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A VIRAL COMEBACK: RECURRENT VARICELLA IN A YOUNG ADULT FEMALE

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ABSTRACT

An otherwise healthy young adult female presented to our clinic with a second episode of varicella. Our patient had a diffuse vesicular rash, reminiscent of childhood varicella, accompanied by constitutional symptoms. This rare presentation of a common virus required careful diagnostic and therapeutic decision-making, with a targeted approach based on clinical presentation and risk factors. As this patient was sexually active, there was concern for a mild case of monkeypox or herpes simplex. A polymerase cain reaction test on a skin vesicle was crucial to distinguish between these viral infections and make a diagnosis. With symptomatic treatment, the outcome was favourable. However, internationally recognised practice guidelines do recommend antiviral treatment. Adolescents and adults are at a higher risk of disseminated varicella, with severe and fatal outcomes. Further investigation of underlying immune impairment is also warranted.

KEYWORDS

Varicella, recurrence, infectious disease

LEARNING POINTS

- There are several possible causes of a diffuse vesicular rash in sexually active individuals.
- Varicella (chickenpox) can occur more than once.
- A polymerase chain reaction test may be required to distinguish between herpes simplex, varicella zoster and monkeypox infections.

INTRODUCTION

We present a case of a presumably immunocompetent young female with recurrent varicella. A second episode of varicella is rare[1]. Usually, an infection with varicella zoster virus (VZV) provokes a single episode of a scattered vesicular rash with constitutional symptoms (commonly known as chickenpox)[1,3]. In rare cases, the infection disseminates to other organs (e.g. central nervous system, lungs)[2,3]. Adults are at a higher risk of these systemic complications[2]. In older patents and/or those with risk factors (e.g. immunodeficiencies) the latent virus may reactivate and cause a rash confined to one or more dermatomes (herpes zoster, commonly known as shingles)[2,3]. Recurrences of a varicella-like rash have been reported in 4 to 13% of

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individuals who have had previous varicella infection[4,5]. The risk factors identified for these recurrences were young age (<12 months) at the first infection and having a milder first infection[4,5]. Confusion may arise as to whether the second episode indicates reinfection with exogenous VZV or is a reactivation of latent, endogenous VZV[1]. Moreover, some first infections are misclassified as varicella, because the diagnosis usually relies on clinical and epidemiological data[4]. Varicella rarely gets laboratory confirmed with serology or polymerase chain reaction (PCR)[4]. A study by Vazquez et al. found that 5.4% of the nonvaccinated individuals with varicella in clinical practice settings were negative for VZV antigen when tested with PCR[6]. Furthermore, in sexually active individuals it may be difficult to distinguish between varicella, herpes simplex and monkeypox.

CASE DESCRIPTION

An 18-year-old female patient presented to our emergency department. She complained of fatigue, feeling generally unwell and a head- and neck ache. Additionally, she reported seeing a skin lesion one day earlier on her abdomen. This lesion had evolved within 24 hours into an extensive rash on her face, trunk, and limbs *(Fig. 1-4)*. Upon further history taking, she mentioned having unprotected sexual intercourse 2 weeks before the onset of her symptoms. She had had the measles and varicella as a child but no other significant medical or surgical history. The patient briefly used paracetamol and a nonsteroidal anti-inflammatory drug (NSAIDs) for symptom relief. She was not on any long-term medication. She had been vaccinated for the measles and mumps in 2007 and 2016.

Axillary temperature was 37.2 °C. Blood pressure and heart rate were within the normal range. When inspecting the skin, we noticed a diffuse vesicular rash on the face and the trunk. Those vesicles were in different stages. Some had a pustular appearance, and others had already evolved into a crust. In the mouth, we observed multiple aphthous ulcers on the right cheek. Along with these changes, we palpated discreetly enlarged tender lymph nodes bilaterally in the cervical, axillary, and inguinal regions. The genital examination performed by a gynaecologist was normal.

A laboratory examination revealed a normal total white cell count (7.91 ×109/l, normal range 4.23-9.99 ×109/l) with an increased absolute lymphocyte count (4.61 ×109/l, normal range 1.26-3.41 ×109/l). This included some atypical lymphocytes (10.7% of the total white cell count). C-reactive protein was mildly elevated (18 mg/l, normal range <6 mg/l). Liver and kidney function were normal. The patient did not have any electrolyte disturbances. Serological tests ruled out active infections with cytomegalovirus, Epstein-Barr virus, human immunodeficiency virus, hepatitis A, B and C viruses and Bartonella henselae. Furthermore, tests for syphilis were negative. A cervical swab failed to detect the following micro-organisms: Chlamydia trachomatis, Neisseria gonorrhoeae, Mycoplasma genitalis and Trichomonas vaginalis. A nasopharyngeal swab tested negative for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), influenza A and B. In our further workup of her symptoms, we punctured a skin vesicle. We conducted a PCR test on this fluid to detect the following viruses: herpes simplex type I and II, VZV and monkeypox. The test showed a positive result for VZV. This was a surprising finding, as the patient had already undergone a primary VZV infection as a child. Moreover, her current presentation clearly differed from herpes zoster.

A vesicular skin rash with constitutional symptoms in an adult requires the clinician to consider a broad differential diagnosis[7]. Many (sexually transmitted) viral infections can cause a skin rash. Amongst the rashes with a vesicular presentation, measles, herpes simplex and varicella should

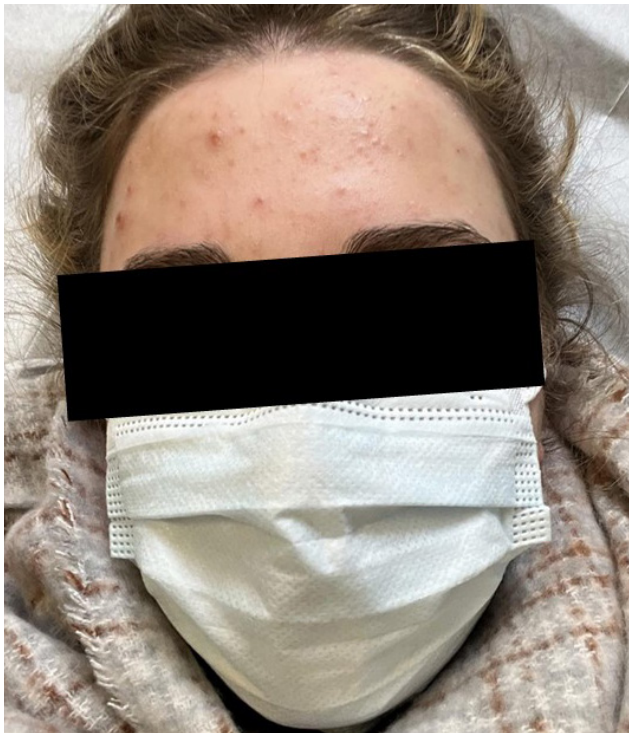

Figure 1. Vesicular exanthema in the face.

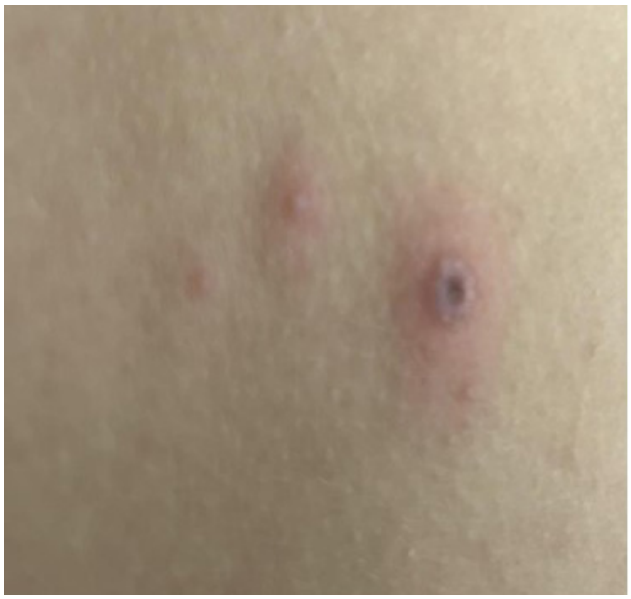

Figure 2. Close-up of a vesiculopustular lesion.

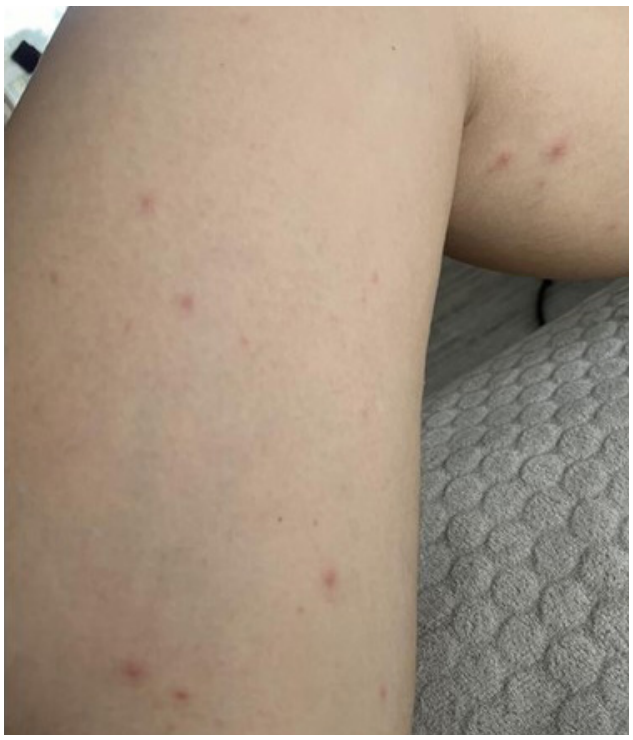

Figure 3. Vesicular exanthema on the leg.

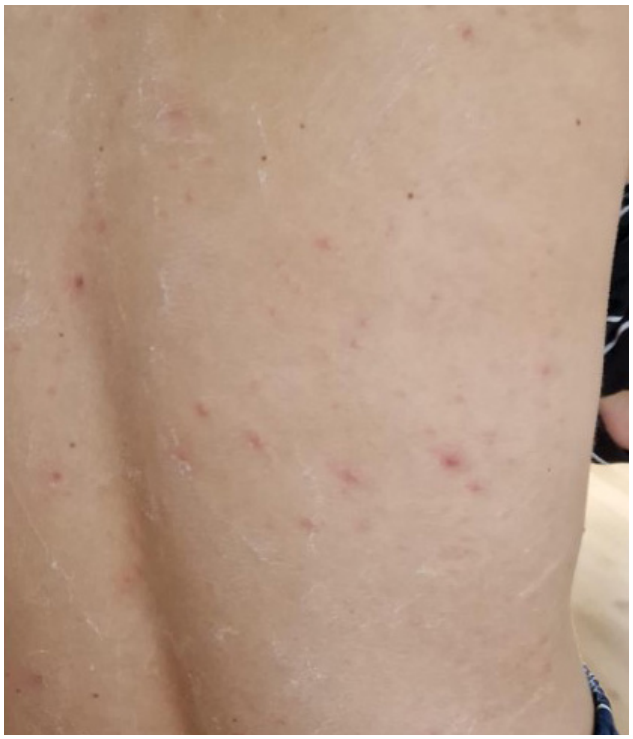

Figure 4. Vesicular exanthema on the back.

be considered as possible causes. Accounting for the recent SARS-CoV-2 and monkeypox epidemics, these viruses should also be included in the diagnostic workup[8]. Genetic bullous diseases, insect bites, burns, cellulitis, erythema multiforme and contact dermatitis may also present with vesicular skin disease[7].

We continued to treat her symptomatically by prescribing paracetamol and NSAIDs. The patient was considered fit enough to be treated as an outpatient. Prior to obtaining the definitive test results, we advised her to exercise caution during interpersonal interactions to avoid contamination.

DISCUSSION

An important limitation of this case report is that the diagnosis of the first varicella infection in this patient was made by history and physical examination only. There is no laboratory confirmation with serology or PCR. As already mentioned in our introduction, clinical and epidemiological data may, in rare instances, lead to misdiagnosis as varicella[4]. Vazquez et al. found that 5.4% of the nonvaccinated individuals with varicella in clinical practice settings were negative for VZV antigen when tested with PCR[6].

Second, in 2025 the investigation of a young sexually active patient with a diffuse vesicular rash requires a broad differential diagnosis, including other viral and bacterial infections, as well as drug-related hypersensitivity reactions[9,10]. Key infections like herpes simplex virus, VZV, and other sexually transmitted infections (STIs) should not be missed. A targeted approach based on clinical presentation and risk factors, rather than a blanket PCR test, is recommended for a cost-effective and accurate workup[9,10]. As mentioned, genetic bullous diseases, insect bites, burns, cellulitis, erythema multiforme and contact dermatitis may also present with vesicular skin lesions[7]. We did not run any tests to check for an autoimmune or autoinflammatory condition[7]. Additionally, we did not obtain any tissue for histopathological examination. Given the unequivocally positive test for VZV, these tests would have probably not been of any additional value. Conversely, viral and bacterial skin infections should be detected and treated before starting any immunosuppressive therapy for an autoimmune or autoinflammatory condition[7].

Furthermore, a recurrence of varicella may be associated with an underlying congenital or acquired immunodeficiency[2,3]. Except for human immunodeficiency virus testing, we did not rule out a possible immune disorder in this patient (e.g. haematological neoplasm, nephrotic syndrome, etc.). We did not screen for disseminated disease (e.g. central nervous system and pulmonary involvement). As previously mentioned, adults are at a higher risk for these systemic complications[2,3].

Despite guidelines recommending antiviral treatment for individuals over 13 years old[3], we did not start any antiviral medication. Large-scale placebo-controlled studies have demonstrated the clinical efficacy and safety of acyclovir in healthy children and adults[2,3]. The drug should be started within 24 hours after the first skin lesion appears[2,3]. It modifies the disease course in all age groups by reducing the number of days of fever, the process of new lesion formation and the total number of varicella lesions[2,3]. These effects may be more important in children[2,3]. We considered our patient to be at a relatively low risk for VZV dissemination[2]. Regardless of our risk assessment, this age group is at a higher risk for severe and fatal outcomes[3]. The patient did not seek any further medical contact to report disease progression.

CONCLUSION

The diagnosis of recurrent varicella still heavily relies on clinical and epidemiological data, without laboratory confirmation. We did not explore any non-infectious causes. A more extensive diagnostic workup covering non-infectious causes should, however, have been performed. Additionally, rather than performing a blanket PCR test, the clinical presentation and risk factors should determine whether to proceed with laboratory testing. Nevertheless, a PCR test may be required to distinguish between herpes simplex, varicella zoster and monkeypox infections. When facing an atypical disease course of VZV infection, screening for systemic involvement and any precipitating factors (e.g. immunodeficiency) is also warranted. Despite our choice for conservative treatment, oral antiviral therapy is recommended in adolescents and adults given the increased risk of a severe or fatal outcome. While exploring the many possible causes of this skin rash with systemic symptoms, we faced challenges in striking the right balance between over and under investigation. In retrospect, the unequivocally clear diagnosis and our clinical judgment may have led to some diagnostic and therapeutic shortcuts. To conclude, we would like to alert our fellow clinicians for these pitfalls when encountering rare presentations of such a common disease.

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