



## Coxsackie virus vs Dengue, clinical case: Differential diagnosis in syndemic

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**ABSTRACT:** In tropical regions, the simultaneous presence of multiple infectious agents complicates diagnosis and treatment. This clinical case describes a 4-year-old boy presenting with fever, malaise, and pruritic rashes on the palms and soles, initially suspected as dengue. Laboratory results showed normal platelet and hematocrit levels, excluding dengue fever. The dermatological pattern and self-limiting course were consistent with hand-foot-and-mouth disease caused by Coxsackievirus A. Differential diagnosis between Coxsackievirus and dengue is crucial in endemic settings due to overlapping symptoms such as fever and rash. Recognition of specific dermatological manifestations—particularly vesicular or pruritic lesions on acral regions—and the absence of thrombocytopenia are key diagnostic clues. The case emphasizes the importance of clinical vigilance and basic laboratory testing to distinguish between similar viral syndromes, thereby avoiding unnecessary interventions and ensuring appropriate management in pediatric populations from dengue-endemic areas.

**KEYWORDS:** Coxsackievirus, Dengue fever, Differential diagnosis, Hand-foot-and-mouth disease

### INTRODUCTION

In tropical and subtropical regions, where arbovirus transmission is constant, the coexistence of multiple infectious agents is not only possible but frequent. This phenomenon has given rise to the concept of syndemic, understood as the simultaneous interaction of two or more diseases that, by coinciding in the same territory and population, generate greater clinical, diagnostic, and epidemiological complexity. In this context, the co-occurrence of enterovirus infections, particularly Coxsackievirus, and dengue virus represents a significant challenge for health services in Latin America and Southeast Asia <sup>(1)</sup>.

Both viruses share initial clinical characteristics: acute fever, malaise, headache, irritability, and variable rashes. These manifestations, which are usually nonspecific in the first few days, lead to Coxsackievirus infections, such as hand, foot, and mouth disease or certain forms of febrile viral rash, being confused with classic dengue, especially in young children <sup>(2)</sup>.

The risk of confusion increases when Coxsackievirus skin lesions present atypically, with itching or erythematous plaques that, in early stages, can mimic a generalized viral rash.

From a pathophysiological standpoint, both infections have different transmission routes, fecal-oral in Coxsackievirus and vector-borne in dengue but they both generate systemic inflammatory responses, affect the skin and mucous membranes, and cause significant malaise. <sup>(3)</sup> However, the fundamental differences lie in the appearance of warning signs typical of dengue, such as progressive thrombocytopenia, hemoconcentration, severe abdominal pain, and spontaneous bleeding, which are not part of the usual behavior of the Coxsackie virus. <sup>(4)</sup>

In dengue-endemic areas, differential diagnosis is critical. Thorough clinical evaluation, timely interpretation of complete blood counts, and recognition of characteristic dermatological patterns, such as vesicular and pruritic lesions on the palms and soles in cases of Coxsackievirus, allow for accurate diagnosis. <sup>(5)</sup> Proper differentiation not only avoids unnecessary treatments, but also allows for the early identification of dengue cases that could evolve into severe forms.

### Coxsackievirus

The Coxsackievirus, belonging to the Enterovirus genus within the Picornaviridae family, is one of the most common infectious agents in childhood and, at the same time, one of the least understood by the general population. Although its name may sound distant or intimidating, it is actually part of the broad group of viruses that commonly circulate in our community and, in most cases, cause mild and self-limiting illnesses. In recent years, molecular surveillance analyses have demonstrated significant changes in the predominant serotypes, especially those associated with hand, foot, and mouth disease. <sup>(6)</sup>



From a scientific perspective, Coxsackieviruses A and B possess a simple, single-stranded RNA genome that is efficient at invading the gastrointestinal epithelium and replicating rapidly. This basic viral design contrasts sharply with the wide variety of clinical manifestations it can produce. Recent reviews highlight the need for a clinical and preventative approach due to its high transmissibility in pediatric settings. <sup>(7)</sup>

Global molecular surveillance shows that serotypes circulate widely and are associated with diseases such as herpangina, aseptic meningitis, and myocarditis. <sup>(8)</sup>

## Pathophysiological Background

Coxsackieviruses are small, non-enveloped viruses that enter the body orally and initially replicate in the gastrointestinal tract. They then disseminate to other organs, including the skin, central nervous system, and heart <sup>(9)</sup>.

In group B coxsackieviruses, their role in myocarditis has been extensively documented. These viruses invade cardiomyocytes, induce direct cell lysis, and activate innate and adaptive immunity. If the immune response fails to eliminate them, chronic inflammation and progression to dilated cardiomyopathy can develop <sup>(10,11)</sup>.

Recent studies have also identified truncated forms of viral RNA that are associated with greater severity and persistence of myocarditis <sup>(12)</sup>.

## Classification

### Coxsackievirus group A (CVA)

Primarily associated with HFMD, herpangina, and rashes. Serotypes A6 and A16 predominate in recent outbreaks <sup>(13,14)</sup>.

### Coxsackievirus group B (CVB)

Includes serotypes B1–B6, associated with myocarditis, pleurodynia, pancreatitis, and systemic neonatal disease <sup>(9,15)</sup>.

## Clinical Presentation of Coxsackievirus

The clinical spectrum varies according to serotype, age, and immune status:

### Mild Cases

- Low-grade or moderate fever
- General malaise
- Sore throat
- Herpangina
- Hand, foot, and mouth disease (HFMD), especially due to CV-A6 <sup>(2)</sup>

### Cardiac Involvement

- Myocarditis and myopericarditis due to CVB <sup>(10,15)</sup>
- Fulminant cases in neonates, some treated with ECMO <sup>(16)</sup>

## Diagnosis

- RT-PCR is the test of choice for enterovirus detection <sup>(17)</sup>
- VP1 genomic typing, useful for molecular surveillance <sup>(6,18)</sup>
- Serology, with limited utility, but employed in specific contexts <sup>(15)</sup>

**The patient's medical history is presented below.**

## Clinical History

### Present Illness

A previously healthy 4-year-old male patient presented **48 hours** prior with an **unquantified fever**, accompanied by malaise, irritability, and decreased appetite. His parents reported that he remained drowsy and showed less interest in his usual activities.

Within 24 hours of the onset of symptoms, **pruritic lesions began to appear on the palms of his hands and soles of his feet**. These were initially described as small, reddish papules, which progressed to erythematous and pruritic plaques. Extensive bullous lesions and oral mucosal involvement were not reported at the beginning, as shown in **Figures 1 and 2**.



Figure 1



Figure 2

Due to the history of fever and the presence of a rash, a **differential diagnosis of classic dengue** fever was considered. A **complete blood count** was ordered, which was within normal limits for his age (platelets 265,000; white blood cells 7,800; hematocrit 37%).

The condition persists with moderate itching and occasional low-grade fever, without signs of bleeding, vomiting, diarrhea, and respiratory symptoms.

#### **Non-Pathological Personal History**

- Complete vaccination schedule for age.
- Adequate housing, no exposure to stagnant water.
- Attends daycare.
- No recent travel.
- No known contact with sick individuals.

#### **Pathological Personal History**

- Denies previous hospitalizations.
- Denies chronic illnesses.
- No known allergies.
- No surgeries.



## Review of Systems

- **Neurological:** Mild irritability with pruritus; alert and responsive.
- **Respiratory:** No cough, no respiratory distress.
- **Cardiovascular:** No palpitations, no chest pain.
- **Gastrointestinal:** Decreased appetite, no vomiting or diarrhea.
- **Genitourinary:** Normal urine output.
- **Dermatological:** Pruritic lesions on hands and feet.

## Physical Examination

### Vital Signs

Within normal limits

### General

Patient alert, slightly irritable on examination, hydrated.

### Head and Craniofacial Region

- Normocephalic, without abnormalities.
- Oral mucosa without aphthous ulcers or vesicles.
- Pharynx slightly hyperemic without exudate.
- Ears without abnormalities.

### Cardiopulmonary

- Clear lung fields, without crackles or wheezes.
- Breath sounds present.
- Regular heart sounds, without murmurs.

### Abdomen

- Flat, soft, and non-tender.
- No pain on palpation.
- Bowel sounds present.

### Skin and appendages

- **Hands:** No vesicular lesions, maculopapules, or desquamation were observed during the examination. The skin was intact, with no signs of inflammation or visible alterations at the time of examination.
- **Feet:** Two erythematous lesions were observed on the lateral aspect of the left leg. One presented a tense vesicle with yellowish serous fluid, while the other showed a reddish area with peripheral desquamation. Both lesions showed mild inflammation, without purulent discharge or signs of superinfection. The pattern corresponded to vesiculoinflammatory lesions, compatible with a viral process such as hand, foot, and mouth disease or with post-inflammatory dermatitis in the resolution phase (Figures 1 and 2).
- No petechiae, no ecchymosis.
- No hemorrhagic lesions.

### Extremities

- Good capillary refill.
- Pulses present and symmetrical.
- No edema.

## LABORATORY RESULTS

### Complete Blood Count

- White Blood Cells: 7,800/ $\mu$ L
- Hemoglobin: 12.4 g/dL
- Hematocrit: 37%



- Platelets: 265,000/ $\mu$ L
- Neutrophils: 54%
- Lymphocytes: 40%

**Interpretation:** Normal values; **no evidence of thrombocytopenia or hemoconcentration**, ruling out classic dengue.

## Differential Diagnosis Considered

1. Classic Dengue

### Ruled out by:

- Absence of severe headache, severe myalgia, or retro-orbital pain.
- Normal complete blood count without thrombocytopenia.
- Pruritic lesions on palms and soles not typical of dengue.

## Diagnostic impression

Hand-foot-and-mouth disease secondary to probable Coxsackievirus type A infection.

Self-limiting febrile illness.

Normal complete blood count, with no findings suggestive of dengue.

## Evolution

Forty-eight hours after the start of symptomatic management, the patient experienced a decrease in pruritus and resolution of the fever. The lesions followed their typical course, with progressive resolution without complications. No signs of dehydration, respiratory compromise, or neurological symptoms were observed. The child gradually resumed his usual activities and remained in stable condition.

## CLINICAL CASE CONCLUSION

This case involved a previously healthy pediatric patient who presented with an acute febrile illness accompanied by malaise and the progressive appearance of pruritic skin lesions on the palms of the hands and soles of the feet, as well as vesicular-inflammatory lesions on the lower extremities. Complete blood counts remained within normal limits, which helped rule out classic dengue fever as the cause of the rash and fever.

The clinical pattern, the distribution of the lesions, the self-limiting course, and the absence of alarm symptoms were consistent with hand, foot, and mouth disease, likely secondary to Coxsackievirus type A infection. Management focused on supportive measures, including fever control, hydration, and pruritus relief, with an adequate clinical response.

Overall, this case highlighted the importance of differential diagnosis among viral infections with similar cutaneous manifestations and reinforced the value of targeted physical examination and basic diagnostic tests to guide clinical decision-making.

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