. For instance, 5-14% of adults with chickenpox will develop pulmonary involvement, and patients with pre-existing lung disease, smokers, immunocompromised and pregnant are at a higher risk of life-threatening pneumonitis [7]. Involvement of CNS may result in acute cerebellar ataxia in recovering children, but is usually benign and self-limiting. Encephalitis however, may entail mortality up to 20% [8].

Helmuth, et al. found reported case fatality rates among hospitalized children in Europe at 0.1 to 0.4% but up to 2.7% among adults in another report [9]. An older study also found case fatality rate highly age-dependent and stated that adults account for 85% of deaths [10].

The Danish childhood vaccination program does not include routine VZV vaccination as it does in USA and other European countries [1]. However, according to Danish guidelines, fertile non-immune women planning pregnancy should receive vaccination at the latest one month prior to conception in order to reduce complication rates. Guidelines also suggest vaccination in healthy seronegative children, immunocompromised and their relatives, e.g. leukemia and prior to organ transplantation. Vaccination can also be used as post-exposure prophylaxis within three days after infection. Vaccination is protective in approximately 98% of cases after two doses [4].

Case Presentation

We here describe a primary VZV infection in a 26-year-old male refugee from Eritrea who had resided in Denmark for over 2 years. Upon admission to the emergency unit, the man was somnolent and unresponsive to pain, and had slight tachycardia, heavy breathing, and a high fever (39.6 °C). He scored 8-9 on GCS. There was no headache, petechiae or neck stiffness, and no lumbar puncture was performed. Meningitis and encephalitis were dismissed as etiology based on clinical assessment and recovery of consciousness on hospitalization, while impetigo, molluscum contagiosum, varicella-zoster and other herpes viruses were considered as differential diagnoses as well as other childhood diseases.

A friend of his functioned as interpreter as the patient did not speak Danish. Through 3-4 days the patient had been feeling ill with a lower back pain, vomiting and had over the last two days developed a rash on the face, upper body and extremities (Figure 1). The patient complained that the rash was itchy and painful. At the institution where the patient was residing, several individuals had supposedly experienced similar symptoms. He was residing at an adult language education college with boarding school facility with other residents of both sexes, same age and a majority of young male immigrants. There were no pregnant women residing there according to the local general practitioner whom the Public Medical Officer contacted. Besides back pain and past malaria infection, the patient was previously healthy.

During physical examination he was found moderately acute affected, although with stable circulation and respiration. GCS had improved to 14. He denied headache. A brief neurological examination was conducted, which showed natural eye movement and reaction to light. His eyes were often closed, but opened when he was addressed. Nuchal rigidity had not developed. All extremities moved upon request. Also, auscultation of heart and lungs was without any pathological findings. However, on the face, forehead, scalp and down the neck was observed a vesicular exanthema and to a lesser extent on the upper body and extremities with both fluid-filled vesicles and small craters.

Only positive findings were the rash and paravertebral tenderness. No doorbell phenomenon was present, and there was no pain to percussion. The tenderness was ascribed to his history of back pain.

Biochemically, CRP was 18 mg/L and D-dimer 1.6 mg/L both attributed to infection. Overall leucocyte count was normal at first contact (5.9×10^9/l, normal range 3.5-10) and remained normal during the entire hospitalization. At admission there was a slight lymphopenia a 1.0×10^9/l (normal range 1.3-3.5), which was normalized on the next day and remained normal for the rest of the hospitalization. Additional biochemistry was normal.

The patient was assumed to have a severe systemic VZV infection and was treated with aciclovir 10/mg/kg intravenously every 8 hours

for three days, sodium chloride infusion (isotonic saline 0.9%) and paracetamol. He was transferred to a specialized department of infectious diseases, where swabs from vesicle fluid were negative for herpes simplex virus 1/2 and positive for VZV based on PCR. HIV serology was negative. Varicella-zoster IgM was positive and IgG negative. HSV-1 IgM was negative, IgG positive. Blood was tested for presence of HHV-6, HHV-7 and HHV-8 DNA, which were all negative. An IgM positive result suggests primary infection, although it does not exclude re-infection or reactivation of latent infection [11]. However, when comparing the laboratory results and the clinical presentation, the case seems to be an incident of primary VZV infection. No pathology was found on chest X-ray and the patient recovered quickly. He was discharged the day after the transfer with 800 mg aciclovir tablets (5 times a day for 5 days), paracetamol and certrizine for pain and itching.

Discussion

Varicella is a common childhood disease, which in adults and other susceptible patients is able to trigger a severe clinical infection. The different pattern of transmission in tropic climates means that some refugees will be non-immune when travelling to Northern Europe. As VZV infection is very contagious, the risk of infection is particularly high in Danish asylum centers, refugee camps etc. due to close person-to-person contact, lacking vaccination and previous infection and thus lack of herd-immunity. Individuals from tropical regions are also at a higher risk of having tuberculosis or HIV making them particularly vulnerable to VZV infection and complications. Also, the contagious nature of the virus also implies a considerable risk of secondary household attacks in non-immune families, due to a high attack rate affecting up to 90% of seronegative [8]. Immigrants are more likely to be seronegative, presumably resulting a higher risk of serious infection in these households.

As described in the literature, complications to VZV infection can be severe, and our case report is an example of such. We have no clear indication of why the patient was so severely affected and appeared somnolent at first contact with a response team at the institution where the patient was staying. He was febrile, but had not neck stiffness. Somnolence could be a part of the clinical presentation, it is well described that considerable viremia of herpes viruses may lead to spill-over into CNS [12]. Once the patient came to the hospital, there were no longer cerebral symptoms, and a lumbar puncture was not found indicated although clearly relevant with the initial presentation. Another possibility is that this patient, who is a refugee from a war-stricken country and perhaps traumatized, was psychologically affected by the whole situation, when a doctor was called and chose not to respond.

In the light of the ongoing European migration crisis, it is evident that changes in demography entail great challenges to the international community, including health care. Challenges demanding both short- and long-term guidelines for management of health and disease in refugees. Our case report, is an example of such a challenge, as it questions whether fertile, non-pregnant women or girls and refugees in family reunification should be vaccinated routinely to prevent an increase in severe chicken pox infections in this population. Although, hospitalization and complications due to varicella, as seen in our case, is not common, vaccination is potentially able to prevent disease and lower the incidence, both in immigrants and ethnic Danes. The high effect of universal vaccination experienced in USA and other European countries, underlines this [1]. Instituting routine vaccination of immigrants should strongly be considered. Additionally, this case may instigate discussion on whether Denmark and other countries should reconsider implementing universal VZV vaccination, due to the fact that most complications and the greatest burden of disease occur in previously healthy children and disabilitating reactivation may occur, even in early age [13]. Describing benefits, drawbacks and capacity for national vaccinations programs is however not within the scope of this report, which concludes that primary VZV infection can be acute and require hospitalization upon late onset in adults, and with a growing population of non-immune adult immigrants the vaccination policy in asylum centers may need reconsideration.

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