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Case Report

Kaposi Varicelliform Eruption: A Deep Study of a Singular Dermatological Condition

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Received: March 13, 2024; **Published:** April 12, 2024

Abstract

Kaposi's varicelliform eruption (KVE) is a rare but serious complication that can occur in patients with atopic dermatitis (AD) affected by the herpes simplex virus (HSV). It is characterized by the rapid dissemination of HSV in AD-affected skin, resulting in widespread vesicular lesions mimicking the presentation of chickenpox. This condition can be triggered by various causes, such as bacterial or viral infections, or the use of immunosuppressants. KVE presents with an acute clinical course and can cause severe systemic complications, such as herpetic encephalitis, making early diagnosis and appropriate treatment crucial. Management includes systemic antiviral therapy, treatment of underlying dermatitis, and supportive measures. Although KVE is uncommon, its potential to cause significant morbidity underscores the importance of clinical surveillance in patients with AD and the need for appropriate therapy to prevent serious complications. A greater understanding of predisposing factors and underlying mechanisms is required to improve prevention and management of this unique clinical entity. At same time is presented one case of KVE with severe affection of the skin.

Keywords: *Kaposi's Varicelliform Eruption (KVE); Atopic Dermatitis (AD); Herpes Simplex Virus (HSV)*

Introduction

Kaposi varicelliform eruption (KVE) is a rare but significant dermatological condition characterized by the appearance of vesicular skin lesions resembling chickenpox or herpes zoster. This disorder is closely associated with herpes simplex virus (HSV) infection, particularly HSV-1 and typically manifests in individuals with preexisting skin conditions such as eczema.

KVE can arise as a result of primary HSV infection or reactivation of latent herpetic infection, and its unique clinical presentation distinguishes it from other skin conditions. This eruption, often painful and prone to complications, poses challenges in both diagnosis and clinical management.

In this review, we will thoroughly explore Kaposi varicelliform eruption, addressing its clinical manifestations, risk factors, pathogenic mechanisms, diagnosis, treatment, and preventive considerations. By delving into the understanding of this condition, we aim to provide a comprehensive insight that benefits both healthcare professionals and those seeking detailed information about KVE. Through this analysis, we hope to contribute to knowledge and awareness surrounding this peculiar cutaneous manifestation associated with herpetic infection.

Epidemiology and risk factors

The epidemiology and risk factors associated with Kaposi varicelliform eruption (KVE) are primarily influenced by herpes simplex virus (HSV) infection and the presence of preexisting skin diseases.

It was first described in 1887 by the Austrian dermatologist Moritz Kaposi in 10 children with "eczema larvae infantum" that evolved into a vesiculopustular eruption, which he termed "eczema herpetiformis" [1]. Subsequently, the German dermatologist Fritz Juliusberg in 1898 defined it as "pustulosis acuta varioliformis" [2].

KVE is a rare condition but can occur in various population groups. Its exact incidence is not well established due to its rarity and variability in clinical presentation, although it is estimated to occur in 3% of patients with Atopic Dermatitis, and although it is a local affectation, it can progress to a situation of systemic infection that compromises the patient's life [3,4].

In more than 90% of cases, KVE is caused by HSV-1 [5]. Risk factors in patients with AD for developing KVE include other allergic diseases such as food allergy and asthma, lymphopenia, increased erythrocyte sedimentation rate and high levels of circulating IgE and eosinophils [6].

KVE can occur at all ages but is more common in children and young adults. Exposure to HSV at these ages may predispose to Kaposi's varicelliform eruption. It can occur in immunocompetent individuals, but the incidence is higher in individuals with weakened immune systems, such as those with primary or secondary immunodeficiencies.

Regarding its seasonality, like with herpetic infections, KVE may have some seasonality, with an increase in cases during the winter months and early spring.

Understanding the epidemiology and risk factors of Kaposi varicelliform eruption is essential for identifying at-risk populations and adopting preventive strategies. Education about the importance of skin care and the management of preexisting skin diseases are key aspects in preventing this dermatological condition.

Etiology and pathogenic mechanisms

Kaposi varicelliform eruption (KVE) is closely associated with primary infection or reactivation of the herpes simplex virus (HSV), specifically HSV-1. Below, the etiology and pathogenic mechanisms involved in this unique dermatological condition are explored: Herpes simplex viruses are double-stranded DNA viruses belonging to the Herpesviridae family and Alphaherpesvirinae subfamily, strictly human pathogens with skin and mucosal lesions [7]. We can differentiate between HSV-1 and HSV-2, which share 50% of homologous sequences [8]. HSV-1 primarily affects the lips and oral area, while HSV-2 mainly affects the genital area, and both viruses usually remain in neural ganglia, mainly the trigeminal ganglia for HSV-1 [9] and others such as ciliary ganglia [10], superior cervical ganglia, thoracic ganglia, and vagus nerve ganglia [11].

Transmission of herpes simplex virus (HSV) occurs through contact with infected secretions. During recurrent infections, whether symptomatic or asymptomatic, the virus can spread through viral shedding. In the typical form, HSV infects the skin or mucosa and multiplies in stratified squamous epithelium. Therefore, keratinocytes, which are the main cells in the epidermis, are the first cells attacked by HSV on the skin [12]. The penetration of HSV into cells depends on the interaction of viral glycoproteins B and D with certain molecules on the cell surface, such as heparan sulfate 3-O, nectin-1, and the HSV entry mediator (also known as TNFRSF14) [13], facilitating fusion between the cell and viral membranes. Keratinocytes, having all these receptors, allow rapid entry of the virus; approximately 90% of

viral particles are internalized within 30 minutes after infection [14]. Other cells present in the skin, such as dendritic cells (DC), can also be infected by HSV, especially Langerhans cells (LC) resident in the epidermis, which express receptors involved in HSV entry. Infection of DC inhibits their maturation and thus reduces cytokine production. Dermal fibroblasts are also potential targets of HSV due primarily to high expression of nectin-1 [15].

Furthermore, receptors allowing entry of the herpes simplex virus are found in various types of cells such as monocytes, B and T lymphocytes, as well as endothelial cells and mast cells [16]. After completing its lytic life cycle, herpes simplex virus initiates long-lasting persistence, known as latency, established in sensory ganglia innervating the infected area. Reactivation of latent viruses can be triggered by various factors such as exposure to ultraviolet light, emotional stress, fever, tissue injury, or immune system suppression [17]. It is recognized that herpes simplex virus employs several strategies to evade the host's innate immune response, contributing to infections [18]. Although herpes simplex virus generally causes mild infection in the mucocutaneous membranes of healthy patients, disseminated infection can occur in the damaged skin of patients with atopic dermatitis [19].

Understanding the pathogenic mechanisms of Kaposi varicelliform eruption is essential for accurate diagnosis and the development of treatment strategies that address both viral infection and underlying skin conditions. Continuous research remains crucial to improving understanding of this unique dermatological condition.

Clinical manifestations

The clinical manifestations of Kaposi varicelliform eruption (KVE) are distinctive and characterized by the presence of skin lesions that can vary in appearance and severity.

The clinical presentation of herpetic eruption (EH) is characterized by the appearance of scattered blisters and pustules, not grouped in reddish lesions, predominantly affecting the head, neck, chest, and arms. These blisters can cause erosions between 2 and 7 days later [20].

The skin's appearance is often accompanied by general symptoms such as fever, malaise, headache, and lymphadenopathy. Additionally, the clinical picture may worsen due to additional bacterial infections, especially with streptococci and staphylococci [21].

It has been found that individuals suffering from acute EH show lower lymphocyte counts and higher monocyte counts. EH may be accompanied by herpetic encephalitis or hepatitis, which can also occur in patients with a competent immune system [22].

At least 20% of patients with EH report recurrent episodes of herpes in their medical history. In a minority set of patients, recurrent HSV infections appear to be widespread.

Recently, Seegräber and colleagues published a multicenter European retrospective analysis examining 224 cases of EH, finding a recurrence rate of 26.5% [23]. Recurrence was linked to an earlier onset of atopic dermatitis; however, no discrepancies were evidenced regarding total IgE levels. Many patients exhibited atopic dermatitis lesions without EH, although the skin without lesions of this disease was never affected by herpetic lesions. Wheeler and colleagues evidenced that recurrent EH is less intense compared to the initial presentation [24]. The average age of adult individuals with EH was estimated at 22.5 years. In 1985, Wutzler and colleagues provided information indicating that most cases of EH were attributable to HSV-1 infection, which frequently coincides with the experience of most healthcare professionals; however, there are no current data available on the distribution between HSV-1 and HSV-2 in EH [25]. Individuals with atopic dermatitis and EH experience significantly earlier onset of atopic dermatitis. Elevated levels of total IgE, asthma frequency, and sensitizations to air, food, and *Malassezia sympodialis* allergens signal more robust type 2 immune responses [26].

It is important to highlight that KVE can present a wide variability in lesion appearance and symptom severity, and its manifestation may depend on various factors, such as the patient's immune status and the presence of preexisting skin diseases. Accurate diagnosis, based on clinical evaluation and laboratory tests, is crucial for proper management and ruling out other skin conditions with similar presentations. Consultation with a dermatologist or infectious disease specialist may be necessary for complex cases.

Diagnosis and evaluation

The diagnosis and evaluation of Kaposi varicelliform eruption (KVE) require a combination of clinical assessment, laboratory tests, and, in some cases, consideration of the patient's medical history.

Clinical evaluation

Medical history: Obtain a detailed medical history, paying special attention to the presence of preexisting skin diseases, such as eczema, and any history of previous herpetic infections. Identify potential triggers, such as stress, that may have precipitated KVE.

Skin examination: Conduct a thorough examination of skin lesions. KVE is characterized by vesicles and ulcers similar to those of chickenpox or herpes zoster but with a more widespread distribution.

Observe the progression of lesions, from vesicles to pustules and ulcers, to aid in differential diagnosis.

Laboratory tests

PCR (Polymerase chain reaction): PCR to detect HSV DNA is a key tool to confirm the diagnosis of KVE. It allows specific identification of the presence of HSV-1 or HSV-2 [27]. PCR, however, cannot differentiate between active virions and viral proteins.

Samples from skin lesions, such as vesicle contents, are examined for the presence of the virus.

Viral culture: Viral culture may be performed to isolate and culture the virus, providing additional information about the identity of the causative agent.

Detecting herpes simplex virus in viral cultures can reveal the presence of active viral particles; however, this involves an additional period of 60 - 130 hours compared to PCR. The use of indirect immunofluorescence to identify herpes simplex virus antigens is routinely performed. Additionally, methods such as direct detection of herpes simplex virus through electron microscopy or the Tzanck test are available, although rarely employed. The latter constitutes a practical and rapid method that reveals multinucleated viral cells of large size, but its use is infrequent due to the extensive availability of PCR and the absence of specific detection of herpes simplex virus. The Tzanck test cannot distinguish between herpes simplex virus and varicella-zoster virus infections on the skin [28].

Blood analysis: Serology, including determination of HSV antibody levels, can help confirm the infection but is not as specific as PCR.

Differential diagnosis

Chickenpox and shingles: KVE may present similarities with chickenpox and shingles. The more widespread distribution and clinical context help differentiate them.

Impetigo and other skin infections: Other skin infections need to be ruled out, especially if there are signs of secondary bacterial infection.

Herpetic dermatitis and contact dermatitis: Distinguish KVE from other herpetic dermatitis or contact dermatitis through clinical evaluation and laboratory findings.

Eczema coxsackium: EC is most often caused by Coxsackie A6 virus. In 2013, Mathes and colleagues stated that blisters and erosions in areas of atopic dermatitis are distinctive clinical signs of EC. Additionally, rashes related to Coxsackie A6 virus exhibit several additional clinical features: a generalized eruption of vesicles and blisters, a rash similar to Gianotti Crosti with papules and vesicles on the face and limbs, a rash with petechial and purpuric spots, and late cutaneous manifestations such as scaling on the limbs [29].

Imaging (Occasional)

Computed tomography (CT) or magnetic resonance imaging (MRI): In severe cases or in the presence of systemic complications, imaging may be used to assess the extent of infection and involvement of internal organs.

Systemic evaluation

Monitoring of systemic symptoms: Evaluate any systemic symptoms, such as fever and general malaise, to determine the severity of the infection and the need for more intensive interventions.

The accurate diagnosis of Kaposi varicelliform eruption involves comprehensive evaluation combining clinical information, laboratory test results, and, in some cases, imaging. Differential diagnosis is crucial to ruling out other conditions with similar presentations and ensuring proper treatment and management. Consultation with a dermatologist or infectious disease specialist may be necessary for complex or recurrent cases.

Treatment and management

The treatment and management of Kaposi varicelliform eruption (KVE) involve addressing acute herpetic infection, managing associated complications, and, in some cases, managing preexisting skin diseases that may have contributed to the development of KVE.

Antivirals

Acyclovir, valacyclovir, or famciclovir

The primary treatment consists of antiviral medications such as acyclovir, valacyclovir, or famciclovir. These medications help control the replication of herpes simplex virus (HSV) and reduce the severity of lesions.

Antiviral treatment should be initiated as soon as KVE is suspected because in severe forms, it can be potentially fatal with mortality rates between 10 to 75% [30].

The first-line drug that should be considered for use is acyclovir (ACV, the first-line treatment since the 1980s), at a dose of 5 - 10 mg/kg intravenously, three times daily for 5 - 7 days [31]. ACV has very low bioavailability, so the molecule valacyclovir (VACV) was developed, with a recommended dose of 500 mg orally twice daily for 5 days. Famciclovir (FCV) acts similarly to ACV, and the dose is 5 mg/kg/dose or 500 mg, twice daily for 7 days [32].

These antiviral treatments should not be used topically except in cases of herpetic keratitis, in which case topical ocular creams should be used [33].

In addition to these classical treatments, new therapeutic approaches may be considered, especially in patients infected with a resistant strain. Among them, therapy with IFN-γ may be a good alternative in infection with resistant strains, particularly for patients with AD with

a low level of IFN-γ [34,35]. Indeed, IFN-γ allows for the control of HSV replication and spread and may be of considerable benefit in cases of EH. However, to date, clinical improvement of patients is not sufficient, given the high cost of this therapy.

Management of skin lesions

Skin care

Maintaining proper skin hygiene is crucial to prevent secondary infections. Gently washing the affected areas is recommended, and excessive scratching should be avoided, using antihistamines such as cetirizine, which may also sedate the patient.

It is necessary to apply moisturizing creams to prevent dry skin and avoid chemical irritants or allergens that may exacerbate skin lesions.

Treatment of complications

Management of secondary bacterial infections: If there are signs of secondary bacterial infections, topical or systemic antibiotics may be administered depending on severity [36].

Ophthalmological care: In cases where KVE affects the eyes, consultation with an ophthalmologist is crucial to prevent ocular complications.

Management of preexisting skin diseases

Treatment of eczema or other skin diseases

If KVE occurs in individuals with preexisting skin diseases such as eczema, treating these underlying conditions is essential to prevent recurrences.

Hospitalization in severe cases

Monitoring and support

In severe cases, especially in immunocompromised individuals, hospitalization may be necessary for close monitoring and intravenous administration of antiviral medications.

Additional support, such as intravenous fluids, may be provided in cases of dehydration [37].

Dermatological follow-up

Evaluation of scarring and pigmentation: After the resolution of lesions, dermatological follow-up is crucial to assess scarring and changes in pigmentation. Cosmetic options may be offered as needed.

Prevention of recurrences: Continuous management of underlying diseases

To prevent recurrences, it is important to continue managing preexisting skin diseases and follow healthcare professionals' recommendations.

Psychological support: Counseling and psychological support

Since KVE can have a psychological impact, counseling and emotional support may be recommended to help the patient cope with the situation.

Important considerations

Treatment adherence: Strict adherence to prescribed treatment, including the full course of antivirals, is essential for successful management.

Patient education: Providing detailed education to the patient about the importance of seeking early medical attention for any new symptoms or worsening of lesions [38].

The treatment and management of KVE should be tailored to the individual characteristics of the patient, including their overall health status and the presence of comorbidities. A multidisciplinary approach, involving dermatologists, immunologists, and other healthcare professionals, is key to comprehensive and effective management.

Case Report

A 19-month-old girl, weighing 15kg, presented to our pediatric outpatient department with a sudden onset of monomorphic vesicles on the face, right shoulder and arm, and back 2 days prior. The patient has a history of atopic dermatitis (AD) for 12 months, primarily affecting the head and face areas.

The patient had a fever (39 - 40°C) 3 days prior and was treated with intravenous amoxicillin-clavulanate and dexamethasone (5mg/d) due to suspected AD complication and bacterial infection. A rash appeared on the third day of treatment, considered an exacerbation of AD, worsening the eruption.

On physical examination, the girl had a temperature of 38.7°C and diffuse erythematous vesicles on the face, arm, and back (Figure 1-4). Crusting was present on the head and face regions. Some yellow crusts were observed on the face as a residual sign of AD.

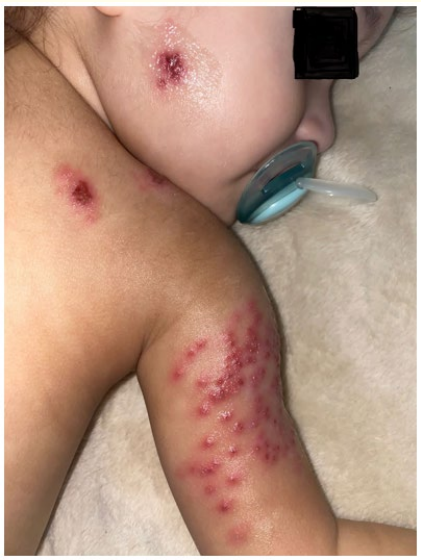

Figure 1

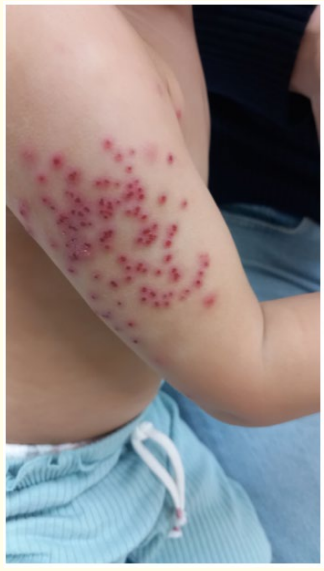

Figure 2

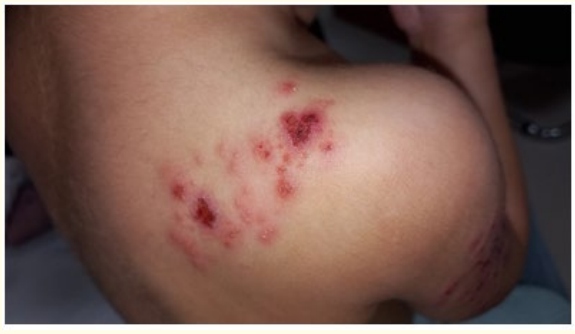

Figure 3

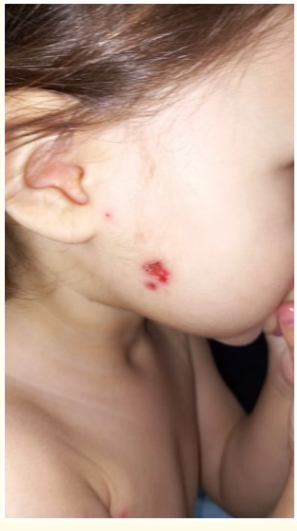

Figure 4

Vesicles in various stages appeared on the lateral aspect of the right arm. Her HSV IgG serum antibody was positive, while IgM was negative.

Based on clinical characteristics, the patient was initially diagnosed with Kaposi varicelliform eruption (KVE) and was prescribed oral acyclovir at a dose of 40 mg/kg/day divided into 3 doses every 8 hours. Topical acyclovir was also applied to the lesions. Vesicle and crust samples were taken for further confirmation as described earlier. Transmission electron microscopy (TEM) examination of the blister wall revealed numerous viral particles within the keratin fibers and the nuclei of keratinocytes. Vesicle fluid and crust were positive for specific HSV-1 DNA.

After 4 days of treatment (Figure 5), the patient's condition had significantly improved with all vesicles crusting over and her temperature returning to normal. The antiviral regimen was continued for another 5 days. Herpetic lesions had nearly disappeared by the seventh day of treatment initiation (Figure 6).

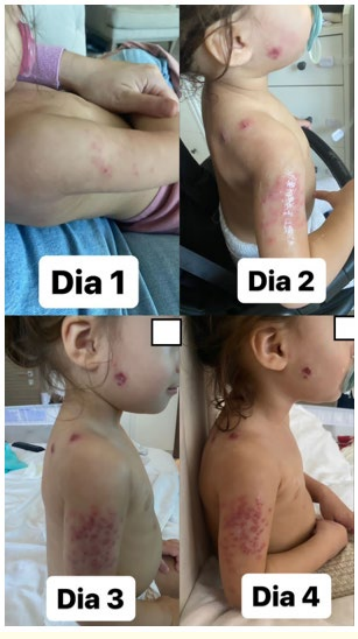

Figure 5

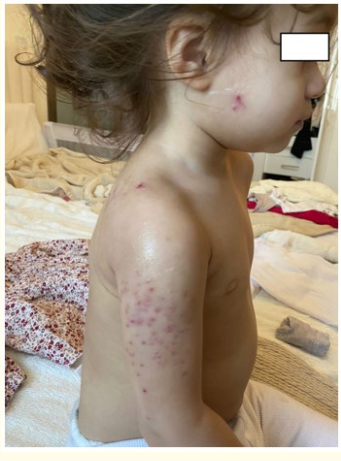

Figure 6

Complications and prognosis

Kaposi varicelliform eruption (KVE) can present various complications and its prognosis may vary depending on the severity of the condition, the presence of comorbidities and the response to treatment. Below, we explore some common complications and examine the prognosis associated with KVE.

Secondary bacterial infections: Open skin lesions and ulcers associated with KVE can increase the risk of secondary bacterial infections, complicating the clinical course of the condition.

Spread of herpetic infection: In severe cases or in immunocompromised individuals, herpetic infection can spread beyond the affected skin areas, affecting other organs and systems.

Ocular complications: In exceptional situations, KVE can affect the eyes, leading to herpetic conjunctivitis and other ocular complications that may have long-term implications for vision.

Systemic complications: In severe cases, especially in patients with weakened immune systems, herpetic infection can spread to internal organs, resulting in systemic complications.

Psychological impact: KVE, with its noticeable cutaneous lesions, can have a significant psychological impact on patients, affecting their quality of life and emotional well-being.

Prognosis of Kaposi varicelliform eruption

Mild to moderate: In mild to moderate cases, where KVE is diagnosed and treated promptly, the prognosis is usually good. Early use of antivirals can help limit the severity of lesions and prevent complications.

Severe or in immunocompromised patients: In severe situations or in individuals with compromised immune systems, the prognosis can be more challenging. Management of systemic complications and prevention of secondary infections become crucial.

Recurrence: Some patients may experience recurrences of KVE, especially if they have pre-existing skin conditions such as eczema. Comprehensive management addressing underlying conditions can help reduce the likelihood of recurrence.

Long-term skin impact: KVE can leave scars and altered pigmentation on the skin after resolution of acute lesions. Dermatological follow-up and aesthetic interventions may be necessary depending on the severity of these cutaneous alterations.

Need for continuous management: Patients with KVE may require long-term follow-up to assess and manage potential recurrences, as well as to address any residual psychological impact.

The prognosis of Kaposi varicelliform eruption largely depends on the promptness of diagnosis, the severity of the infection, the presence of comorbidities, and the effectiveness of treatment. Collaboration among dermatologists, immunologists, and other healthcare professionals is essential to provide a comprehensive and personalized approach in managing this dermatological condition.

Discussion

The presentation of herpetic eruption is characterized by the sudden appearance of disseminated, uniform, dome-shaped vesicles, typically accompanied by fever, general malaise, and lymph node enlargement. Herpetic eruptions often begin in areas previously affected by atopic disease, such as the head, hands, and upper body, and can spread to unaffected skin within a period of 7 to 10 days. After 2 weeks,

the blisters dry up, crust over, and eventually heal without leaving scars over a span of 2 to 6 weeks. Diagnosis of herpetic eruption is primarily based on clinical signs. Polymerase chain reaction (PCR) technique can rapidly identify herpes simplex virus (HSV) with high sensitivity and specificity, while transmission electron microscopy (TEM) can reveal the location and morphological characteristics of viral particles in infected cells. Detection of virus-specific DNA or viral particles through both methods, from blister fluid and viral culture, can confirm the disease. Immunofluorescence testing is also valuable for diagnosis.

Herpetic eczema or Kaposi's varicelliform eruption represents a dermatological emergency with potentially life-threatening complications, such as septicemia and ocular disorders, so physicians should be familiar with this condition. The primary type of the disease occurs predominantly in children, while the recurrent type is more common in older ages and has a milder course, with skin lesions generally more localized. Although atopic dermatitis is the most known risk factor, it can also coexist with several additional skin disorders. The underlying pathophysiology is not fully understood; however, defects in the skin barrier and immune dysfunction appear to contribute to the development of the disease. Moreover, the onset of herpetic eczema after HSV activation may be related to underlying proliferation of regulatory T cells and proinflammatory monocytes, along with enhancement of their effector functions.

Clinically, it is easy to misdiagnose herpetic eruption as an exacerbation of the patient's underlying chronic eczematous skin conditions, with serious consequences. High-dose systemic corticosteroid administration led to the progression of his HSV-1 ocular infection to bilateral keratitis, which can cause scarring and blindness. Additionally, overlooking the diagnosis of herpetic eruption, common in pediatric patients with atopic disease, can lead to disseminated cutaneous and systemic infections by herpes simplex, which may be associated with bone marrow suppression and disseminated intravascular coagulation, causing even death, as was the case with a baby. In our case, failure to recognize early herpetic eruption in the context of atopic disease led to systemic steroid therapy for a week, resulting in the spread of herpes simplex. Therefore, it is crucial to be alert to the possibility of herpetic eruption and recognize the connection between chronic dermatitis and possible herpetic infection.

Regarding treatment, the introduction of effective antiviral agents is fundamental. Currently, acyclovir is the most potent drug for pediatric patients with herpetic eruption. Although there are no clear guidelines describing specific treatment for these patients, a retrospective study that included 79 patients aged 0 to 18 years with herpetic eruption found that oral acyclovir, intravenous and oral acyclovir, or intravenous acyclovir alone were effective in treating the disease of various severities. In children, intravenous acyclovir is generally administered in severe cases and oral acyclovir in mild cases [39]. However, the clinical utility of acyclovir is limited by its low oral bioavailability and the need for frequent dosing.

Valacyclovir, a prodrug of acyclovir, has superior oral bioavailability and can be administered less frequently than oral acyclovir, achieving plasma concentrations of acyclovir similar to those observed with intravenous acyclovir in adults. In children, the recommended dose of oral valacyclovir has been shown to be effective and well tolerated. Although there are few reports on the efficacy of valacyclovir in the treatment of herpetic eruption, its use has been recommended in adults. Additionally, glycyrrhizin, a licorice extract, has pharmacological effects such as anti-inflammatory activity and antiviral effect against viruses of the Herpesviridae family. Its application during the acute phase of herpetic eruption may reduce inflammation and strengthen antiviral therapy.

Conclusion

In summary, herpetic eruption is a rare condition, and it is important to increase awareness of its signs when diagnosing children with chronic skin diseases. The sudden onset of vesiculopapular eruptions with fever in a pediatric patient with atopic disease should raise a high suspicion of herpetic eruption. Oral valacyclovir may be a convenient and effective treatment option for ambulatory pediatric patients with herpetic eruption.

Bibliography

1. Kaposi M. "Pathologie und Therapie der Hautkrankheiten für prak tische Ärzte und Studirende". 3rd edition. Wien: Urban & Schwarzenberg (1887).

2. Juliusberg F. "Über Pustulosis acuta varioliformis". *Arch. f. Derm. u. Syph.* 46 (1898): 21-28.

3. Wollenberg A. "Eczema herpeticum". *Chemical Immunology and Allergy* 96 (2012): 89-95.

4. Buxbaum S., *et al*. "Epidemiology of herpes simplex virus types 1 and 2 in Germany: what has changed?" *Medical Microbiology and Immunology* 192.3 (2003): 177-181.

5. Beck LA., *et al*. "Phenotype of atopic dermatitis subjects with a history of eczema herpeticum". *Journal of Allergy and Clinical Immunology* 124.2 (2009): 260-9, 269.e1-7.

6. Wollenberg A., *et al*. "Predisposing factors and clinical features of eczema herpeticum: a retrospective analysis of 100 cases". *Journal of the American Academy of Dermatology* 49.2 (2003): 198-205.

7. Traidl S., *et al*. "Eczema herpeticum in atopic dermatitis". *Allergy* 76.10 (2021): 3017-3027.

8. Bussmann C., *et al*. "Molecular pathogenesis and clinical implications of eczema herpeticum". *Expert Reviews in Molecular Medicine* 10 (2008): e21.

9. Baringer JR and Swoveland P. "Recovery of herpes-simplex virus from human trigeminal ganglions". *New England Journal of Medicine* 288.13 (1973): 648-650.

10. Bustos DE and Atherton SS. "Detection of herpes simplex virus type 1 in human ciliary ganglia". *Investigative Ophthalmology and Visual Science* 43.7 (2002): 2244-2249.

11. Warren KG., *et al*. "Isolation of latent herpes simplex virus from the superior cervical and vagus ganglions of human beings". *New England Journal of Medicine* 298.19 (1978): 1068-1069.

12. Rahn E., *et al*. "Entry pathways of herpes simplex virus type 1 into human keratinocytes are dynamin- and cholesterol-dependent". *PLoS One* 6.10 (2011): e25464.

13. Suazo PA., *et al*. "Evasion of early antiviral responses by herpes simplex viruses". *Mediators of Inflammation* (2015): 593757.

14. Spear PG and Longnecker R. "Herpesvirus entry: an update". *Journal of Virology* 77.19 (2003): 10179-10185.

15. Thier K., *et al*. "Entry of herpes simplex virus 1 into epidermis and dermal fibroblasts is independent of the scavenger receptor MARCO". *Journal of Virology* 92.15 (2018): e00490-18.

16. Petermann P., *et al*. "Role of nectin-1 and herpesvirus entry mediator as cellular receptors for herpes simplex virus 1 on primary murine dermal fibroblasts". *Journal of Virology* 89.18 (2015): 9407-9416.

17. Nicoll MP., *et al*. "The molecular basis of herpes simplex virus latency". *FEMS Microbiology Reviews* 36.3 (2012): 684-705.

18. Su C., *et al*. "Evasion of host antiviral innate immunity by HSV-1, an update". *Virology Journal* 13 (2016): 38.

19. Damour A., *et al*. "Eczema herpeticum: clinical and pathophysiological aspects". *Clinical Reviews in Allergy and Immunology* 59.1 (2020): 1-18.

20. Higgins CR., *et al*. "Natural history, management and complications of herpes labialis". *Journal of Medical Virology* 1 (1993): 22-26.

21. Swart RN., *et al*. "Treatment of eczema herpeticum with acyclovir". *Archives of Dermatology* 119.1 (1983): 13-16.

22. Yeh TC., *et al*. "Kaposi's varicelliform eruption in herpes simplex encephalitis". *Internal and Emergency Medicine* 11.6 (2016): 885-887.

23. Seegräber M., *et al*. "Recurrent eczema herpeticum - a retrospective European multicenter study evaluating the clinical characteristics of eczema herpeticum cases in atopic dermatitis patients". *Journal of the European Academy of Dermatology and Venereology* 34.5 (2020): 1074-1079.

24. Wheeler CE Jr and Abele DC. "Eczema herpeticum, primary and recurrent". *Archives of Dermatology* 93.2 (1966): 162-173.

25. Wollenberg A., *et al*. "Predisposing factors and clinical features of eczema herpeticum: a retrospective analysis of 100 cases". *Journal of the American Academy of Dermatology* 49.2 (2003): 198-205.

26. Wutzler P., *et al*. "Klinische und virologische Untersuchungen zum Ekzema herpeticatum [Clinical and virological studies of eczema herpeticum]". *Dermatologische Monatschrift* 171.4 (1985): 222-229.

27. LeGoff J., *et al*. "Diagnosis of genital herpes simplex virus infection in the clinical laboratory". *Virology Journal* 11 (2014): 83.

28. Traidl S., *et al*. "Eczema herpeticum in atopic dermatitis". *Allergy* 76.10 (2021): 3017-3027.

29. Mathes EF., *et al*. ""Eczema coxsackium" and unusual cutaneous findings in an enterovirus outbreak". *Pediatrics* 132.1 (2013): e149-e157.

30. Wheeler CE Jr and Abele DC. "Eczema herpeticum, primary and recurrent". *Archives of Dermatology* 93.2 (1966): 162-173.

31. Khan A., *et al*. "Fifteen-minute consultation: eczema herpeticum in a child". *Archives of Disease in Childhood: Education and Practice Edition* 100.2 (2015): 64-68.

32. Piret J and Boivin G. "Resistance of herpes simplex viruses to nucleoside analogues: mechanisms, prevalence, and management". *Antimicrobial Agents and Chemotherapy* 55.2 (2011): 459-472.

33. Wollenberg A. "Eczema herpeticum". *Chemical Immunology and Allergy* 96 (2012): 89-95.

34. Frisch S and Siegfried EC. "The clinical spectrum and therapeutic challenge of eczema herpeticum". *Pediatric Dermatology* 28.1 (2011): 46-52.

35. Darji K., *et al*. "Characterization of children with recurrent eczema herpeticum and response to treatment with interferon-gamma". *Pediatric Dermatology* 34.6 (2017): 686-689.

36. Morata Alba J and Morata Alba L. "Erupción variceliforme de Kaposi. A propósito de un caso". *Revista de Pediatría de Atención Primaria [online]* 19.74 (2017): 157-161.

37. Wang V., *et al*. "The infectious complications of atopic dermatitis". *Annals of Allergy, Asthma and Immunology* 126.1 (2021): 3-12.

38. Napolitano M., *et al*. "Children atopic dermatitis: Diagnosis, mimics, overlaps, and therapeutic implication". *Dermatologic Therapy* 35.12 (2022): e15901.

39. Luca NJ., *et al*. "Eczema herpeticum in children: clinical features and factors predictive of hospitalization". *Journal of Pediatrics* 161.4 (2012): 671-675.

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