Varicella-Zoster Virus Encephalitis in an Immunocompetent Adult with Disseminated Cutaneous Herpes Zoster after Testosterone Booster Supplements: Case Report

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Abstract
Disseminated zoster affects immunocompromised individuals and has a nondermatomal distribution. We report a 28-year-old male who initially presented to the dermatology clinic with pinprick sensation over the right side of his face that was followed by vesicular eruption. Upon which he was diagnosed with herpes zoster and discharged on topical mupirocin ointment three times a day and valacyclovir 1 g oral three times a day. A few hours later, he presented to the emergency department with drowsiness and an episode of loss of consciousness. He was then admitted by neurology and found to have herpetic encephalitis. During admission, he was started on intravenous acyclovir 10 mg/kg three times a day. After 3 weeks of intravenous acyclovir, the patient improved clinically; and all the vesicular lesions have crusted. Up to this date, there are only a few cases of immunocompetent adult patients with disseminated cutaneous herpes zoster (DCHZ), most of whom were over the age of 65 years or taking immunosuppressive medication. We report a case of DCHZ and varicella-zoster virus encephalitis in a young immunocompetent patient using daily testosterone supplements and a history of emotional and physical stress, in contrast to all previously reported cases, which presented significant risk.

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Introduction

Athletes and bodybuilders use different types of performance-enhancing drugs, mainly to boost their strength and muscle growth. Anabolic-androgenic steroids (AAS) contain a combination of synthetic and natural hormones that are like testosterone in structure [1]. A variety of side effects have been linked to AAS use, such as organ damage (e.g., liver, heart, and kidneys), alopecia, higher risk of tendinitis and tendon rupture, severe acne, and immune suppression [2, 3]. On the other hand, androgens suppress immunity by affecting B and T cell development, suppressing antibody response, dendritic cells, and macrophages [2]. Due to the aforementioned reasons, testosterone booster supplements have a suppressive effect on immunity.

Varicella-zoster virus (VZV) most commonly affects children and causes chickenpox [4]. The reactivation of latent VZV usually occurs in the elderly and immunocompromised individuals and leads to herpes zoster [5]. The Centers for Disease Control reports that a minimum of one herpes zoster outbreak is reported by 30% of all individuals [5]. It is usually localized to one dermatome. However, disseminated zoster affects immunocompromised individuals and has a nondermatomal distribution.

Disseminated cutaneous herpes zoster (DCHZ) is defined as the eruption of more than twenty lesions outside the primary dermatome and involvement of more than two noncontiguous dermatomes [6]. In addition to end-organ damage that presents as hepatitis, pneumonitis, and encephalitis [7].

Few cases of disseminated zoster in immunocompetent individuals have been reported in the literature [8]. A study by Price and Grose [9] highlighted the severe infection with VZV in patients treated with high doses of corticosteroids.

We report an unusual case of VZV encephalitis in a healthy 28-year-old male with disseminated herpes zoster. He was an athletic bodybuilder, and the symptoms were preceded by 8 weeks of strenuous exercise and testosterone-booster supplements in preparation for a bodybuilding Olympic competition. The purpose of this study is to shed light on disseminated VZV encephalitis in immunocompetent young adults.

Case Report

A 28-year-old male with no previous medical history presented initially to our dermatology clinic with a complaint of severe burning pain and pinprick sensation on the right side of his scalp, face, and upper chest that was followed by vesicular eruptions on these sites. He denied any past medical history, smoking, alcohol, or illicit drug use. No history of receiving a varicella-zoster vaccine. However, he is a professional bodybuilder and in preparation for an Olympic competition; therefore, he has been undergoing strenuous exercise and taking daily testosterone supplements for the past 2 months.

On examination, the right side of the face, scalp, and shoulder had few vesicles and crusted erosions. With an impression of herpes zoster, he was discharged on topical mupirocin ointment three times a day for 7 days and valacyclovir 1 g oral three times a day. A few hours later, he presented to the emergency department with drowsiness and an episode of loss of consciousness. He was then admitted by neurology to rule out herpetic encephalitis.

A lumbar puncture was done, and it showed an elevated white blood cell count of 18 with 99% mononuclear cells, normal protein, and glucose level. VZV polymerase chain reaction test was negative. At that time the diagnosis of VZV encephalitis was made, and the patient was admitted to be started on intravenous acyclovir 10 mg/kg three times a day. Magnetic resonance
imaging of the brain showed no lepto-meningeal enhancement. Human immunodeficiency virus screening was negative.

After 3 weeks of intravenous acyclovir, the patient improved clinically; and all the vesicular lesions have crusted. The patient was counseled about the immunosuppressive effects of AAS and testosterone boosters and the impact of stress on immunity.

**Discussion**

Reactivation of latent primary varicella-zoster led to opportunistic herpes zoster, and this occurs when the host’s natural or active immune system to the VZV-specific antigen wanes off [10]. In 33% of immunocompetent patients, they might have a few scattered lesions outside their sharply demarcated and localized rash but not yet completely disseminated [11]. Even though disseminated HZ occurs more often in immunocompromised patients, VZV viremia can happen in all patients with HZ irrespective of T-cell immune status or clinical evidence of dissemination [12].

Up to this date, there are only a few cases of immunocompetent adult (age 16 or older) patients with DCHZ, most of whom were over the age of 65 years, taking immunosuppressive medication, or with a history of failure to complete an entire course of antiviral therapy for herpes zoster [3]. Apart from one study published by Burdett et al. [13], where the patient was not on immune suppressive medications but was 75 years old and known diabetic; from the previously mentioned risks, none were applicable in our case.

VZV also can affect multiple organs including the central nervous system (CNS), which presents a spectrum of conditions, such as meningitis, encephalitis, and vasculopathy, which can present as primary or reactivation infections with possible neurological sequelae [14]. In patients with suspected meningitis or encephalitis and other CNS complications due to VZV, the diagnosis should be on clinical suspicion, with confirmation that can be done using viral DNA demonstrable in cerebrospinal fluid [15]. Identifying the VZV DNA by polymerase chain reaction depends on the timing of sampling as some studies found it to be negative in 56% of the patients [16].

Notably, VZV encephalitis can follow or proceed the appearance of rash by approximately 1 week in a patient with DCHZ, forty percent of whom will have asymptomatic CNS infection and have a higher risk of ischemic attacks, making it crucial to institute early treatment to prevent its fatal complications. From these cases, all of the reported patients were above the age of 75 years or being immunocompromised status, including human immunodeficiency virus or post-transplant patients [17–19].

The risk of VZV encephalitis is around 0.1–0.2% in patients with disseminated herpes zoster or having VZV eruption in the head and neck location [20]. Emotional tension within 6 months duration has doubled the probability of developing shingles [21]. At the same time, intensified training for long periods in athletes may lower T-cell functionality; this effect is not usually observed for persons with a sedentary lifestyle; the aforementioned are known risks of reactivation of latent varicella but not the appearance of DCHZ. These risks were present in our patient, as he was emotionally and physically stressed prior to the reactivation of HZ [22].

Few cases attributed the use of daily testosterone supplements or using AAS with reactivation of varicella-zoster. A study by LoBue et al. [1] described a case of recurrent herpes zoster ophthalmicus preceded by anabolic steroids and the use of testosterone 500 mg a week. In relation to our case, this patient did not develop complete dissemination of the virus, and he had an additional use of AAS. Nevertheless, these hormones have been well-documented to have immunosuppressive effects [3].
Numerous studies have shown that androgens are related to immunomodulation, hence influencing the innate and adaptive arms of the immune system. They have also been shown to induce immunosuppressive effects by reducing T cell numbers activation capacity, lowering anti-inflammatory cytokine production, and finally decreasing the antibody production levels through the effect on B-cell [23].

The use of commercial testosterone booster, identified as an independent risk of increasing aspartate transaminase, alanine transaminase, and gamma-glutamyl transferase, which led to idiosyncratic drug liver injury [24], thus perhaps lowering the patient immunity and inducing DCHZ as well as VZV encephalitis. Our case presented with DCHZ and VZV encephalitis in a young immunocompetent patient using only daily testosterone supplements and a history of emotional and physical stress, in contrast to all previously reported cases, which presented significant risk factors or appeared as a case of shingles only.

**Conclusion**

In conclusion, we present a healthy 28-year-old athlete who was under emotional and physical stress and was taking testosterone booster supplements for 2 months prior to the reactivation of VZV. The patient then developed DCHZ and VZV encephalitis. DCHZ and VZV encephalitis usually affect the elderly and immunocompromised individuals; however, clinicians should keep an eye for VZV infection in young and healthy adults who develop shingles and altered mental status. More large-scale studies are needed to determine the relation between testosterone booster and VZV reactivation to establish a true association.

**Statement of Ethics**

The study was done in accordance with the World Medical Association Declaration of Helsinki. It was also reviewed and approved by the Institutional Review Board at Prince Sultan Military Medical City in Riyadh, Saudi Arabia, on January 5, 2022. Written informed consent was obtained from the patient for publication of the details of their medical case.

**Conflict of Interest Statement**

The authors have no conflicts of interest to declare.

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**Author Contributions**

Ghada Alhayaza contributed by working on the literature review, data collection, writing, and reviewing the manuscript. Abdullah Al-Omair contributed by working on the literature review, writing, and reviewing the manuscript. Hind Almohanna contributed substantially in the conception of the paper, writing of the draft, and critically revised the manuscript. All authors
Data Availability Statement

All data generated or analyzed during this study are included in this article. Further inquiries can be directed to the corresponding author.

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