*Salud Integral y Comunitaria*. 2026; 4:276
doi: 10.62486/sic2026276

CASE REPORT

# Atypical rash, a diagnostic challenge in clinical practice: A Case Report from Bolivia

## Exantema atípico, un desafío diagnóstico en la práctica clínica: Reporte de Caso en Bolivia

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**Cite as:** Paz-Román CA, Auza-Santivañez JC, Fuentes Luzcuber PN, Rivero Castedo L, Kubatz La Madrid ME, Robles-Nina SM, et al. Atypical rash, a diagnostic challenge in clinical practice: A Case Report from Bolivia. Salud Integral y Comunitaria.2026; 4:276. https://doi.org/10.62486/sic2026276

**Submitted:** 23-07-2025 **Revised:** 13-09-2025 **Accepted:** 17-11-2025 **Published:** 01-01-2025

**Editor:** Dr. Telmo Raúl Aveiro-Róbalo

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## ABSTRACT

Hand-foot-and-mouth disease, commonly caused by Coxsackievirus A16, can manifest in atypical and severe forms associated with the CVA6 serotype, termed “eczema coxsackium,” which may mimic serious pathologies. This report describes the case of a 10-year-old boy with a diffuse maculopapular rash, targetoid and bullous lesions, and systemic compromise, initially diagnosed as erythema multiforme major. The discussion focuses on the differential diagnostic challenge with eczema herpeticum, highlighting that despite the alarming clinical presentation, etiological confirmation via PCR for CVA6 was crucial to rule out other infections, discontinue unnecessary acyclovir, and focus treatment on supportive care, leading to a favorable outcome. In conclusion, eczema coxsackium due to CVA6 should be considered in severe vesiculobullous rashes, with PCR being essential for an accurate diagnosis and proper management, as its prognosis is generally benign.

**Keywords:** Eczema Coxsackium; Coxsackievirus A6; Erythema Multiforme; Differential Diagnosis; PCR.

## RESUMEN

Un “exantema atípico” es una erupción cutánea aguda que difiere en apariencia de las erupciones virales clásicas, como el sarampión, Coxsackievirus, la rubéola o el eritema infeccioso. La enfermedad de mano-pie-boca es una infección viral común en la infancia, que generalmente es causada por las cepas del Coxsackievirus A16 (CVA16) y enterovirus 71 (EV71), manifestándose como erupciones vesiculares en manos, pies y boca. Las formas atípicas son presentadas por lesiones cutáneas mucosas más extensas, variadas y a menudo más graves que la HFMD clásica. El eccema coxsackium se caracteriza por erupciones papulovesiculosas, eccematosas e incluso costrosas, especialmente por las extremidades, nalgas y la región perioral. Estas características pueden simular a otras enfermedades dermatológicas severas, tales como el eccema herpeticum, la varicela, el herpes zóster diseminado o el eritema multiforme mayor, lo que convierte a estos casos en un desafío diagnóstico. En nuestro caso clínico describimos una presentación clínica atípica del CVA6, el diagnóstico, manejo y tratamiento de las complicaciones, destacando a su vez el diagnóstico diferencial.

**Palabras clave:** Eccema Coxsackium; Coxsackievirus A6; Eritema Multiforme; Diagnóstico Diferencial; PCR.

## INTRODUCTION

An "atypical rash" is an acute skin eruption that differs in appearance from classic viral eruptions, such as those caused by measles, Coxsackievirus, rubella, or infectious erythema. They are usually preceded or associated with nonspecific systemic symptoms, such as fever, malaise, or upper respiratory tract or gastrointestinal tract infection. Hand, foot, and mouth disease (HFMD) is a common childhood viral infection, typically caused by strains of Coxsackievirus A16 (CVA16) and enterovirus 71 (EV71), characterized by vesicular rashes on the hands, feet, and mouth.[1] In recent years, concerns have arisen about atypical manifestations of HFMD, particularly those caused by CVA6.[2,3,4] These atypical forms are characterized by more extensive, varied, and often more severe mucocutaneous lesions than classic HFMD, leading to the name "coxsackium eczema" in cases where the lesions are located in areas of pre-existing dermatitis.[3,5,6] Coxsackium eczema is characterized by papulovesicular, eczematous, and even crusted eruptions, especially on the extremities, buttocks, and perioral region, and is frequently associated with patients who have a history of atopic dermatitis (AD).[4,7,8] These characteristics can mimic other severe dermatological diseases, such as eczema herpeticum, chickenpox, disseminated herpes zoster, or erythema multiforme major, making these cases a significant diagnostic challenge.[3,4,9]

Our clinical case aims to describe the atypical clinical presentation of CVA6, the diagnostic process, and the management of a particular case of coxsackium eczema with features of erythema multiforme major in a 10-year-old boy, highlighting the importance of differential diagnosis and etiological confirmation by PCR.

## CLINICAL CASE

A 10-year-old male patient was admitted to the hospital with a clinical picture that had been developing for a week. Initially, the patient presented with symptoms of the common cold, followed by a fever of 38°C and the appearance of maculopapular lesions on the chest, as well as on the upper and lower limbs. On the third day, a progressive spread of the rash and persistent fever was observed. Upon arrival at our hospital, the patient was experiencing general discomfort, accompanied by a sore throat and a very high fever. Physical examination revealed the presence of a diffuse maculopapular rash, target-like lesions with a central blistering area, as well as vesicular-bullous lesions scattered across the face, trunk (figure 1), and upper and lower extremities (figure 2), slightly dry mucous membranes, tachycardia, blood pressure within normal limits, and the rest of the physical examination within normal parameters.

Laboratory tests on admission revealed elevated neutrophils (7,650/mm$^3$) and a C-reactive protein (CRP) level of 24 mg/dL, with normal liver and kidney function parameters. The chest X-ray showed no pulmonary infiltrates, and the skin lesion culture was negative for bacteria. Forty-eight hours after admission, the CRP level increased further to 48 mg/dL, confirming a significant increase in acute-phase reactants.

Given the severity of the condition and the morphology of the lesions, a presumptive diagnosis of major polymorphic erythema secondary to herpes or coxsackievirus infection was considered. Empirical treatment was therefore initiated, along with supportive measures, including the administration of albumin at a pediatric dose, intravenous rehydration, and broad-spectrum intravenous antibiotics (intravenous cefotaxime), due to suspicion of bacterial superinfection. Intravenous acyclovir was also started due to the possibility of eczema herpeticum, given the patient's systemic condition and the characteristics of the lesions.

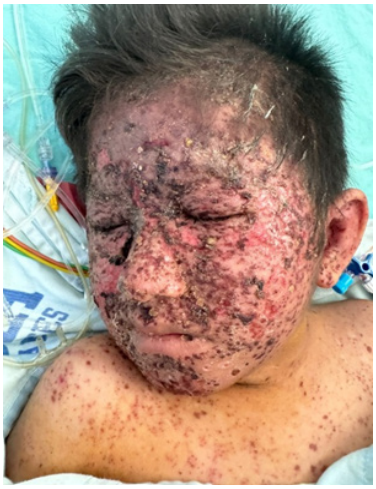

**Figure 1.** Facial lesions, vesicular-bullous lesions, and meliceric-appearing crusts are observed

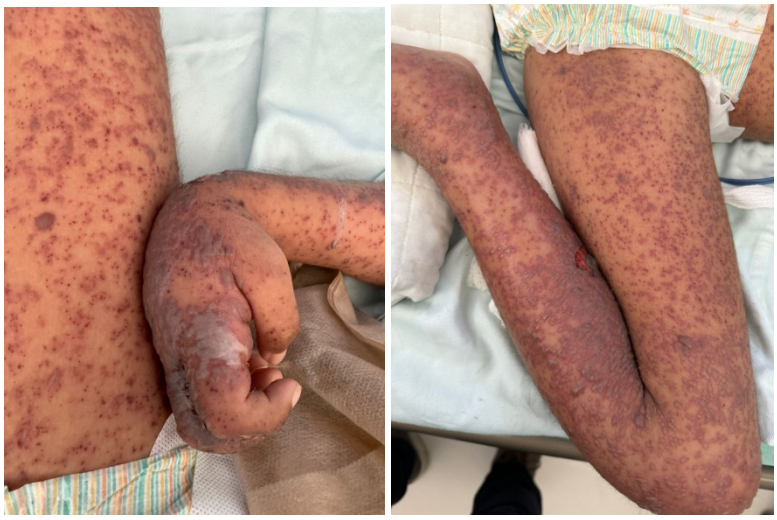

**Figure 2.** Vesicular-bullous lesions on the back of the hands and feet, calves, forearms, and trunk

Polymerase chain reaction (PCR) tests were requested on swabs of the skin lesions to detect Coxsackievirus and Herpes Simplex Virus. The PCR results, received within 72 hours, were positive for Coxsackievirus A6 and negative for Herpes Simplex Virus. This finding reoriented the diagnosis toward atypical coxsackium eczema with features of major polymorphic erythema and secondary bacterial superinfection.

After etiological confirmation, acyclovir was discontinued. Supportive care, rehydration, and antibiotics for the superinfection were maintained. Additionally, medium-potency topical corticosteroid therapy and local zinc sulfate treatments were introduced. The outcome was favorable, with progressive resolution of the lesions over the following 2-3 weeks, followed by palmoplantar desquamation (figure 3). The patient was discharged in good general condition with no scarring.

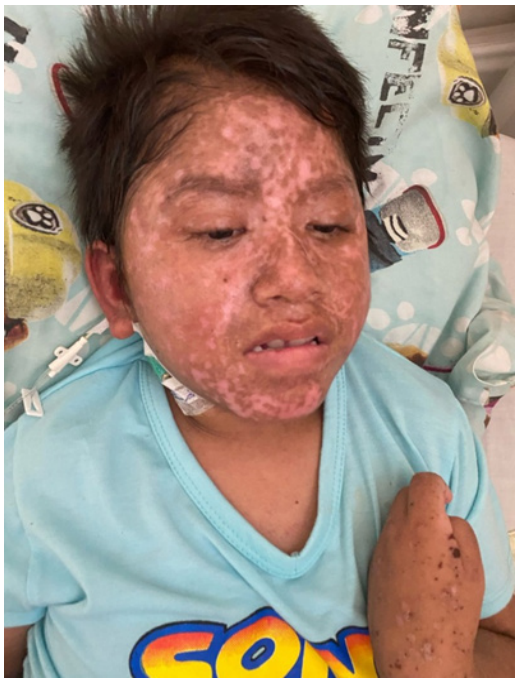

**Figure 3.** Lesions undergoing desquamation

## DISCUSSION

This clinical case illustrates the diagnostic difficulty that coxsackium eczema can present, especially in cases with atypical manifestations that mimic other severe dermatological pathologies.[2] The patient's initial presentation, with target-like lesions, disseminated vesicles and bullae, and systemic involvement, made erythema multiforme major (EMM) and eczema herpeticum (EH) the primary differential diagnoses.[9,10]

EMM is a hypersensitivity reaction, often triggered by infections (frequently caused by the herpes simplex virus or Mycoplasma pneumoniae) or medications, characterized by classic target lesions.[1,9] Eczema herpeticum, on the other hand, is an infection caused by the herpes simplex virus (HSV) that affects skin with preexisting conditions (such as atopic dermatitis), presenting as vesicles and "punched-out" erosions with the potential

for serious dissemination and systemic involvement.[1,2,4] The similarity is such that coxsackium eczema can be clinically indistinguishable from eczema herpeticum in its initial presentation.[10] The differential diagnosis of atypical HFMD includes herpetic eczema, varicella-zoster virus infection, MPOX (monkeypox) infection, and bullous impetigo. Coxsackievirus A6 (CVA6) has emerged as a key serotype in HFMD outbreaks with atypical presentations, which are characterized by being more extensive, severe, and varied, differing from the classic forms.[1,2] These atypical manifestations include generalized vesicular-bullous and erosive eruptions, which are similar to Gianotti-Crosti syndrome; petechial/purpuric exanthems; and, notably, coxsackium eczema, where lesions are accentuated in areas of previously inflamed or damaged skin.[1,2,5] Although in our case, the patient had no history of atopic dermatitis, the predilection of CVA6 for areas of previous trauma or inflammation explains the severity of the rash in a host without underlying chronic dermatosis. The patient's age, 10 years, is also relevant, since although HFMD is more common in children under 5 years of age, CVA6 outbreaks have also affected older children and even adults.[9,11]

Histopathology in cases of coxsackium eczema may show spongiotic dermatitis, focal interface dermatitis with subepidermal clefts, and edema in the papillary dermis.[1] In more severe cases, extensive epidermal necrosis with dyskeratosis and blister formation has been reported, which can mimic severe adverse skin reactions such as EMM or Stevens-Johnson syndrome (SJS).[9] In fact, in the index case, the initial histopathological findings were consistent with erythema multiforme, before the epidemiological context and PCR reoriented the diagnosis.[11]

Establishing an accurate diagnosis in these types of atypical presentations relies on clinical suspicion and the use of appropriate laboratory tests. Polymerase chain reaction (PCR) is the most effective method for detecting enteroviruses, including CVA6, from vesicular fluid, oropharyngeal swabs, perirectal swabs, or stool samples.[7,11] These tests are necessary because clinical differentiation from other bullous diseases can be challenging.[2,3] In our case, a positive PCR for CVA6 and a negative PCR for HSV was decisive in confirming coxsackium eczema and de-escalating unnecessary antiviral treatment.[4] The treatment of coxsackium eczema is based primarily on supportive care, as this disease is usually self-limiting and rarely causes serious systemic complications, with hydration being a fundamental pillar in these cases.[1,10] The administration of antibiotics is only indicated in cases of bacterial superinfection, as in the clinical suspicion of the patient in our case. Unlike herpetic eczema, which can be associated with serious complications and mortality, coxsackium eczema generally has a good prognosis.[1,4] In children with darker skin, extensive post-inflammatory pigmentation often occurs, which can last for months or years but eventually resolves.

## CONCLUSIONS

This case highlights an atypical rash associated with hand, foot, and mouth disease caused by Coxsackievirus A6. Despite its rarity, this condition highlights the importance of thorough epidemiological surveillance and underscores the need to recognize uncommon presentations of viral infections in children. Early molecular testing, such as PCR, enables accurate etiological identification, facilitating effective treatment and a more precise prognosis. By fostering collaboration among healthcare professionals, implementing preventive measures, and raising community awareness, we can collectively mitigate the burden of eczema.

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## CONSENT

The patient's consent was obtained for this study.

## FUNDING

The authors did not receive funding for the implementation of this study.

## CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

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