ILLUSTRATIVE CASE

Crawling Toward a Diagnosis: Vesicles and Thrombocytopenia in a Neonate

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CASE

A previously healthy 25-day-old boy presented to a tertiary children's hospital with a diffuse vesicular rash worsening over the previous 2 weeks. Per parental report, the rash was not accompanied by any other symptoms and did not appear to be pruritic or painful; specifically, he had no history of fever and was formula feeding well. The infant was the product of a full-term pregnancy, complicated only by a maternal diagnosis of pruritic papules and plaques of pregnancy at ~34 weeks of gestation. There was no known maternal history of herpes simplex virus (HSV) infection, and the mother denied any recent personal or family history of rashes or other skin lesions. The infant did not have any known allergies and no offending topical agent could be identified from the parental interview. He was not taking any medications.

WHAT ARE KEY HISTORY POINTS THAT MUST BE CONSIDERED WHEN PRESENTED WITH A VESICULAR AND PUSTULAR RASH IN A NEONATE?

This differential includes both relatively benign conditions and diseases associated with significant morbidity and mortality. Key history points include pertinent birth events, maternal health status, onset timing of the rash, presence of systemic symptoms, such as fever or poor feeding, location of rash, potential allergen exposure, contacts with similar rashes, trauma to the skin, and family history of skin diseases. The duration of the rash is important because a well-appearing infant with a rash of 2 weeks' duration is less concerning than a febrile infant who developed vesicles 24 hours prior.

On physical examination, the infant was fussy but consolable when held. He was afebrile with vital signs within the normal limits for his age. Examination was otherwise unremarkable except for vesicles on an erythematous base and pustules on the face, torso, extremities, soles, hands, palms, and occipital scalp (Fig 1). There were no interdigital lesions, and his mucous membranes were lesion-free. Neurologic examination showed no focal abnormalities.

WHAT DISEASES SHOULD BE CONSIDERED IN THE DIFFERENTIAL DIAGNOSIS FOR AN INFANT WITH A PUSTULAR VESICULAR RASH?

Wagner[1] proposes that the disease should be differentiated into infectious and noninfectious categories, which do not necessarily indicate the severity of illness. Noninfectious diseases to be considered include erythema toxicum, transient neonatal pustular melanosis, malaria neonatorum, acne neonatorum, eosinophilic pustular folliculitis, acropustulosis of infancy, mastocytosis, and incontinentia pigimenti. Infectious etiologies include impetigo neonatorum,

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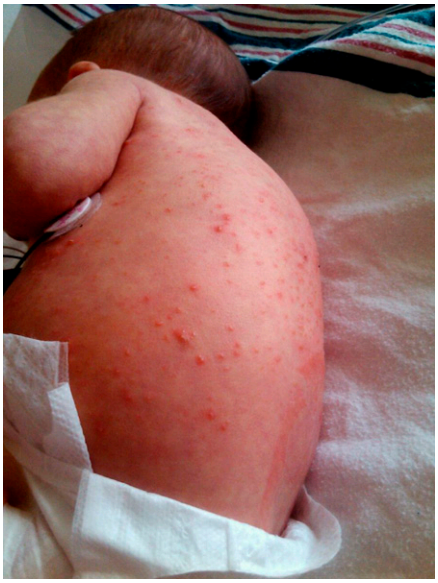

FIGURE 1 Vesicles and pustules on an erythematous base on the torso.

staphylococcal scalded skin, scabies, candidiasis, bacterial sepsis, syphilis, herpes simplex infections, and varicella infections.[1]

Given the appearance of the lesions and the patient's age, HSV was strongly suspected. The infant received a full sepsis evaluation; studies including spinal fluid HSV polymerase chain reaction (PCR) and skin scrapings for HSV were sent from the emergency department, and he was started on intravenous acyclovir 20 mg/kg every 8 hours. Initial bloodwork was notable for thrombocytopenia (107 k/mm^3) but normal liver function tests and white blood cell count. Additionally, pediatric ophthalmology was consulted and noted multiple unilateral dendritic lesions on examination, thereby increasing the suspicion for HSV infection. The infant was then started on erythromycin ophthalmologic ointment and polymyxin/trimethoprim-sulfamethoxazole eye drops and admitted to the hospital.

WHAT CLINICAL INDICATORS SHOULD INCREASE THE CLINICAL SUSPICION OF NEONATAL HERPES INFECTION?

Infants with disseminated or central nervous system HSV infections are often clinically ill appearing and may present with seizures, lethargy, and poor feeding; this presentation is identical to other causes of bacterial sepsis that are common in the neonatal period.[2] The most common presentation of neonatal HSV infections is grouped vesicles or crusted papules over the presenting part of the infant.[1] Neonates with HSV infections commonly have elevated liver enzymes and thrombocytopenia.[3] HSV is known to cause a characteristic inclusion body keratoconjunctivitis if ocular involvement is present.[4] Although a maternal history of HSV infection is helpful, it is often not present. An infant born to mother with a primary herpes infection has the highest risk of infection,[4] and there is an increased risk of infection if fetal scalp electrodes were used during labor.

Forty-eight hours after initial admission, the HSV skin cultures and spinal fluid HSV PCR were reported as negative. Seventy-two hours after admission, the rash had evolved from vesicular lesions as described previously into numerous pustules, many with overlying brown/yellow crust and minimal erythema (Fig 2). The patient also developed worsening thrombocytopenia (67 k/mm^3).

WHAT DISEASES AND WORKUP SHOULD BE CONSIDERED IN A NEONATE PRESENTING WITH A RASH AND THROMBOCYTOPENIA?

Infants with classic TORCH infections (to include *Toxoplasma gondii*, *Treponema pallidum*, congenital rubella, cytomegalovirus, HSV, and fetal parvovirus) commonly present with rashes and thrombocytopenia. The rash is usually petechial or purpuric, although HSV is classically vesicular. Age at presentation varies, with toxoplasmosis and congenital syphilis often being asymptomatic at birth. Hepatosplenomegaly and ocular involvement are universally present; other examination findings may include growth retardation, microcephaly, and cardiac defects. Workup generally involves disease-specific serology or PCR testing.[8] Maternal prenatal care and immunization status are important risk factors in disease development. Thrombocytopenia is generally the result of either a consumptive hypersplenism or decreased production secondary to bone marrow infiltration. Any sepsislike presentation, regardless of underlying etiology, may present with thrombocytopenia and should be considered in an ill-appearing patient. The thrombocytopenia may be further evaluated with peripheral smear, coagulation panel to evaluate for disseminated intravascular coagulopathy, or bone marrow biopsy as indicated by the patient's clinical course. Bleeding risks should be considered by treating physician.

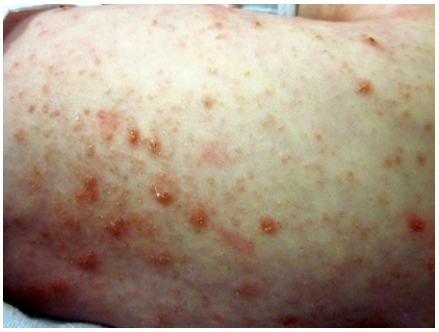

FIGURE 2 Evolution of rash with pustules and brown/yellow crusting.

The infectious disease service was consulted, and given the progression of the rash, believed our patient had neonatal scabies despite the finding of thrombocytopenia. Dermatology was consulted and a skin scraping evaluated with mineral oil preparation was positive for *Sarcoptes scabiei* mites and feces, confirming the diagnosis of neonatal scabies.

WHAT IS THE TYPICAL RASH AND EXAMINATION PRESENTATION FOR SCABIES?

Adults and older children classically present with intensely pruritic inflamed papules and excoriations to the interdigital web spaces, volar surface of the wrists, belt line, inframammary folds and periareolar region in women, and genitalia in men. Skin proximal to the neck is usually spared. Burrows may be present and are pathopneumonic for the disease.[5,6] Neonatal scabies is markedly different; patients

generally have large numbers of vesicles, papules, and pustules that are more diffuse, often involving face, scalp, neck, and trunk. Burrowing is rarely seen, and infants frequently do not exhibit pruritis due to their young age.[1] *Sarcoptes scabiei* is a human itch mite that buries itself under the outer layers of the skin. There are 4 life stages: eggs, larvae, nymphs, and adults. During the transition between stages, intermittent burying and migration to the skin surface result in the classic burrows seen on examination.[10]

Our patient was treated with permethrin 5% cream once and showed rapid improvement in his rash. The day after treatment, his platelet count normalized to 302 k/mm^3. Repeat ophthalmologic evaluation resulted in a revised diagnosis of corneal abrasion, likely secondary to pruritis. The patient was then discharged from the hospital in good condition. On further evaluation of the patient's mother's pruritic papules and plaques of pregnancy rash, it too was likely scabies.

WHAT IS THE TREATMENT OF NEONATAL SCABIES?

Permethrin 5% cream applied once from neck to toe for 8 hours is the standard treatment of scabies infections in adults and children >2 months; a Cochrane review in 2009 confirmed this as the most effective treatment.[7] Only 1 application is generally necessary but may be repeated after 1 to 2 weeks if itching persists or new papules or vesicles are seen. In infants younger than 2 months, the recommended treatment is topical sulfur in petroleum, but this must be compounded, so may be difficult for some families to access. Given the relatively low risk of side effects, we chose to treat with permethrin 5%. The family was advised to wash all clothing, blankets, towels, and bedding in hot water before using again to prevent reinfection. Families need to be educated that itching can last for days to weeks after initial treatment and may not be indicative of continued infections. Patients can generally return to work or school the day after treatment is complete.[10]

DISCUSSION

Due to presentation differences and the relatively low incidence of scabies in neonates, it is frequently lately diagnosed (or misdiagnosed altogether). Infants do not present with the "classic" pattern of burrows noted in the interdigital web spaces and the extremities. Our patient's presentation is typical of scabies in the neonate: widespread vesiculopustular lesions, present for 14 to 21 days. In contrast with older children and adults, the face, neck, and torso are commonly affected. The rash often will not appear to be particularly pruritic or uncomfortable, as was reported in this case. Despite a well-recognized pattern of presentation, the diagnosis is often delayed because scabies is relatively rare in the neonatal period and the differential diagnosis of vesiculopustular lesions includes more serious conditions that must often be first investigated. The addition of marked thrombocytopenia and an incorrect physical examination finding of corneal dendritic lesions in this infant further complicated the diagnosis. We could find no previous case reports of thrombocytopenia in the setting of neonatal scabies; an isolated case report of an adult with Norwegian scabies and thrombocytopenia[9] demonstrates a potential association, but it is likely that if the correct diagnosis is initially identified, no laboratory work is performed. As a result, the prevalence of thrombocytopenia in scabies infestation may be unknown. It is important, however, for providers to know that thrombocytopenia may be present during a scabies infection and is not necessary indicative of a more severe disease. Infants younger than 2 months can generally be safely treated with topical permethrin cream, but families should receive guidance on home cleaning, expected clinical course, and return to day care guidelines.

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