Chapter 2
Viral Infections

Patrick McMahon and Robert James Smith

Abstract Cutaneous manifestations of viral infections in pediatric patients can provide the first critical clues to disease development. While often self-limiting, viral infections can cause serious morbidity and mortality in vulnerable pediatric populations. In this chapter, we review the clinical presentation, differential diagnosis and treatment of hand foot mouth disease, neonatal herpes simplex virus infection, disseminated varicella zoster in an immunocompromised patient and Lipschütz ulcers.

Keywords Viral exanthem • Coxsackievirus • Enterovirus • Herpes simplex virus • Varicella zoster virus • Epstein–Barr virus • Lipschütz ulcer • Acyclovir

Case 2.1

A 13-month-old female is admitted to the hospital for a severe flare of atopic dermatitis (AD). Her parents report that this flare began 2 days ago with a fever (T_{max} 101°F) and fussiness. She has been able to drink, but has been eating less solid foods. She has developed blisters and sores on the arms, legs, buttocks, and around her mouth. They especially noticed redness and sores within the areas affected by AD, including her antecubital and popliteal fossae. She has had both increased itching of the arms and legs as well as tenderness in some of the areas with open sores. Today, they noticed a few new bumps on the hands and feet. The patient has had mild AD since the age of 6 months that has been controlled well on low potency topical steroids until this flare. They have not applied medications or emollients since this flare began due to perceived discomfort upon attempted applications. The patient is otherwise healthy. There were no known sick contacts and no contact with active cold sores or herpes virus. However, today the mother began noticing painful

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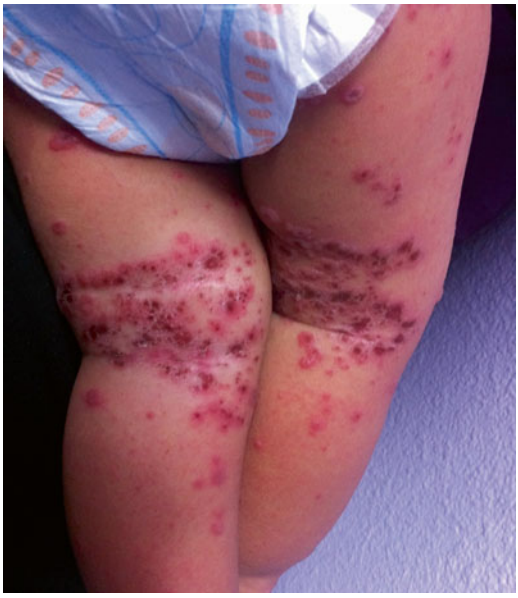

Fig. 2.1 Scattered vesicles and erosions on legs with accentuation in the popliteal fossae

blisters on her own palms. On physical exam, the child appears nontoxic, but fussy with scattered intact individual vesicles noted on the arms, legs, and buttocks; vesicles, crusting, and erosions around the mouth and within the antecubital and popliteal fossae; three vesicles noted on the soft palate and several papulovesicles on the dorsal hands, dorsal feet and on the soles. The vesicles are mostly not clustered, but in and around the scaly pink plaques of the antecubital and popliteal fossae the erosions appear accentuated and more concentrated (Fig. 2.1).

Questions

1. What is your differential diagnosis?
2. How would you treat the rash?
3. What are some delayed sequelae of this infection?

Presentation

Hand, foot, and mouth disease (HFMD) is a common pediatric illness due to enterovirus that typically presents with fever, painful erosions on the oral mucosa, and small, gray-white, oval vesicles on the palms, soles, and buttocks [1]. While the most common culprits of HFMD are Coxsackievirus A16 and enterovirus 71, starting in 2012, the Center for Disease Control reported a growing number of severe, atypical cases of HFMD attributed to a different stain of the virus, Coxsackievirus A6 (CVA6) [2]. In addition to classical HFMD symptoms of low-grade fever,

malaise, and gastrointestinal or respiratory complaints, patients with CVA6 often present with more extensive cutaneous lesions [1]. Outbreaks have been reported in Asia, Europe, and the United States [3, 4]. While classical HFMD affects children under the age of 6, CVA6 manifests in adults as well [4, 5]. Transmission occurs via oral or respiratory droplets with viral replications occurring in the pharynx and intestine. Subsequent viral amplification within the lymphatics results in viremia with distant multiorgan spread, including the skin.

The cutaneous manifestations of CVA6 infection are characterized by widespread vesiculobullous and erosive lesions extending beyond the palms and soles to include the trunk, extremities, and perioral region [1, 6]. A concurrent enanthem also consists of small vesicles and erosions on the oral mucosa. Perioral involvement may, in fact, be a hallmark of CVA6 infection [7]. In patients with a history of atopic dermatitis, as with the patient in presented case, lesions tend to concentrate in areas most affected by the individual's eczema, leading to the specific diagnosis of "eczema Coxsackium" or "eczema enteroviricum" [8, 9]. In these individuals, lesion morphology can appear quite similar to eczema herpeticum, except that in "eczema coxsackium" the vesicles tend to be less clustered and involvement of the palms and soles can be a clue that the patient has HFMD. Eruption patterns reveal a predilection for the virus to congregate in areas of previous trauma, friction or irritation, which may explain why disease severity is often worse on the palms, soles, and buttocks [1, 8].

Differential Diagnosis (Table 2.1)

The differential diagnosis for HFMD depends on the general presence or absence of cutaneous involvement. When there is only involvement of oral mucosa, the differential for these lesions includes orolabial HSV infection, aphthous stomatitis, and primary herpangina [8]. When there is widespread cutaneous involvement, other entities to consider within the differential for "eczema Coxsackium" include eczema herpeticum (HSV), varicella (VZV), disseminated zoster, bullous impetigo, erythema multiforme major, and bacterial superinfection of atopic dermatitis [5–8].

Diagnosis, Management, and Sequelae

Diagnosis of Coxsackie A6 HFMD is based primarily on clinical presentation. The diagnosis of an enteroviral infection can be confirmed via polymerase chain reaction (PCR) detection of the virus within the vesicle fluid, crusting or an erosion. For confirmation of the A6 serotype, nucleotide sequencing can be performed on PCR-positive specimens [1]. A skin biopsy is usually not necessary. If performed, it may reveal a spongiotic dermatitis, focal interface dermatitis with areas of subepidermal separation, and edema of the papillary dermis [1]. In patients with suspected "eczema Coxsackium," given the similarity in morphological appearance to eczema herpeticum, it is prudent to collect a sample of vesicular fluid for HSV PCR and consider empiric treatment with acyclovir if the eruption is severe [7].

Table 2.1 Differential diagnosis of viral exanthems by lesion morphology

Description of lesion morphology	Small, gray-white, oval vesicles on the palms, soles, and buttocks	Disseminated clustered, coalescing vesicles with surrounding erythema *in a neonate*	Dermatomal papulo-vesicular lesions	Disseminated papulo-vesicular lesions with crusting in various stages of development	Necrotic, painful, acute ulcer of the labia
Etiological category					
Infection/infestation	Eczema Coxsackium, eczema herpeticum, primary or disseminated VZV, bacterial superinfection of eczema	Neonatal HSV, disseminated VZV, Group B streptococcal infection, staphylococcal skin infection, toxoplasmosis, syphilis, rubella, cytomegalovirus	VZV, dermatomal HSV	Primary VZV, disseminated zoster, generalized HSV, enterovirus, scabies	HSV, syphilis, chancroid, HIV, tuberculosis, Lipschütz Ulcer (EBV, CMV)
Autoimmune	Linear IgA disease, bullous pemphigoid	Bullous mastocytosis		Guttate psoriasis, dermatitis herpetiformis	Behcet's disease, Crohn's disease, autoimmune bullous disease
Drug reaction					Fixed drug reaction
Other	Erythema multiforme (secondary to HSV or medication)		Contact dermatitis, burns, arthropod reaction	Kaposi's varicelliform eruption, papular urticaria, Langerhans cell histiocytosis, PLEVA	Trauma, contact dermatitis, pyoderma gangrenosum aphthous vulvar ulcer

The course of the illness is acute and self-limited. Treatment of concurrent atopic dermatitis with topical steroids and emollients may be indicated. Systemic symptoms typically resolve within a few days, and skin lesions resolve without scarring within days to weeks. Serious systemic complications in otherwise healthy patients are rare, but can include dehydration and viral meningoencephalitis. A known sequelae of CVA6 infection is delayed onychomadesis due to temporary arrest of the nail matrix, typically occurring 3–8 weeks after disease onset [6]. Patients typically experience full regrowth of their nails [9]. Patients may also experience desquamation of the palms and soles in the weeks following resolution of the vesicobullous eruption [1, 6].

Case 2.2

A 10-day-old male is admitted to the neonatal intensive care unit with fever, lethargy, and a widespread eruption. His parents report that he was born via normal spontaneous vaginal delivery at 39 weeks after an uncomplicated pregnancy. He was discharged home with his mother on day 2 of life and had been feeding well until yesterday when he began appearing excessively sleepy and refused to feed. Overnight, they noticed a small cluster of blisters on his abdomen. This morning he has several more blisters forming on his body, felt hot to the touch, and was found to have a temperature of 103°F. The mother has a remote history of genital herpes, but has not had any known active lesions for several years and, therefore, has not been on antiviral treatment recently. He was brought into the emergency department and underwent a full sepsis work-up for neonatal fever. Swabs were sent for viral and bacterial cultures from the vesicles on the skin. On physical exam, the child is found to be very irritable with widespread bright red clusters of erosions with scalloped borders on the abdomen, flanks, back, arms, legs, scalp, and buttocks. Upon close inspection he is also found to have intact clustered vesicles on the abdomen and an individual vesicopustule on the right forearm (Fig. 2.2).

Questions

1. What are the three types of presentation of this disease?
2. What is your differential diagnosis?
3. What is your treatment?

Presentation

Neonatal herpes simplex virus (HSV) is a herpetic infection that manifests within the first 28 days of life. While rare, with about 1500 cases annually, the infection carries significant morbidity and mortality [10]. Neonatal HSV can be transmitted

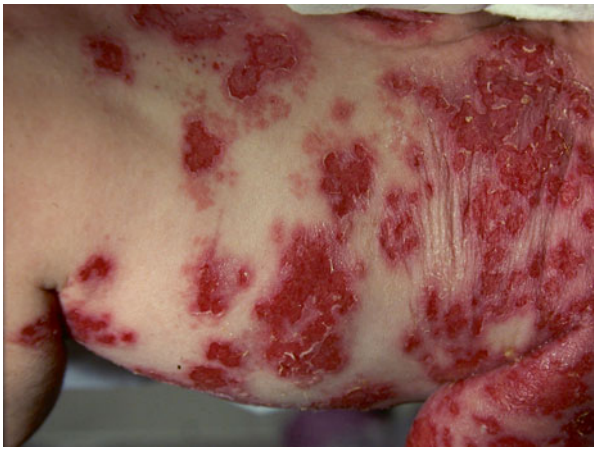

Fig. 2.2 Widespread cropped erosions with scalloped borders on the torso of a neonate (Photograph courtesy of Paul Honig, M.D.)

in three distinct periods: intrauterine, peripartum, and postnatal [11]. The majority (85 %) of neonatal HSV infection are acquired in the perinatal period when infants are directly exposed to HSV infection in the mother's genital tract. An additional 10 % of patients acquire the infection postnatally, typically via transmission from a caretaker with HSV-1. The remaining 5 % of patients acquire the infection through intrauterine transmission [11].

For purposes of treatment and prognosis, neonatal HSV infections are divided into three types: localized "skin, eye, and mouth" (SEM) disease, central nervous system (CNS) disease, and disseminated disease. All three forms of neonatal HSV can be caused by either HSV-1 or HSV-2, though HSV-2 infections have been associated with poorer outcomes [11].

Localized SEM disease accounts for 45 % of neonatal HSV cases and classically presents with clustered, coalescing small 2–4 mm vesicles on an erythematous base [12]. Lesion morphology can also take the appearance of pustules, blisters, or ulcerations. While it can occur at any point within the first 6 weeks of life, lesions will typically manifest within the first 2 weeks [13]. Early signs of HSV infection of the eye include excessive watering, conjunctival erythema, and crying from apparent eye pain. Keratoconjunctivits from HSV can progress to chorioretinitis and cataracts, causing permanent vision impairments [14]. HSV of the oropharyngeal cavity is characterized by ulcerative lesions of the mouth, tongue, and palate. While benign appearing, treatment is critical to prevent progression to CNS or disseminated disease. If antiviral treatment is initiated prior to development of further disease, outcomes are favorable.

CNS neonatal herpes, also described as HSV meningoencephalitis, accounts for 1/3 of neonatal HSV infections [14]. It can occur through either hematogenous spread from disseminated disease or localized retrograde spread from the nasopharynx and olfactory nerves to the brain. CNS disease typically presents in the second or third week of life and can occur with or without localized or disseminated diseases. Clinical manifestations include seizures, irritability, poor feeding, tremors, full anterior fontanelles, and temperature instability [15]. Lumbar puncture for cerebrospinal

fluid [CSF] may appear normal early in the disease course, but classically shows a mononuclear cell pleocytosis, normal glucose, and mildly elevated protein. An electroencephalogram is often abnormal early in the disease course, showing multifocal periodic epileptiform discharges [11, 16]. Of note, without vesicular skin findings, it may be impossible to distinguish HSV meningoencephalitis from other forms of neonatal meningitis. If clinical and laboratory findings are suggestive or inconclusive for aseptic meningitis, treatment with acyclovir is recommended [17].

The least common form of neonatal HSV is disseminated disease, accounting for 25 % of cases. Disseminated illness can involve multiple organs, including the liver, lungs, and adrenals, in addition to CNS and/or SEM disease [14]. These neonates typically present in the first week of life with signs and symptoms of neonatal sepsis, including fever or hypothermia, irritability, poor feeding, lethargy, abdominal distension, and respiratory distress [11]. Disseminated disease progresses quickly, often resulting in respiratory failure, necrotizing enterocolitis, acute liver failure secondary to hepatitis, meningoencephalitis, and/or shock, similar to multiorgan involvement of bacterial sepsis. Since most (80 %) patients with disseminated illness have vesicular skin findings, the identification of skin findings can be significant for halting disease progress [14].

Differential Diagnosis

The differential diagnosis for vesicular skin findings in neonates includes other infectious etiologies, such as varicella zoster virus (VZV), enteroviral infection, group B streptococcal (GBS) infection, staphylococcal skin infection, listeriosis, and other congenital "TORCH" infection (toxoplasmosis, syphilis, rubella, cytomegalovirus) [12, 18]. The differential diagnosis also includes bullous mastocytosis, bullous impetigo, incontinentia pigmenti, and other blistering disorders.

Treatment and Management

Given the severity of disease progression, prompt recognition and treatment of neonatal herpes is of critical importance in infants with mucocutaneous vesicles, CNS abnormalities, or sepsis-like syndromes. Detection of HSV may be achieved through isolation of HSV in viral cell culture, detection of viral DNA via polymerase chain reaction (PCR), or rapid direct fluorescence antibody (DFA). However, negative cultures, PCR, or DFA cannot always rule out neonatal HSV. Alternatively, a Tzanck smear can be conducted to provide rapid diagnosis via visualization of multinucleated giant cells, though a positive result will not distinguish between HSV and VZV, and it may be unreliable due to interpreter variability [12].

Mortality exceeds 80 % in patients with untreated disseminated HSV disease, and serious morbidity can result, even with patients who receive early intervention [12]. The recommended antiviral treatment for suspected neonatal HSV is intravenous acyclovir [19]. Localized infections should be treated for a minimum of

14 days, while CNS and disseminated disease should be treated for a minimum of 21 days. Since the advent of antiviral therapy, mortality for CNS disease has declined from 85 to 29 % and for disseminated disease from 50 to 4 % [19–21]. Early treatment of localized disease effectively prevents the disease course from progressing to CNS or disseminated illness [22]. Following parenteral treatment, suppressive oral therapy of acyclovir should be administered for 6 months.

While approximately 20–30 % of pregnant women in the United States are infected with HSV-2, most neonates with HSV are born to mothers without a known prior history of the infection [12, 23]. Risk of maternal-fetal transmission is much higher [25–50 %] in women who acquire primary genital HSV during their pregnancy compared to women with long-standing HSV-2 infections who experience viral reactivation in their genital tract at term [<1 %] [24]. As such, infants born to mothers with high suspicion of primary HSV should be treated empirically [25].

Case 2.3

A 16-year-old female with a recent diagnosis of acute lymphoblastic leukemia (ALL) presents with spreading pink papulovesicles on the hands, arms, and now trunk. The lesions were first noticed 2 days ago on the bilateral forearms and have since spread. The patient is currently undergoing consolidation chemotherapy and is pancytopenic. She has been afebrile, denies pain or itching associated with these lesions, and denies having any lesions in the mouth or genital region. Besides the new diagnosis of ALL, the patient has no other past medical history and was fully immunized. Upon physical exam, she is tired, but well appearing and has scattered individual pink intact papules and papulovesicles accentuated on the bilateral arms and hands with limited involvement of the trunk and two papulovesicles noted on the buttocks. The lesions are in a linear distribution on the right forearm and some are crusted. Upon palpation of these lesions, the patient denies pain. There are not relevant findings in the oral or genital mucosae. Follow-up physical exam the following day revealed several new lesions on the trunk, arms, and legs, frank vesiculation of several lesions on the distal arms, and crusting of two lesions on the trunk. A diagnostic swab was sent from one of the vesicles (Fig. 2.3).

Questions

1. What are the differences in presentation of this virus for immunocompetent and immunosuppressed patients?
2. What is your differential diagnosis?
3. What is your treatment?

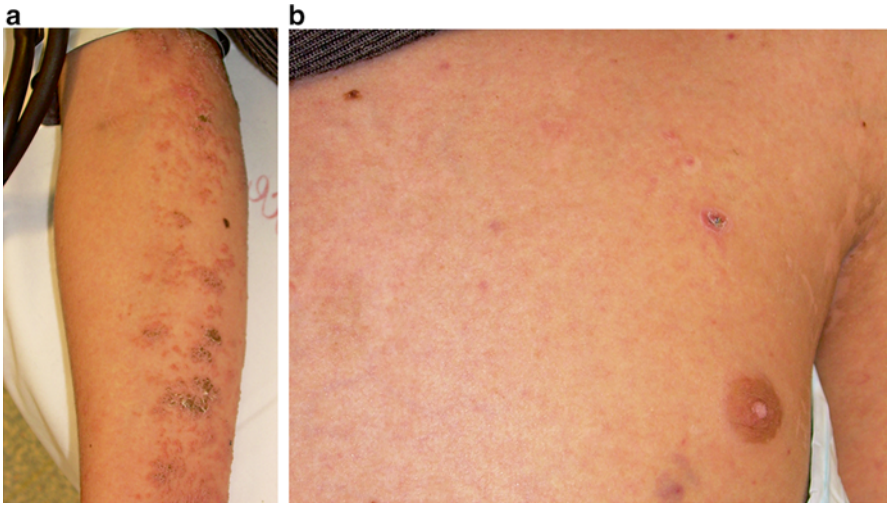

Fig. 2.3 Linear crusted papulovesicles on the arm (*left*), and scattered violaceous to pink papules on the chest (*right*)

Presentation

Varicella zoster virus (VZV) is a herpes virus that classically manifests as two different disease syndromes: primary infection (chickenpox) and reactivation ("herpes zoster" or "shingles") [26]. Primary infection is characterized by the presence of lesions in various stages of development on the face, trunk, and extremities that transition from macules to papules, pustules, vesicles, and crusts [26]. Lesions are typically most abundant on the central trunk and proximal upper extremities with relative sparing of the distal and lower extremities. Pruritus is an almost universal symptom associated with the lesions, along with fever and malaise [27]. Primary varicella is typically a self-limited disease in immunocompetent children, lasting about 7–10 days. However, complications can occur, such as bacterial superinfection, central nervous system (CNS) involvement (such as Reye's syndrome, Guillain–Barré, acute cerebral ataxia, and encephalitis), and varicella pneumonia [28, 29].

Primary VZV can have significant morbidity and mortality in immunocompromised hosts [30]. These patients may experience a prolonged febrile period, persistent viremia, and a more severe cutaneous presentation, often with purpuric or hemorrhagic lesions. These patients are also more likely to have involvement of the lungs, liver, and CNS [27]. Primary VZV can occur in previously immunized patients if their immunity has waned.

Herpes zoster is caused by reactivation of dormant varicella virus residing in the dorsal ganglia of previously infected patients. The zoster syndrome characterized by a painful, unilateral, dermatomal rash consisting of erythematous macules and papules, which then progress to vesicles, pustules, and crusts [31]. While the rash is

preceded by intense pain and paresthesia in greater than 90 % of adults with this condition, lack of pain or limited pain is common in children with herpes zoster infections. Regional lymphadenopathy may or may not be present. Complications associated with zoster infections are rare in children, but include persistent regional pain, known as post-herpetic neuralgia [PHN], and ocular disease in patients with ophthalmic zoster [28].

As with primary VZV infection, the pain and rash associated with zoster may be more severe in immunocompromised patients [32]. Zoster can disseminate in up to 20–40 % of affected individuals [30]. Disseminated cutaneous zoster is defined as a patient having 20 or more vesicles *outside* of the primary affected and adjacent dermatomes. Visceral involvement of the lungs, liver, and CNS subsequently affect 10 % of these patients. Of note, as in the patient presented, atypical presentations and morphologies are possible in an immunocompromised host—specifically reactivated disseminated zoster is not always dermatomal in distribution, resembling acute varicella infection, and may be painless.

Differential Diagnosis

The differential for primary VZV infection includes other viral exanthems (generalized herpes simplex virus, disseminated herpes zoster, Kaposi's varicelliform eruption, or enterovirus), bacterial infections (bullous impetigo), drug eruptions (Stevens–Johnson syndrome), papular urticaria, pityriasis lichenoides et varioliformis acuta (PLEVA), Langerhans cell histiocytosis, guttate psoriasis, scabies, and dermatitis herpetiformis [26, 27]. In an immunocompromised host with atypical papular lesions, infectious etiologies such as disseminated candidiasis or atypical mycobacteria should also be considered.

The differential diagnosis for classical herpes zoster infections includes dermatomal HSV infections, contact dermatitis, localized viral or bacterial infections, arthropod reactions, and burns [26]. For disseminated zoster, the differential will be similar to that of disseminated primary varicella.

Diagnosis

Diagnosis is of primary varicella is often clinical based on characteristic lesion findings and a history of recent exposure to the virus within the previous 2–3 weeks. However, the diagnosis can also be confirmed through a number of laboratory methods [26]. The initial test of choice for patients with vesicular lesions in various stages of development is a viral PCR for HSV and VZV. Tzanck smear can also be done for rapid detection of multinuclear giant cells; however, the Tzanck will not distinguish VZV from herpes simplex virus [HSV] [12]. Viral culture and serological tests are alternative laboratory options. Serology may be helpful for distinguishing between primary VZV infection and reactivation, particularly when a history of primary chickenpox is uncertain [33].

Management

In healthy pediatric patients with uncomplicated primary varicella, treatment is symptomatic with antipyretics, antihistamines, and cool compresses [26]. In contrast, in immunocompromised pediatric patients, the treatment of choice for either primary varicella or herpes zoster is intravenous acyclovir [34, 35]. Early antiviral treatment prevents visceral dissemination of the virus [30, 32, 35]. To monitor the development of varicella complications in immunocompromised patients, laboratory evaluation should include a complete blood count, liver function tests, renal function test, and a chest radiograph [35]. Frequent clinical and laboratory evaluation should be rendered to monitor for the development of such complications. In otherwise immunocompetent patients who develop complications of varicella infections, such as pneumonia, encephalitis, or hepatitis, intravenous acyclovir is also indicated [35]. In rare cases of acyclovir-resistant VZV infections, foscarnet is the best drug available for treatment [36].

Prevention

Varicella is highly contagious, with infectivity rates in susceptible, unvaccinated patients ranging from 61 to 100 % [27]. The virus spreads in two forms: (1) via aerosolized droplets in the 2 days prior to appearance of skin lesions; and (2) via direct skin contact with the lesions 5–7 days after appearance of the rash. In immunocompromised hosts, the contagious period can last for several weeks. As such, patients in inpatient settings should be placed on droplet precautions. The live, attenuated varicella vaccine can safely be administrated to children as young as 9 months and is highly effective, with prevention rates typically reaching 80–85 % [27].

Passive immunization with varicella zoster immunoglobin may be administrated to some susceptible groups who have been exposed to the virus. Eligible patients include immunocompromised children and adults for whom live vaccines are contraindicated, pregnant women, premature infants, and neonates whose mothers present with varicella infection in the period 5 days prior to 2 days after birth [37].

Case 2.4

A 15-year-old otherwise healthy female is admitted to the adolescent medicine service due to fever and severe, painful swelling and ulceration of the left labia majora and minora. The symptoms began 5 days ago with fever (T_{max} 102.5°F), mild swelling, and pain and have progressed to include ulceration and extreme dysuria prompting admission. The patient denies sexual activity. A preliminary work-up for sexually transmitted infections is negative including gonorrhea, chlamydia, human immunodeficiency virus (HIV), and a syphilis screen with rapid plasma reagin

(RPR). Bacterial swab from the left labial ulcer was negative as was HSV PCR. Monospot screening for Epstein–Barr virus (EBV) was positive and EBV serologies are pending. Upon physical exam, the well-appearing patient is noted to have left labial edema with mild pink erythema surrounding an ulceration between the labia major and minora with another more shallow ulceration noted on the inferior labia majora. Left inguinal lymphadenopathy is appreciated and painful to palpation. The physical exam overall is incredibly painful for the patient (Fig. 2.4).

Questions

1. What is your differential?
2. What is your management?

Presentation

Acute genital ulcers, also described as Lipschütz ulcers (LU), ulcus vulvae acutum, or nonsexual acute genital ulcers, are characterized by the sudden appearance of a single or multiple necrotic, painful ulcerations of the vulva, often in young prepubertal or adolescent women who are typically immunocompetent and nonsexually active [38, 39]. The ulceration is frequently large (>1 cm) and deep with a violaceous border, necrotic base, and grayish exudate or eschar. Ulcers can involve the labia minora, labia majora, perineum, and lower vagina. The ulceration are often preceded and accompanied by fever, dysuria, malaise, and inguinal lymphadenopathy [40, 41].

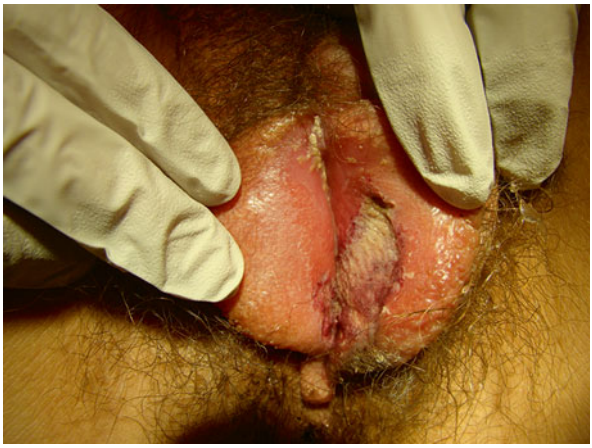

Fig. 2.4 Deep ulceration on the left labia with clean edges and minimal surrounding erythema (Photograph courtesy of Lara Wine-Lee, M.D., Ph.D.)

Differential Diagnosis

A Lipschütz ulcer is a diagnosis of exclusion. These lesions can be particularly distressing for patients, families, and providers, as their morphology and distribution can be mistaken for sexually transmitted infections and, consequently, as potential signs of abuse [39]. As such, their presence warrants a work-up to rule out multiple concerning etiologies. The diagnosis for LU should be distinguished from other venereal etiologies, such as herpes simplex virus (HSV), syphilis, and chancroid, as well as non-venereal infections, such as HIV, ulcerative tuberculosis, and paratyphoid fever. The differential also includes physical trauma, rheumatologic disease, such as Behcet's or Crohn's disease, pyoderma gangrenosum, fixed drug eruption, contact or irritant dermatitis, and autoimmune bullous diseases [39–41].

The cause of Lipschütz ulcers is most often linked to acute infection with EBV, though it has been associated with cytomegalovirus (CMV), influenza A virus, salmonella, toxoplasmosis, mycoplasma, Lyme, and paratyphoid fever virus [42]. In most patients, however, no specific etiology is ever identified [42, 43].

Diagnosis and Management

Initial work-up for these ulcers should first include a viral culture swab or polymerase chain reaction (PCR) for herpes simplex virus [HSV], as genital herpes simplex is the most common cause of genital ulcers. Serological tests for other causes of sexually transmitted genital ulcerations, such as syphilis, chancroid, chlamydia, and lymphogranuloma venereum, should also be performed, based on clinical suspicion and history. Serological testing for EBV is also indicated. Bacterial cultures of the ulcer should be obtained to assess for vulvar cellulitis and bacterial superinfection. Biopsy of the site is not initially indicated, as histology will appear nonspecific [40].

The lesion typically resolves without intervention within 2–6 weeks. Treatment entails reassurance, wound care in the form of Sitz baths, and pain control with acetaminophen, topical anesthetics, and systemic pain medications in severe cases or during painful physical exams [44]. Oral corticosteroids or high potency topical steroids may be used for the treatment of particularly painful, deep, or long-lasting ulcers [45]. Recurrence has been reported in up to a third of cases [40, 44].

References

1. Mathes EF, Oza V, Frieden IJ, Cordoro KM, Yagi S, Howard R, et al. "Eczema coxsackium" and unusual cutaneous findings in an enterovirus outbreak. Pediatrics [Internet]. 2013;132(1):e149–57.
2. McIntyre M, Stevens K, Todd R. Notes from the field. MMWR Morb Mortal Wkly Rep [serial online]. 2012;61(12):213–4.
3. Wu Y, Yeo A, Phoon MC, Tan EL, Poh CL, Quak SH, et al. The largest outbreak of hand; foot and mouth disease in Singapore in 2008: the role of enterovirus 71 and coxsackievirus A strains. Int J Infect Dis [Internet]. 2010 [cited 2015 Jul 6];14(12):e1076–81.

4. Ben-Chetrit E, Wiener-Well Y, Shulman LM, Cohen MJ, Elinav H, Sofer D, et al. Coxsackievirus A6-related hand foot and mouth disease: skin manifestations in a cluster of adult patients. J Clin Virol [Internet]. 2014;59(3):201–3.
5. Downing C, Ramirez-Fort MK, Doan HQ, Benoist F, Oberste MS, Khan F, et al. Coxsackievirus A6 associated hand, foot and mouth disease in adults: clinical presentation and review of the literature. J Clin Virol [Internet]. 2014 [cited 2015 Jun 7];60(4):381–6.
6. Wei S-H, Huang Y-P, Liu M-C, Tsou T-P, Lin H-C, Lin T-L, et al. An outbreak of coxsackievirus A6 hand, foot, and mouth disease associated with onychomadesis in Taiwan, 2010. BMC Infect Dis [Internet]. 2011 [cited 2015 Jul 6];11:346.
7. Flett K, Youngster I, Huang J, McAdam A, Sandora TJ, Rennick M, et al. Hand, foot, and mouth disease caused by coxsackievirus A6. Emerg Infect Dis. 2012;18(10):1702–4.
8. Lott JP, Liu K, Landry ML, Nix WA, Oberste MS, Bolognia J, et al. Atypical hand-foot-and-mouth disease associated with coxsackievirus A6 infection. J Am Acad Dermatol [Internet]. 2013;69(5):736–41.
9. Feder HM, Bennett N, Modlin JF. Atypical hand, foot, and mouth disease: a vesiculobullous eruption caused by Coxsackie virus A6. Lancet Infect Dis [Internet]. 2014;14(1):83–6.
10. Flagg EW, Weinstock H. Incidence of neonatal herpes simplex virus infections in the United States, 2006. Pediatrics [Internet]. 2011 [cited 2015 Jul 14];127(1):e1–8.
11. Kimberlin DW. Neonatal herpes simplex infection. Clin Microbiol Rev [Internet]. 2004 [cited 2015 Jun 29];17(1):1–13.
12. Ladizinski B, Rukhman E, Lee KC. A 4-day-old neonate with a widespread vesicular rash. JAMA. 2013;310(9):9–10.
13. Kimberlin DW, editor. Herpes simplex. Red Book: 2015 Report of the Committee on Infectious Diseases. Elk Grove Village: American Academy of Pediatrics; 2015. p. 432.
14. Kimberlin DW. Herpes simplex virus infections of the newborn. Semin Perinatol [Internet]. 2007 [cited 2015 Jul 14];31(1):19–25.
15. Toth C, Harder S, Yager J. Neonatal herpes encephalitis: a case series and review of clinical presentation. Can J Neurol Sci [Internet]. 2003 [cited 2015 Jul 14];30(1):36–40.
16. Mizrahi EM, Tharp BR. A characteristic EEG pattern in neonatal herpes simplex encephalitis. Neurology [Internet]. 1982 [cited 2015 Jul 14];32(11):1215–20.
17. Long SS. In defense of empiric acyclovir therapy in certain neonates. J Pediatr [Internet]. 2008 [cited 2015 Jul 14];153(2):157–8.
18. Marquez L, Levy ML, Munoz FM, Palazzi DL. A report of three cases and review of intrauterine herpes simplex virus infection. Pediatr Infect Dis J [Internet]. 2011 [cited 2015 Jul 15];30(2):153–7.
19. Kimberlin DW, Lin CY, Jacobs RF, Powell DA, Corey L, Gruber WC, et al. Safety and efficacy of high-dose intravenous acyclovir in the management of neonatal herpes simplex virus infections. Pediatrics [Internet]. 2001 [cited 2015 Jun 29];108(2):230–8.
20. Whitley R, Arvin A, Prober C, Burchett S, Corey L, Powell D, et al. A controlled trial comparing vidarabine with acyclovir in neonatal herpes simplex virus infection. Infectious Diseases Collaborative Antiviral Study Group. N Engl J Med [Internet]. 1991 [cited 2015 Jul 14];324(7):444–9.
21. Pinninti SG, Kimberlin DW. Neonatal herpes simplex virus infections. Pediatr Clin North Am [Internet]. 2013 [cited 2015 Jun 5];60(2):351–65.
22. Turk DC, Swanson KS, Gatchel RJ. Predicting opioid misuse by chronic pain patients: a systematic review and literature synthesis. Clin J Pain [Internet]. 2008;24:497–508.
23. Caviness AC, Demmler GJ, Selwyn BJ. Clinical and laboratory features of neonatal herpes simplex virus infection: a case-control study. Pediatr Infect Dis J [Internet]. 2008 [cited 2015 Jul 14];27(5):425–30.
24. Corey L, Wald A. Maternal and Neonatal HSV Infections. N Engl J Med. 2009;361(14):1376–85.
25. ACOG Practice Bulletin. Clinical management guidelines for obstetrician-gynecologists. No. 82 June 2007. Management of herpes in pregnancy. Obstet Gynecol [Internet]. 2007 [cited 2015 Jul 15];109(6):1489–98.

26. McCrary ML, Severson J, Tyring SK. Varicella zoster virus. J Am Acad Dermatol [Internet]. 1999 [cited 2015 Jul 18];41(1):1–14; quiz 15–6.
27. Heininger U, Seward JF. Varicella. Lancet (London, England) [Internet]. 2006 [cited 2015 Jul 19];368(9544):1365–76.
28. Gilden DH, Kleinschmidt-DeMasters BK, LaGuardia JJ, Mahalingam R, Cohrs RJ. Neurologic complications of the reactivation of varicella-zoster virus. N Engl J Med [Internet]. 2000 [cited 2015 Jul 19];342(9):635–45.
29. Breuer J, Fifer H. Chickenpox. BMJ Clin Evid [Internet]. 2011 [cited 2015 Jul 19];2011.
30. Nyerges G, Meszner Z, Gyarmati E, Kerpel-Fronius S. Acyclovir prevents dissemination of varicella in immunocompromised children. J Infect Dis [Internet]. 1988 [cited 2015 Jul 18];157(2):309–13.
31. Wareham DW, Breuer J. Herpes zoster. BMJ [Internet]. 2007 [cited 2015 Jul 19];334(7605):1211–5.
32. Shepp DH, Dandliker PS, Meyers JD. Treatment of varicella-zoster virus infection in severely immunocompromised patients. A randomized comparison of acyclovir and vidarabine. N Engl J Med [Internet]. 1986 [cited 2015 Jul 19];314(4):208–12.
33. Petrun B, Williams V, Brice S. Disseminated varicella-zoster virus in an immunocompetent adult. Dermatol Online J [Internet]. 2015 [cited 2015 Jul 19];21(3).
34. Prober CG, Kirk LE, Keeney RE. Acyclovir therapy of chickenpox in immunosuppressed children—a collaborative study. J Pediatr [Internet]. 1982 [cited 2015 Jul 18];101(4):622–5.
35. Arvin AM. Antiviral therapy for varicella and herpes zoster. Semin Pediatr Infect Dis [Internet]. 2002 [cited 2015 Jul 18];13(1):12–21.
36. Piret J, Boivin G. Antiviral drug resistance in herpesviruses other than cytomegalovirus. Rev Med Virol [Internet]. 2014 [cited 2015 Jul 19];24(3):186–218.
37. Centers for Disease Control. A new product (VariZIG™) for postexposure prophylaxis of varicella available under an investigational new drug application expanded access protocol. MMWR Morb Mortal Wkly Rep [Internet]. 2006 [cited 2015 Jul 19];55:209–10.
38. Haidari G, MacMahon E, Tong CYW, White JA. Genital ulcers: it is not always simplex …. Int J STD AIDS [Internet]. 2015 [cited 2015 Jul 25];26(1):72–3.
39. Truchuelo MT, Vano-Galván S, Alcántara J, Pérez B, Jaén P. Lipschütz ulcers in twin sisters. Pediatr Dermatol [Internet]. 2012 [cited 2015 Jul 25];29(3):370–2.
40. Hernández-Núñez A, Córdoba S, Romero-Maté A, Miñano R, Sanz T, Borbujo J. Lipschütz [corrected] ulcers—four cases. Pediatr Dermatol [Internet]. 2008 [cited 2015 Jul 25];25(3):364–7.
41. Rosman IS, Berk DR, Bayliss SJ, White AJ, Merritt DF. Acute genital ulcers in nonsexually active young girls: case series, review of the literature, and evaluation and management recommendations. Pediatr Dermatol [Internet]. 2012 [cited 2015 Jul 25];29(2):147–53.
42. Farhi D, Wendling J, Molinari E, Raynal J, Carcelain G, Morand P, et al. Non-sexually related acute genital ulcers in 13 pubertal girls: a clinical and microbiological study. Arch Dermatol [Internet]. 2009 [cited 2015 Jul 25];145(1):38–45.
43. Deitch HR, Huppert J, Adams Hillard PJ. Unusual vulvar ulcerations in young adolescent females. J Pediatr Adolesc Gynecol [Internet]. 2004 [cited 2015 Jul 25];17(1):13–6.
44. Lehman JS, Bruce AJ, Wetter DA, Ferguson SB, Rogers RS. Reactive nonsexually related acute genital ulcers: review of cases evaluated at Mayo Clinic. J Am Acad Dermatol [Internet]. 2010 [cited 2015 Jul 25];63(1):44–51.
45. Dixit S, Bradford J, Fischer G. Management of nonsexually acquired genital ulceration using oral and topical corticosteroids followed by doxycycline prophylaxis. J Am Acad Dermatol [Internet]. 2013 [cited 2015 Jul 25];68(5):797–802.

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