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Toe Herpetic Whitlow as presenting HSV symptom in an 8-Month Old Infant

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Abstract

Herpetic whitlow of the toe as the primary presenting manifestation of herpes simplex virus (HSV) is rarely reported in the pediatric literature. We report the case of an 8-month-old African American male who presented with an erythematous and swollen right great toe. Originally diagnosed as an infected insect bite, the lesion failed to respond to amoxicillin, sulfamethoxazole/trimethoprim, topical mupirocin, or topical permethrin (when scabies was suspected) prescribed treatment regimens. Observation of the clinical course yielded the diagnosis of herpetic whitlow. We present this unusual case as an important reminder to healthcare providers that herpetic whitlow is not limited to the fingers and can mimic other infectious processes or serious bacterial infections which may require surgical debridement. Herpetic whitlow of the great toe as the first presenting symptom of HSV infection in 8-month-old child with no known prior diagnosis of HSV is also unusual. This report highlights the need to include herpetic whitlow in the differential diagnosis of an isolated digit infection in an otherwise healthy child in order to minimize prolonged diagnostic quests and accompanying pain and burden to the pediatric population and their caregivers.

Keywords

herpetic whitlow; herpes simplex virus; herpes toe infection

Abbreviations

DFA: direct fluorescent antibody; DNA: deoxyribonucleic acid; ED: emergency department
HIV: human immunodeficiency virus; HSV: herpes simplex virus; IV: intravenous; MRSA: Methicillin-resistant Staphylococcus aureus; PCR: polymerase chain reaction

Introduction

Herpes simplex virus (HSV) affects 90% of the population by adulthood [1], and one-third of the pediatric population are reported to contract a primary HSV-1 infection by the age of five [2]. In the United States, neonatal HSV disease occurs in approximately 1 in 3200 deliveries, or 1500 new cases every year [3]. Enveloped double-stranded deoxyribonucleic acid (DNA) in structure, the Herpes virus family contains more than 80 known types of which 8 cause human infection [4]. Contagious and ubiquitous, both HSV-1 and HSV-2 are transmitted through exposure to active lesions on the skin or direct exposure to virus shed in secretions such as respiratory droplets or saliva. Initial HSV-1 or HSV-2 infection incubation periods range from 2 to 12 days with an average of 4 days [5]. Viral shedding can last from one to several

weeks, during which the host may show clinical signs or may be asymptomatic. Under normal circumstances in an immunocompetent patient the virus then remains latent within the autonomic ganglia of the host, with HSV-1 tending to reside within the trigeminal ganglion and HSV-2 in the sacral ganglia. The virus may then replicate within the ganglia during latency without being detected by the host's immune system.

Stern et al [6] coined the term “herpetic whitlow" in 1959 to describe a specific manifestation that may present during a HSV infection, namely a painful, pus-producing infection of a distal digit in a medical personnel. Technically, however, the term is a misnomer, as herpetic whitlow produces clear or turbid fluid rather than pus [6]. As described in the literature, herpetic whitlow is a self-limited cutaneous infection caused by either HSV-1 or HSV-2 transmitted from an oral, genital, or skin lesion or vesicle. Herpetic whitlow has been reported on fingers, hands, knees, or uncommonly toes [7]. Herpetic whitlow affecting the toes has seldom been reported, with only four pediatric cases described in the literature to our knowledge [8-12]. We describe the case of a 8-month-old African American male who presented with an erythematous and swollen right great toe, repeatedly diagnosed as various other infections.

Case Report

A previously healthy an eight-month-old infant African American male presented to medical attention with a tender, erythematous, and edematous right great toe containing clusters of small blisters. One day after symptom onset, the mother consulted her child's primary care physician (PCP) who felt the symptoms represented a reaction to insect bites, prescribing oral amoxicillin and topical mupirocin. After three days of treatment with no symptom improvement, the mother returned to her child's PCP and received reassurance with instructions to continue the prescribed treatment regimen. As the erythema continued to worsen, the mother brought the infant to an outside hospital emergency department (ED). A diagnosis of an allergic reaction to an insect bite was made, and all previously prescribed medications were discontinued. The patient was then prescribed sulfamethoxazole/trimethoprim. The ED also had concern for possible scabies infestation, so topical permethrin was prescribed and the mother was instructed to apply the medication on both legs between his knees and toes. During the course of this treatment, he developed multiple pustules on both dorsal and plantar surfaces of his right great toe, which lead to localized loss of skin and a resulting black eschar.

A week and a half after symptom onset, the patient was admitted to the hospital with a concern for cellulitis. His mother denied trauma to the affected area, seeing any puncture wounds, or known exposure to spiders, ticks, fleas, or pets. In addition, no family members or close contacts had recently displayed signs of a rash, scabies, cold sores, or fever blisters. She did note that the patient habitually puts his toes in his mouth. The patient remained afebrile throughout the entire clinical course, displayed no signs of systemic illness, and was quite content on exam. Physical exam on intake demonstrated multiple pustules, two areas of black eschar on the dorsal (Fig 1A) and plantar surface of his right first toe, and an area of desquamation on the medial plantar surface (Fig 1B). Erythema was limited to the right great toe with no additional swelling noted on either foot or leg. The patient's lower extremities were cool to touch. A plain radiograph of the right foot obtained upon admission revealed no abnormalities. The patient was started on oral clindamycin and intravenous (IV) cefepime on admission to cover causes of bacterial cellulitis, including the potential for ecythema gangrenosum secondary to *Pseudomonas aeruginosa*. Bedside

debridement was performed after antibiotic initiation, followed by local wound care with normal saline foot soaks and topical bacitracin. Wound cultures and Gram stain, peripheral blood cultures, and Methicillin-resistant *Staphylococcus aureus* (MRSA) polymerase chain reaction (PCR) yielded no positive results. The patient showed clinical improvement by the second day of admission, with decreased erythema and tenderness to palpation (Fig 1C and 1D). After considering the child's history of sucking on his toes, the initial failure to respond to antibiotics, and the physical appearance of the patient's toe over time, a Pediatric Infectious Diseases consulting physician felt the clinical course was most consistent with a diagnosis of herpetic whitlow of the right great toe.

Discussion

There are fewer reports of herpetic whitlow in medical personnel today due to use of protective gloves, with most cases now resulting from autoinfection during HSV gingivostomatitis or genital infections in adults and with HSV gingivostomatitis in children [13-15]. In total, there is an estimated annual incidence of 2.4 cases per 100,000 people [15]. Herpetic whitlow is most commonly transmitted through direct contact with an HSV lesion, nail-biting autoinfection, or contact with infected bodily fluids [2]. Peak age of occurrence in children is within the first two years of life, during which the most common mode of HSV autoinfection is finger sucking [9,15]. While secondary autogenous infection attained from the child's primary herpeticgingivostomatitis is the most likely source [16], a digit may become infected from autogenous or exogenous sites following traumatic injury [17]. Of note, the transmission route remains unknown in 21% of cases [18].

Herpetic whitlow may present with a prodromal tingling, burning or pruritic sensation of the affected digit or entire limb. This is followed by erythema and vesicle formation. Pain at the affected fingertip is the most frequently reported presentation of herpetic whitlow of the finger. With a primary infection systemic complaints including fever, malaise, lymphangitis, and/or local adenopathy may be present [14]. The dermatologic findings progress through a classic evolution, beginning with the coalescence of one or more vesicles and often followed by necrosis of the skin surrounding these vesicles. Pertinent to an accurate diagnosis, the vesicles may appear to contain pus, but closer inspection typically reveals opalescent, clear, or serosanguineous fluid instead. This finding is key in distinguishing herpetic whitlow from paronychia or bacterial felon [19]. The coalesced vesicular bullae and non-purulent fluid remain clinically apparent for approximately 10 to 14 days, after which the lesions become crusted and peel, revealing normal skin beneath [4].

Herpetic whitlow is diagnosed clinically based on suspicion of characteristic lesions following the sequence of changes described above [14,19]. Features that may assist in correctly identifying herpetic whitlow include: a recent history of orolabial or genital HSV lesions in the child or close contacts, recurring symptoms presenting at an identical anatomical location, any history of nail biting or trauma to digits permitting easy viral entry [20], or identification of the non-purulent vesicular fluid. It is important to note that the vesicle fluid appearance may not be a reliable sign if bacterial super infection exists within the herpetic whitlow lesion [19]. A clinical diagnosis can be confirmed with viral culture, PCR, or direct fluorescent antibody (DFA) test. The Tzank test, classically utilized to diagnose HSV, is no longer recommended due to limited sensitivity [21]. Incision and drainage of the lesion should be avoided in order to prevent worsening symptoms, risks of increased infection duration, or further viral or

bacterial infection [18,19]. Once vesicular lesions are crusted and eschar has formed, viral replicative activity may be low, making culture difficult (sensitivity 19 to 27% for late-stage crusted lesions). Furthermore, HSV PCR sensitivity and specificity of skin lesions in pediatric patients has not been well-established. As such, as we try to establish in our case report, herpetic whitlow of the digits is primarily a clinical diagnosis which is often made only after failure to respond to antibiotic therapy and following the clinical course. As such, making the clinical diagnosis without confirmatory HSV testing may help to avoid surgical intervention and additional unnecessary antibiotic therapy.

In an immunocompetent host, herpetic whitlow is usually self-limited over a span of a few weeks; therefore, treatment is largely supportive [10,19]. The lesions should be covered with a dry dressing to prevent viral shedding [19,22]. Treatment may also include analgesics, as well as antibiotics in cases with possible bacterial super infection [20]. Studies report that topical acyclovir provides no clear benefit for herpetic whitlow. Using oral or IV antiviral medications to treat primary herpetic whitlow has not been extensively studied, thus the efficacy of utilizing this course of therapy is unknown [18]. However, oral acyclovir for recurrent HSV-2 herpetic whitlow reduces both symptom duration and positive viral cultures [23], and systemic acyclovir is definitively indicated in immunocompromised patients with herpes virus infection of any form [24]. Despite the lack of conclusive evidence, anecdotal reports of existing whitlow lesions successfully treated with acyclovir have been reported [25], with some advocating for IV acyclovir treatment for initial episodes of herpetic whitlow or any severe whitlow infections accompanied by constitutional symptoms [26].

Although not commonly seen in the pediatric population, herpetic whitlow should be carefully considered in the differential diagnosis of a finger or toe infection. Often mistaken for cellulitis, paronychia, or bacterial felon [10,19,2], a 2001 review of 26 pediatric herpetic whitlow cases revealed that a correct diagnosis upon initial presentation occurred in only 6 (23%) [18]. This delay in establishing a correct diagnosis led to inappropriate antimicrobial use in 15 cases (65%) [18]. Other studies have also found pediatric herpetic whitlow misdiagnosis to be quite common, with many physicians even unaware of the existence of this rare HSV manifestation [19,27,28].

In addition to unnecessary antibiotic exposure and delayed diagnoses, failing to identify herpetic whitlow as the presenting symptom of HSV can result in severe and suboptimal clinical outcomes. Encephalitis has been reported following surgical incision in a pediatric patient with herpetic whitlow [18], and an elevated risk of HSV-2 meningitis should likewise be considered with only subtle central nervous system symptoms in children presenting with herpetic whitlow [29]. Herpetic whitlow also can be the first sign of an underlying immunocompromised state, as reported in a 10-year-old girl later diagnosed with human immunodeficiency virus (HIV) [9]. Immunocompromised patients are at increased risk of developing atypical, severe, prolonged, and invasive herpes infections [24,30]. Other known complications of herpetic whitlow include bacterial superinfection, nail dystrophy, permanent nail loss, local hypoesthesia, secondary ocular involvement, and systemic viremia [31,32].

There are four pediatric cases of pedal herpetic whitlow in the literature. Szinnai reviewed published pediatric herpetic whitlow case reports between 1970–2000 (n = 43); of which only three cases involved the toes [11,18,33]. Two of these cases were the result of mothers with herpes labialis sucking on orbiting the fingernails of their infants. The third case, which involved autoinoculation from a

child putting their toes in their mouth, is pertinent due to a history of cold sores reported in multiple family members, including the patient's two siblings [11]. In a case report published after the aforementioned literature review, Murphy describes a nine-month-old girl with recurrent episodes of herpetic whitlow; no inoculation method was determined and the parents denied any endogenous or exogenous “toe sucking” [34]. Although oral-pedal autoinoculation has been previously described in the literature, the patient in this case report is significant due to a lack of known herpes infections or history of oral lesions in any close family members or contacts.

We report a case of herpetic whitlow of the great toe in an otherwise healthy infant to urge healthcare providers to consider this rare infection when evaluating an inflammatory process involving an isolated or few digits. In turn, we hope to prevent futile or harmful interventions that delay appropriate care. This case report should serve as a reminder that herpetic whitlow may present anatomically in locations other than the fingers and may afflict otherwise healthy appearing infants with no past history of HSV infection and no obvious predisposing risk factors, except in this case of the history of toes frequently in the mouth.

Figures

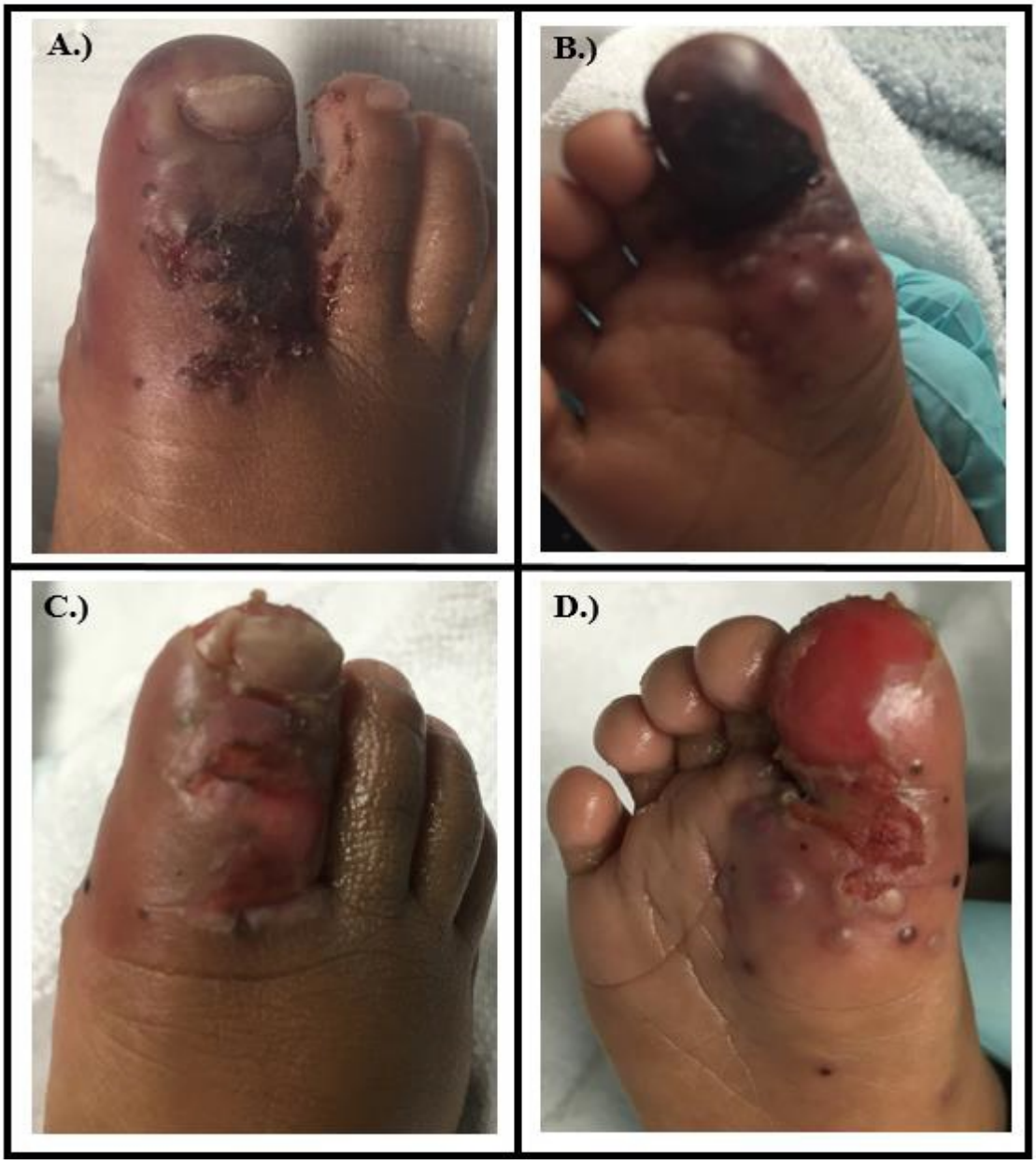

Figure 1: A, Dorsal surface of right foot, 11 days since lesion onset. History of dorsal great toe blister, since popped. Right great toe black eschar, erythema, and swelling present, with partial skin sloughing. **B**, Plantar surface of right foot, 11 days since lesion onset. Erythema, swelling, multiple blisters, and black eschar on great toe and distal medial plantar surface. Discrete pustular, vesicular lesions on a dark purple base, nontender to palpation. Area of desquamation on medial plantar surface.**C**, Dorsal surface of right foot, 12 days since lesion onset (24 hours after Fig1A). Status-post bedside debridement by normal saline foot soaks, great toe eschar sloughed off exposing erythematous denuded skin. Significantly decreased erythema and swelling. **D**, Plantar surface of right foot, 12 days since lesion onset (24 hours after Fig1B). Status-post bedside debridement by normal saline foot soaks, great toe eschar sloughed off exposing erythematous denuded skin. Discrete punctate lesions scattered on distal sole of foot grouped at base of great toe, non tender to palpation, consistent with herpetic whitlow.

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