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Case Report

Varicella bullosa a rare form of chickenpox in an immunocompromised child: a case study

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ABSTRACT

The common human alpha herpesvirus known as varicella-zoster virus (VZV) causes both varicella (chicken pox) and herpes zoster (shingles). The frequent paediatric illness varicella is characterized by fever, viremia, and sporadic vesicular skin lesions. The bullous onset of chickenpox, is a very uncommon symptom that typically affects children who are immunosuppressed. Modern methods, such as polymerase chain reaction (PCR), have shed new light on this issue and strongly suggest that VZV can be involved in the development of bullae. Adequate prophylaxis and vaccination coverage help high-risk populations avoid complications. A7-year-old girl with polymorphic rash all over the body with comorbid diseases, diabetes mellitus type 1 and celiac disease. Past medical history stated suffering from COVID-19 infection. Physical examination revealed vesicular rashes of healing stages on various parts of the body with intense itching along with other symptoms of weakness, lethargy and lack of appetite. Based on the history, physical exam, and laboratory investigations, a definitive diagnosis of uncomplicated chickenpox, bullous form of moderate severity, was made. Treatment with saline infusion, iodinol, brilliant green solution, loratadine, acyclovir, amoklav, topical levofloxacin, and topical noxivin was initiated. The outcomes demonstrated that immunosuppression, autoimmune diseases and unvaccinated state of immunity might be the predisposing factors for development of bullous varicella. Inspite of its rarity, the disease have a good prognosis.

Keywords: Chickenpox, Varicella bullosa, Immunosuppression, Diabetes mellitus, Celiac disease

INTRODUCTION

The common human alpha herpesvirus known as varicella-zoster virus (VZV) causes both varicella (chicken pox) and herpes zoster (shingles). The frequent paediatric illness varicella is characterized by fever, viremia, and sporadic vesicular skin lesions. VZV establishes latency in the dorsal root ganglia cells, as is typical of the alpha herpesviruses. Herpes zoster is a localized, excruciating, vesicular rash affecting one or more nearby dermatomes and is brought on by VZV reactivation.[1]

VZV enters the body through the mucous membranes of the upper respiratory tract during primary infection (incubation period 10-21 days) and undergoes the initial replication in the regional lymph nodes. This is followed by a primary lymphocyte-associated viremia 4-6 days after infection (p.i.) and a secondary peripheral blood mononuclear cell-associated viremia 10-14 days p.i., which spreads the virus to the skin.[1]

The major clinical feature is a vesicular pruritic rash that occurs mainly on the trunk, head, and face. The extremities are somewhat spared; skin vesicles are full of infectious, well-formed virus which are aerosolized and serve to transmit VZV to others who have not had the disease previously. The skin lesions commonly occur in crops and progress from papules to vesicles to crusts over a few days.

There may be anywhere from a few to many hundreds of vesicles, with an average of about 500.[1] Serious complications from chickenpox include: bacterial infections of the skin and soft tissues in children, including group A Streptococcal infections, infection of the lungs (pneumonia), infection or swelling of the brain (encephalitis, cerebellar ataxia), Bleeding problems (hemorrhagic complications), bloodstream infections (sepsis), and dehydration.[2]

Staphylococcus aureus or *Streptococcus pyogenes* are most frequently etiologic agent for the bacterial superinfection of skin lesions, which is the most frequent varicella complication.[3] Other cutaneous complications of varicella include bullous or hemorrhagic varicella (more commonly seen in immunocompromised children) or purpura fulminans, which is associated with thrombocytopenia and disseminated intravascular coagulation.[4]

The following individuals are at a higher risk of complications and may experience a serious case of chicken pox are infants, adolescents, adults, pregnant women, patient with weakened immune systems as a result of illness or medications, such as those who have HIV/AIDS or cancer, transplant recipients, chemotherapy patients, immunosuppressive drug users, and long-term steroid users.[2] Varicella in an immunocompromised host leads to cutaneous and visceral dissemination.[4] The availability of efficient antiviral therapy has significantly decreased the mortality linked to disseminated zoster.[5,6] "Atypical generalized zoster" is a rare form of herpes zoster in immunocompromised hosts. Since the patients are VZV seropositive before the rash appears and have diffuse varicella-like skin lesions without obvious primary dermatomal involvement, the syndrome is not primary varicella.[4]

The clinical presentation makes the diagnosis challenging to make. Rarely is histological confirmation required, but a blood test is offered to look for VZV antibodies. Modern methods, such as PCR, have shed new light on this issue and strongly suggest that VZV can be involved in the development of bullae. Adequate prophylaxis and vaccination coverage help high-risk populations avoid complications.[7]

Early treatment, particularly in cases of zoster, can lessen tissue damage and, as a result, delay or even prevent the death of affected ganglion cells. For antiviral treatment of VZV infections, the primary options are the acyclic nucleoside analogs of acyclovir, including its prodrug valaciclovir, famciclovir (prodrug of penciclovir), and the cyclic nucleoside analog brivudin ((E)-5-(2-bromovinyl)-2'-deoxyuridine, BVDU).

Herein, we have presented a rare case of a child with a bullous form of chickenpox that was successfully treated.

Table 1: Antiviral treatment of VZV infections.[8]

Antiviral drugs	Administration	Indication
Valaciclovir[1]	Orally	Zoster, immunocompetent, adults: 3×1000 mg per day for 7 days
Famciclovir[2]	Orally	Zoster, immunocompetent, adults: 3×250 mg per day for 7 days, immunodeficient adults or adults with zoster ophthalmicus: 3×500 mg per day for 7-10 days
Brivudin	Orally	Zoster, immunocompetent, adults: 1×125 mg per day for 7 days
Foscarnet	i.v.	VZV infections caused by TK-negative VZV strains, adults: 3×40 mg/kg body weight per day for 10 (max 20) days, children (off-label use): 3×60 mg per kg body weight per day for 10 (max 20) days
Acyclovir	i.v./orally	i.v.=Severe and generalized VZV infections, zoster under immunosuppression, adults: 3×5-10 mg/kg body weight per day for 7-10 days, children: 3×500 mg/m^2 body weight per day for 7-10 days. Orally=Zoster, varicella in risk patients, adults: 5×800 mg per day over 7 days, children: 5×15 mg/kg body weight per day (max 4000 mg/day) for 7 days

[1]Prodrug of acyclovir administered orally, [2]prodrug of penciclovir administered orally

CASE REPORT

A 7-year-old girl was brought at Grodno regional infectious diseases clinical hospital by her mother, complaining of a polymorphic rash all over her body, lethargic and weakness. The patient had comorbid conditions such as diabetes mellitus type 1 and celiac disease.

Physical examination revealed vesicular rashes on the scalp, face, neck, chest, abdomen, back, upper limbs, and lower limbs. The rashes were in various stages of healing, including spots, papules, vesicles, erosions, and crusts. On the next day the vesicles progressed to large bullous on hand, legs, neck filled with vesicular fluid with size ranging from 3 mm to 25 mm.

The patient complained of intense itching where the rash was present. Additionally, she had weakness, lethargy, and lack of appetite. Baseline serial glycaemic index measurements were taken on the day of hospitalization, showing readings of 8.4 and 10.5 mmol/l, with a blood glucose level of 9.43 mmol/l noted. Patient was

unvaccinated against varicella infection. Past medical history also stated COVID-19 infection few months' back. With epidemiological history of no contact with any VZV patients, and all the family members were healthy.

A general CBC analysis was performed, which showed lymphocytosis of 52%. A urine analysis was also ordered, which tested positive for slime (mucus). Based on the physical exam and investigations, a preliminary diagnosis of varicella-zoster infection of moderate severity was made.

Further consultation with an ENT specialist found vesicles on external side of right ear and diagnosis of right otitis externa was made. Otitis externa was treated with Levofloxacin ear drops 3-4 drops in the right ear 3 times a day, Noxivin in the nose 2 drops 2 times a day.

Additional investigations were performed on the next day to rule out other possibilities for co-infection or superinfection which included a throat swab and stool test. These tests came back negative for microbial pathogens.

Based on the history, physical exam, and laboratory investigations, a definitive diagnosis of uncomplicated chickenpox, bullous form of moderate severity, was made.

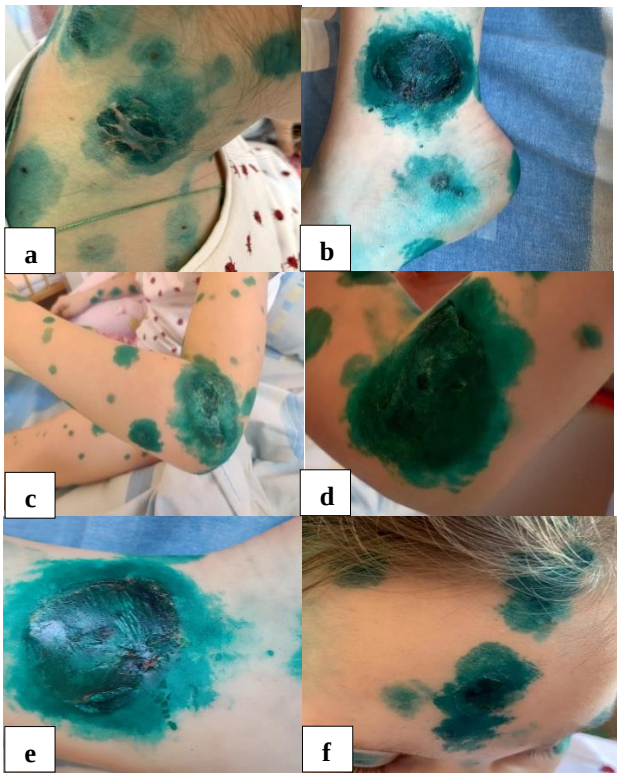

Figure 1 (a-f): Rupture and fluid-filled Bullae of different sizes on the face, neck, hands, and legs.

Treatment with saline infusion, iodol, brilliant green solution 1% solution in 60% alcohol, loratadine 10 mg, acyclovir 20 mg/kg per dose (maximal dose 800 mg), amoxicillin/clavulanate 250 mg/125 mg, topical levofloxacin, and topical noxivin was initiated. After the patient's condition had improved, she was discharged and advised to continue the antibacterial medication, along with topical application of brilliant green solution 2 to 3 times per day. A second consultation was advised only if infiltrative or suppurative changes were seen in rash elements.

DISCUSSION

Bullous chickenpox, also known as varicella bullosa, is a rarely reported variant of chickenpox that can affect both children and adults and occurs in 0.5% of cases. It can happen to both previously healthy people and people with compromised immune systems.[9]

Childhood blistering disorders are frequently challenging to diagnose and present challenging management challenges. Vesicles and bullae can be a symptom of a wide range of illnesses, from harmless conditions to serious systemic issues.[9,10] A "vesicle" is a raised, superficial, fluid-filled lesion that is less than 5 mm in diameter; a "bulla" is a large vesicle that is typically 5 mm or larger in diameter.[10] Herpes simplex viruses type I and type II as well as varicella zoster virus are the most frequently seen vesicobullous viral eruptions. Varicella zoster virus, a common neurotropic human herpes virus, is structurally composed of a DNA core, protein capsid, and lipid envelope.[1]

The presented case here is a 7-year-old girl with polymorphic rash all over the body with comorbid diseases diabetes mellitus type 1 and celiac disease. Past medical history stated suffering from COVID-19 infection. Eventually a clinical diagnosis of uncomplicated chickenpox, bullous form of moderate severity was made. The presence of large vesicular rashes along with characteristic symptoms, confirmed the diagnosis of chickenpox.

Hereby, we want to propose several factors that worsened the course of chickenpox which resulted rare cutaneous complications of varicella infection.

Immunosuppression being major risk factors for development of varicella bullosa. This patient observed with elevated glycaemic index and present comorbid autoimmune condition diabetes mellitus type 1, celiac disease may alter the paradime of immune system and increase the susceptibility for infections.

Diabetes is a metabolic disorder brought on by immune system inflammation. Due to the inhibition of insulin signalling, insulin resistance causes a variety of immunological responses that exacerbate the inflammatory state and result in hyperglycemia. The immune system's resistance to invasive infections in diabetics (including T cells) is thought to be compromised by both problems with the innate immune response (including neutrophil and macrophage dysfunction) and

deficiencies in the adaptive immune response. It is essential for the development of cutting-edge therapies to treat infections in diabetic patients and enhance treatment outcomes to have a deeper understanding of the mechanisms of hyperglycemia that compromise host defence against pathogens.[11] There are evidence indicating that an immunocompromised state occurs only in the context of poor glycemic control with severe complications.[12] Low production of interleukins in response to infection and hyperglycaemia both increase some pathogens' virulence; decreased chemotaxis, decreased phagocytic activity, and immobilization of polymorphonuclear leukocytes.[11]

Unvaccinated children or there is no evidence of VZV immunity are at greater risk at developing severe varicella infection, of which some of the risk factors are immunosuppression, state of pregnancy, child with age >12 years, chronic skin or lung diseases, infancy.[13] A retrospective study conducted complications of varicella in unvaccinated children from Romania, 2002–2013 demonstrated younger patients (10.9 versus 13.8 years, p=0.001), male patients (56.5% versus 43.5% in females, p=0.001), patients diagnosed between 2007 and 2010 (33.7%, p=0.001), and patients diagnosed between 2011 and 2013 (46%, p=0.001) all had significantly higher rates of varicella complications including respiratory tract infections, followed by GIT and ENT complications.[14] Medical history of our patient also states no vaccination against varicella infection.

Despite the fact that toxigenic *Staphylococcus aureus* is considered to play the main role in the aetiology of varicella bullosa, microbiological study and enterobioscopic examination were made to rule out other possibilities of co-infection and superinfection which tested negative for pathogenic flora.[4]

Additionally, infections are more likely to affect diabetic patients. Numerous studies have revealed that people with diabetes are more likely to develop lower respiratory tract illnesses, such as pneumonia, urinary tract infections, pulmonary tuberculosis (TB), and infections of the skin and internal organ tissues.[11] Development of Otitis externa with conjunction of chickenpox in our patient may state that chickenpox can give rise to development of various complication as generally cause of otitis externa are bacterial infections as *Pseudomonas aeruginosa* and *Staphylococcus aureus*.[15]

Antivirals should be administered as soon as possible to immunocompromised people and anyone who appears to be developing severe varicella for the best results.[1] However, the standard recommended doses of acyclovir for 1-2 weeks, depending on the severity of the disease, and antistaphylococcal antibiotics for 10-14 days, along with adequate supportive care, are included in the treatment of varicella bullosa. Patients with streptococcal cutaneous complications may also benefit from adjunctive therapy with intravenous immunoglobulin. This type of chickenpox typically has an excellent prognosis.[16]

The patient's improvement as a result of the started treatment confirms the validity of the diagnosis and the efficacy of the selected therapeutic strategy. The importance of follow-up care and close monitoring for any worsening or suppurative changes in the rash is emphasized by discharging the patient with continued antibacterial medication and topical application of brilliant green solution.

CONCLUSION

A 7-year-old girl with a history of type 1 diabetes mellitus (DM) and celiac disease presented with complaints of a polymorphic rash, which included papules, vesicles, erosions, and crusts. This rash further progressed to bullae ranging from 3 to 25 mm filled with vesicular fluid. Based on her clinical presentation and laboratory examination, a definitive diagnosis of uncomplicated chickenpox in its bullous form with moderate severity was made. The presence of an immunocompromised state and a lack of proper vaccination in this child might have aggravated the condition. Therefore, it's crucial to evaluate the immune status in such patients and administer vaccines. Additionally, introducing antibiotics into the treatment protocol is of utmost importance to prevent bacterial superinfection of the skin. Early recognition and treatment of these secondary bacterial infections can prevent further complications.

Compromised immunity, autoimmune diseases and unvaccinated state might be the predisposing factors for development of bullous varicella. Inspite of its rarity, the disease has a good response to medical therapy as well as good prognosis.

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