CLINICAL IMAGES

Pediatric Nasal Rash

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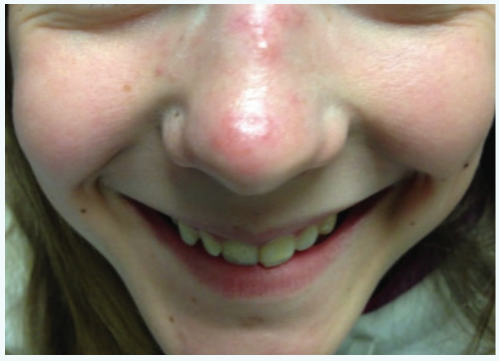
A 13-year-old white female presented with a two-day history of a rash on the dorsum of her nose. The patient stated she was outside all weekend playing soccer in the sun without sun protection prior to appearance of the rash. The patient described an itchy sensation to the dorsum of her nose prior to lesions appearing. The rash has been recurrent on her nose at least one or two times per year for six years and it usually follows history of sun exposure. It presents in a similar manner with each episode: an itchy prodromal period followed by groups of small, fluid filled lesions lasting approximately three days before crusting over. The inflammation and crusting persists for about a month with each episode before resolving completely. Prior occurrences of the rash have been treated with topical antifungals without relief. She denies blurry vision, diplopia, orbital pain, burning sensation on nose, similar lesions elsewhere on her body, or any close contacts with similar rash. The patient denies other medical problems or skin conditions. She does have family history of rosacea.

QUESTIONS:

1. What is the most likely diagnosis?
   a. Acne Vulgaris
   b. Herpes Simplex Virus
   c. Impetigo
   d. Phytophotodermatitis
   e. Solar urticaria

2. How would you diagnose this rash?
   a. History and physical examination
   b. Skin Biopsy
   c. Tzank smear
   d. Viral Culture
   e. All of the above aid in diagnosis

3. What is the appropriate treatment?
   a. Acyclovir
   b. Mupirocin
   c. Benzoyl peroxide wash
   d. Metronidazole cream
   e. Topical clindamycin



ANSWERS

1. What is the most likely diagnosis?

The correct Answer is: B) Herpes Simplex Virus

Fluid filled vesicles in a grouped manner as seen in the patient photograph is consistent with herpes simplex virus. Acne vulgaris would not necessarily have the sensation of pruritus or outbreak after sun exposure, and lesions often appear more pustular in nature. Acne typically begins at puberty due to hormonal influence, yet this patient had onset of this recurrent rash since the age of seven. Solar urticaria may present with pruritus and erythema but is associated with wheal formations that typically resolve 24 hours after cessation of sun exposure.[1] Phytophotodermatitis is an inflammatory skin reaction that develops following cutaneous contact with photoactive compounds and exposure to ultraviolet light. There was no known contact with such compounds on her nose.[2] Impetigo is a very contagious bacterial infection caused by Streptococcus or Staphylococcus. It often is associated with history of trauma to the skin and appears as vesicles or pustules that rupture and leave behind a characteristic honey colored crust.[3]

2. How would you diagnose this rash?

The correct Answer is: E) All of the above aid in diagnosis

All of the above may aid in the diagnosis of the pictured rash. History and physical exam will be the best clue to diagnosis as grouped fluid-filled vesicles with prodromal period is classic for HSV. The most commonly used diagnostic test is the Tzanck smear, a nonspecific test which will reveal to the provider if the skin infection is associated with a member of the herpes virus family.[4] Skin biopsy and viral culture are also effective means of diagnosing the rash.

3. What is the appropriate treatment?

The correct Answer is: A) Acyclovir

Episodic treatment options for recurrent herpes labialis includes acyclovir 500mg five times a day for five days, valacyclovir 2g twice daily for one day, or famciclovir 125mg twice daily for five days (or 1500mg once daily for one day). In order for this episodic therapy to be effective, the patient must start therapy within one to two days of lesion onset or during the prodromal period.[5] Topical antibiotics, such as Mupirocin and topical clindamycin are not indicated for treatment of viral skin infections unless the lesions become secondarily infected with bacteria. Benzoyl peroxide wash is a treatment option for acne vulgaris. Metroniadazole cream is a commonly used topical agent for treatment of rosacea.

DISCUSSION

Herpes Simplex virus is a ubiquitous double-stranded enveloped DNA virus that infects both children and adults.6 Herpes simplex virus type-1 (HSV-1) and type-2 (HSV-2) belong to the Alphaherpesvirinae subfamily of the large Herpesvirus family.[6,7] Worldwide, greater than one-third of people have recurrent HSV infections.[7] The virus infects by destroying the host cell and becoming latent in the sensory ganglia of nerves, most commonly the trigeminal ganglion in HSV-1 and the sacral ganglion in HSV-2.[6] HSV-1 generally infects above the waist as orolabial lesions at the vermillion border called herpes labialis. HSV-2 is most frequently associated with genital herpes and neonatal infections passed along from a mother with genital herpes during the birthing process. HSV-2 has been linked to oral mucosal infections, however the incidence is much less than HSV-1.[6,7] This discussion will be focused on non-genital HSV infections.

Herpes simplex virus infection is one of the most prevalent infections in the world, with humans being the sole reservoir.[4,6] Between 30% and 95% of adults are seropositive for HSV-1 worldwide, with HSV antibodies in nearly 90% of adults by the fifth decade.[8,9] HSV-1 infection is generally transmitted during childhood or adolescence via non-sexual contact with infected saliva, though it may be transmitted in young adulthood through sexual contact.[10] Viral shedding can occur in an asymptomatic state; therefore, it is important to note that all individuals infected with HSV are potentially infectious even with no apparent signs or symptoms of disease.[4]

HSV infections occur in a susceptible host when the virus enters through a break in the skin or mucous membrane. The virus may be transmitted by sharing utensils, sharing towels, or kissing. HSV minimally replicates at the inoculation site before entering the cutaneous neurons. The virus then travels in a retrograde fashion along the axons to the sensory ganglia where it will establish lifelong latency.[11] The classic oral HSV-1 infection reactivates from the trigeminal ganglia which may lead to facial, labial, buccal, or ocular mucosal lesions. A visible skin lesion appears when the virus travels to the original entry site via the sensory nerve fibers. When it reaches the skin, it replicates and destroys the surrounding epithelial cells leading to the appearance of vesicular lesions. These lesions are filled with virus, cell debris, and inflammatory cells.[11] The above patient was likely infected with HSV-1 of the ophthalmic branch of the trigeminal ganglion.[12] Of note, this is not to be confused with Hutchinson's sign caused by Herpes Zoster, which also involves the ophthalmic branch of the trigeminal ganglion. This rash is generally located on the tip of the nose, but typically does not cross the midline.[12]

The establishment of lifelong latency with brief periods of mucocutaneous outbreak is a key feature of the HSV viral infections. The time in latency likely depends on factors including the amount of neurons infected during the primary episode, the amount of neurons involved with the reactivation periods, and recruitment of additional neurons with each recurrent episode.[11] The average number of HSV-1 outbreaks is one to six per year.[13] Reactivation of the virus is stimulated by direct trauma to the skin or mucosa innervated by peripheral nerve, ultraviolet –B exposure, physical or emotional stress, hormonal changes, menstruation, fever, immunosuppressive agents, or other infections.[7,11] The most likely cause of our patient's outbreak was extensive UV-B exposure while playing soccer.

The clinical appearance of herpes simplex lesions characteristically involves a group of small vesicles on an erythematous base about 1 to 2 mm in diameter. The grouping of vesicles is a clue to the diagnosis. These vesicles may contain a clear to cloudy fluid. The vesicles rupture and painfully ulcerate forming a hemorrhagic crust. This crust will resolve and leave an area of erythema that typically clears in 2 to 6 weeks.[13,15]

The primary mucocutaneous lesions appear approximately 3 to 7 days after initial exposure to the virus. This first episode is often accompanied by a generalized flu-like prodrome of tender cervical lymphadenopathy, fever, inability to eat, myalgias and malaise.[8,14] Pain, burning, tingling, or pruritus at the initial site of inoculation are characteristic symptoms of the reactivation prodrome.[14] The primary infection tends to be more severe than the recurrent infections.[16] Subsequent episodes of cutaneous presentation are often associated with fewer vesicles and shorter duration.[14] The differential diagnosis of HSV-1 infection includes aphthous ulcers, Behcet syndrome, herpangina, varicella-herpes zoster infection, impetigo, and pemphigus vulgaris.

HSV-1 or 2 can be diagnosed via specific or nonspecific laboratory tests. The most common diagnostic method is the Tzanck smear, a nonspecific test that will reveal to the provider if the skin infection is associated with a member of the herpes virus family. A more specific means of diagnosis is the direct fluorescent antibody test that identifies the virus subtype. Viral culture is a specific test, and an alternative to serological testing, which will provide results in as little as 2-3 days.[4] This patient was diagnosed with herpes simplex viral infection via viral culture. Polymerase chain reaction (PCR) testing is as specific as, and four times more sensitive than viral culture. A skin biopsy will reveal HSV-induced viropathic changes and special staining techniques may be performed on the tissue sample to confirm the diagnosis. The lesion morphology at the time of presentation and sampling ultimately determines the accuracy of these tests. Vesicular lesions will likely be positive with Tzanck smears, while crusted, ulcerative lesions are best diagnosed by culture, PCR, skin biopsy, or fluorescent antibody testing.[4]

The treatment of herpes infections is personalized to the individual based on a number of factors including frequency of recurrence, the cost of treatment, and impact on quality of life. Since UV-B sunlight is a common trigger for orolabial lesions, applying sunblock daily to the face and lips may reduce the rate of recurrence.[4] Topical antiviral therapy, such as topical acyclovir ointment, has proven to be minimally effective with no impact on symptom relief or healing time.[4,13] The recommended treatment for a primary orolabial herpes infection is acyclovir 15mg/kg orally five times a day for 5-10 days.[5,13] Treatment options for episodic therapy of recurrent herpes labialis infection includes acyclovir 400mg five times a day for five days, valacyclovir 2g twice daily for one day, famciclovir 125mg twice daily for five days, or famciclovir 1500mg once daily for one day.[5,13] In order for this episodic therapy to be affective, the patient must start the medication within one to two days of lesion onset or during the prodromal period.[5,13]

Suppressive therapy is the gold standard treatment option if transmission is a concern or if the patient experiences greater than five episodes per year. Episodic therapy will not reduce the risk of transmission. Acyclovir 400mg twice daily is recommended for suppressive therapy.[5] The patient can also prophylactically treat with antivirals prior to known triggers such as skiing, tropical vacations, or dental/surgical procedures to reduce the risk of a subsequent outbreak.[4] The patient in this case was placed on acyclovir 400 mg by mouth three times day for seven days and reported that her lesions cleared in two days. Application of sunblock to her face was also recommended prior to sporting events to reduce the risk of subsequent outbreak with the UV-B exposure.

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