CLINICAL IMAGE

# Newborn Rash: Distinguishing Benign vs Pathological Skin Lesions

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**KEYWORDS**

**Erythema toxicum neonatorum • Neonatal skin lesions • Herpes simplex virus • Transient neonatal pustular melanosis • Neonatal cephalic pustulosis**

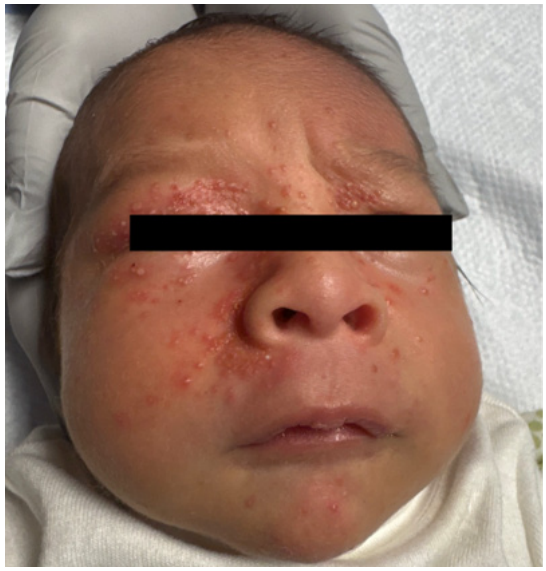
## CASE PRESENTATION

A 17-day-old male infant, born at 39 weeks and 3 days' gestation via spontaneous vaginal delivery, was admitted to the pediatric inpatient service for worsening skin rash over the past 5 days. The patient's mother states that the rash started as scattered erythematous papules over the cheeks and nasal bridge. This was consistent with the patient's newborn exam at day 2 of life. He was later seen by his pediatrician for his routine 2-week well-child check, where diffuse erythematous papules were noted over the face (Figure 1A). The rash gradually worsened over the next 2 days, and the patient was subsequently admitted for further evaluation.

On admission, the infant was afebrile, active, and feeding well with no clinical signs of systemic illness. On physical examination, diffuse maculopapular and pustular lesions with erythematous bases were noted over the face (Figure 1B).

FIGURE 1A

FIGURE 1B



## QUESTION

**1. What is the most likely diagnosis?**

A. Erythema toxicum neonatorum

B. Neonatal herpes simplex virus

C. Impetigo

D. Transient neonatal pustular melanosis

E. Neonatal cephalic pustulosis (neonatal acne)

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**Correct Answer: A. Erythema toxicum neonatorum**

Erythema toxicum neonatorum (ETN) is a benign newborn rash consisting of macules and papules that can develop into yellow pustules with an erythematous base.[1,2] ETN is a nonpruritic rash that typically presents within the first 72 hours of life, with complete spontaneous resolution within 2 weeks, and most commonly affects term male infants.[2,3] ETN can present differently across different skin tones, and erythematous bases may be more subtle on darker skin tones.[3] The rash is typically located on the face and proximal extremities, sparing the palms and soles.[1] The etiology of ETN is still highly debated and unknown.[3-5] Cytologic examination of an ETN pustule would show eosinophilia.[1,2,9] Differentiating benign neonatal rashes like ETN, neonatal cephalic pustulosis, and transient neonatal pustular melanosis (TNPM) from mucocutaneous herpes simplex virus (HSV) and impetigo is vital in clinical practice.

Distinguishing ETN from mucocutaneous HSV is crucial, as HSV requires prompt treatment to avoid potentially life-threatening sequelae like disseminated infection or central nervous system (CNS) disease like meningoencephalitis.[6,7] Neonatal herpes rashes typically appear as mucocutaneous vesicles with erythematous bases around the mouth and eyes with associated systemic signs like fever, lethargy, poor feeding, or irritability. Diagnostic evaluation for neonatal HSV includes surface specimen swabs from the conjunctiva, mouth, nasopharynx, anus, and any vesicular skin lesions for HSV polymerase chain reaction (PCR) or viral culture.[7] Serum PCR can help detect HSV viremia, but it alone is not a definitive indicator of disseminated disease.[7] The diagnostic method of choice for evaluating suspected CNS involvement in neonatal HSV is PCR of cerebrospinal fluid.[7]

Impetigo usually presents as honey-colored crusts (nonbullous) or flaccid bullae (bullous form). Bullous impetigo is commonly caused by Staphylococcus aureus, whereas the nonbullous form is typically caused by Streptococcus pyogenes. Diagnostic testing for impetigo includes lesion culture and gram staining.[8] Except in the rare case of superimposed infection, ETN alone does not normally stain for bacteria on gram stains.

TNPM is a benign, idiopathic, self-limited neonatal skin lesion like ETN.[9] However, TNPM pustules are usually present at birth.[9] TNPM also has a different progression, starting with flaccid and superficial pustules, which progress to scaling and hyperpigmented macules.[4,9] Cytologic examination of a TNPM pustule would show polymorphonuclear neutrophils, unlike the eosinophils seen in ETN.[4,9]

Neonatal cephalic pustulosis (neonatal acne), typically presents later than ETN, usually developing around 2 weeks of life.[10] Neonatal cephalic pustulosis may be caused by an inflammatory reaction to yeast infection from *Malassezia* species, rather than a true acne.[10] However, the current literature is divided regarding the association.[10] Neonatal cephalic pustulosis is usually self-limited but topical 2% ketoconazole or mild topical corticosteroids could be considered for treatment.[10]

Differentiating benign neonatal rashes like ETN, neonatal cephalic pustulosis, and TNPM from impetigo and mucocutaneous HSV is imperative to avoid overtreatment and potentially life-threatening sequelae.

## DISCUSSION

The patient was treated empirically with intravenous acyclovir and nafcillin to target HSV and *Staphylococcus*, respectively, while awaiting confirmatory laboratory results. HSV cultures (from the lesion) and serum PCR testing were both ultimately negative. Bacterial culture from the patient's right periorbital lesion showed heavy growth of *Staphylococcus epidermidis*, likely from skin flora rather than a true pathogen. Based on the clinical course, physical exam, and negative diagnostic testing, the patient's final diagnosis of ETN was concluded, and both antimicrobials were discontinued 3 days after initiation of therapy. No pustules, vesicles, or honey-crusted lesions were noted at his 1-month well-child checkup (19 days after onset). Spontaneous resolution of our patient's lesions took longer than the typical 7- to 14-day course of ETN.[3]

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