

# Painful Bubbles

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A 25 year-old female with a past medical history of well controlled eczema presented to her primary care physician with a one week history of a painful “bubbles” localized to her right antecubital fossa as seen in Figure 1. She noted that the new rash appeared to form overnight, was extremely painful, and would occasionally drain a clear liquid after scratching. It did not respond to her usual over-the-counter regimen of moisturizers prompting her to be evaluated. She had subjective fevers and malaise but denied oral or genital ulcers, vaginal discharge, dysuria, ocular irritation, visual disturbances, and upper respiratory or gastrointestinal symptoms. Review of systems was otherwise unremarkable.

She had no other known medical problems, allergies, and denied drug and alcohol use. She denied any recent travel, sick contacts, pets, or OTC medications/creams. She was sexually active in a monogamous relationship for over a year.

## QUESTIONS

1. What is the most likely diagnosis?
  - A. Cellulitis
  - B. Eczema herpeticum
  - C. Impetigo
  - D. Primary varicella infection
2. Which test should be performed initially?
  - A. Blood culture
  - B. Direct fluorescent antibody staining
  - C. Tzanck smear
  - D. Wound culture
3. What is the best treatment?
  - A. Acyclovir
  - B. Augmentin
  - C. Doxycycline
  - D. Varicella Zoster Immune Globulin

FIGURE 1:



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## ANSWERS

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

Correct answer: B) Eczema herpeticum

Eczema herpeticum is characterized by painful symmetric clear to yellow colored vesicles in areas previously affected by atopic dermatitis or eczema with a superimposed infection with HSV1 or HSV2. The rash appears as fluid-filled blisters that are pruritic and painful typically affecting the face or neck. The blisters are usually monomorphic, meaning that they appear similar to one another and are not in various stages of healing which is classically seen with Varicella zoster. Newly formed blisters may exhibit central umbilication, which could be mistaken for molluscum contagiosum. The fluid within the blisters can be thin yellow fluid or thick and purulent which can leak or weep from the site. The blisters can bleed at times as well.<sup>1</sup>

The differential diagnosis of eczema herpeticum includes impetigo, bacterial superinfection, and primary varicella infection (chickenpox).<sup>2</sup> Chickenpox or primary varicella infection is an infection with Varicella zoster virus typically occurring in children. The incidence has been effectively decreased 79% overall with the Varicella zoster vaccination and active surveillance.<sup>3</sup> A history of non-adherence to vaccination schedules along with vesicles in various stages of healing would help differentiate chickenpox from eczema herpeticum which is characterized by vesicles all of the same stage.<sup>4</sup> Impetigo is a bacterial infection of the soft tissue caused by Staphylococcus or Streptococcus species. Impetigo's appearance is classically described as vesicles with honey-colored crusting near the nose, mouth or on the extremities. This is primarily a clinical diagnosis.<sup>5</sup> Cellulitis is a bacterial infection of the subcutaneous and dermal layers of the skin most commonly caused by Staphylococcus or Streptococcus species. Physical exam will reveal a warm, indurated, homogenous erythematous plaque or patch at the area of infection.<sup>5</sup>

### 2. What test should be performed initially?

Correct answer: C) Tzanck smear

Confirmation of this diagnosis can be made with one of four ways: viral DNA on PCR, viral culture, presence of HSV-infected cells from blister fluid with immunofluorescence(DFA) or through a Tzanck smear.<sup>2</sup> Clinically the first test to be performed is a Tzanck smear which can be helpful when combined with history and physical examination. Tzanck smear has a sensitivity greater than 80% and specificity of 90% that is dependent on the experience of the evaluator.<sup>6</sup> This test is performed by unroofing the vesicular lesions and scraping the base with a scalpel. The skin obtained from the base is then placed onto a slide for evaluation with light microscopy for the presence of multinucleated giant cells which indicates infection with HSV or VZV.<sup>2</sup> Direct fluorescent antibody(DFA) staining and PCR confirm the diagnosis after initial clinical testing.<sup>7</sup> DFA staining has a sensitivity as high as 90% for HSV which is primarily dependent upon proper sampling technique and PCR has a sensitivity of 93% with specificity of 100%.<sup>8,9</sup> DFA staining is resulted within hours while PCR takes at least 48 hours to result lending some benefit to DFA in comparison to PCR if rapid definitive diagnosis is needed.<sup>7</sup>

Blood cultures can be obtained for concern of systemic symptoms with a bacterial soft tissue infection especially in patient that are immunocompromised or of advanced age but would not be helpful in this case.<sup>4</sup> Wound cultures are also indicated in bacterial soft tissue infections when patients have a history significant for an immunocompromised status, large and recurrent abscesses or bites from humans or animals but would not be helpful in this case unless specific requests for viral culture are made.<sup>4</sup>

### 3. What is the best treatment?

Correct answer: A) Acyclovir

Treatment of eczema herpeticum is an antiviral agent such as oral acyclovir as the underlying cause is HSV type 1 or type 2. Acyclovir is a guanosine analog and becomes incorporated into the viral DNA and ceases viral replication.<sup>10</sup> In neonates or extensive systemic cases, intravenous acyclovir is required.<sup>11</sup> Intramuscular Varicella Immune Globulin is prophylactic against chickenpox, VZV, and is reserved for use in neonates exposed in utero and immunocompromised children according to the CDC.<sup>12</sup> Augmentin is used in treatment of impetigo.<sup>4</sup> Doxycycline is used in treatment of soft tissue infection concerning for MRSA involvement.<sup>4</sup>

## DISCUSSION

Eczema herpeticum (EH), also known as Kaposi's varicelliform, occurs when the compromised dermal barrier from atopic dermatitis becomes infected with a primary or reactivation infection with HSV-1 or HSV-2.<sup>2</sup> HSV-1 is widely prevalent in the general population with 20% of children and 60% of adults testing seropositive. Despite the ubiquity of HSV-1, only 3% of patients with eczema will develop eczema herpeticum.<sup>13</sup> The patients will present with widespread monomorphic vesicular lesions typically affecting the head, neck and trunk with systemic symptoms of fever, malaise and lymphadenopathy.<sup>2</sup> Lesions can be expected to dry and become eroded or "punched out" pits at about two weeks after vesicular eruption. The dried lesions can tense the overlying skin and crack during this time. Healing and full resolution can take up to six weeks.

Eczema, also known as atopic dermatitis, affects 15-20% of the population in developed countries such as the United States.<sup>14</sup> This chronic skin disorder can occur in a triad with two other disorders: asthma and allergic rhinitis which when combined constitutes the "atopic triad."<sup>11</sup> Atopic dermatitis (AD) severely affects the epidermal layer and its protective capabilities due to the breakdown of the skin barrier with atopic dermatitis, the skin is more susceptible to infection with bacteria (typically *Staphylococcus aureus*) as well as viruses (Herpes simplex), more rarely.

Diagnosis is typically clinical although can be supported with a Tzanck smear showing multinucleated giant cells from ulcer base sampling in the clinical setting. This test is supportive and not confirmatory in that it is neither sensitive nor specific for HSV. Confirmation can be made with the use of direct immunofluorescent antibody testing, commercial immunofluorescent tests, viral DNA PCR or viral culture.<sup>2</sup> Blood cultures are useful when concern of bacterial soft tissue infection from skin breakdown is suspected, especially in patient that are immunocompromised.<sup>5</sup> Wound cultures could be obtained although a specific request for viral culture must be made when sending the sample to the lab.<sup>5</sup>

Treatment is managed with an oral antiviral (acyclovir) to decrease disease severity and reduce the chance for viremia and other systemic complications.<sup>2</sup> Dosing is 400 milligrams three times a day for 7 to 10 days. In cases indicated by high fevers, inability to maintain adequate nutrition and hydration or superimposed bacterial infection, the patient should be hospitalized and acyclovir administered via intravenous route for 7 days at a dose of 5-10mg/kg per dose at a frequency of three times daily in order to effectively treat these severe systemic cases. For patients less than 12 years old the dose is reduced to 750 mg/m<sup>2</sup> per dose although the frequency and total treatment days remain the same at three times daily and 7 days, respectively.<sup>2</sup> Pre-administration baseline creatinine levels should be drawn before the use of oral acyclovir to monitor for nephrotoxic complication. Before the administration of antiviral medication was widely accepted the mortality rate was 75%.<sup>2</sup> Appropriate measures to moisturize the vesicles should be made to avoid dry skin and subsequent cracking leading to a greater likelihood of bacterial infection.<sup>2</sup>

Complications include herpetic keratitis, meningitis and encephalitis making the need for ophthalmic evaluation essential, especially patients complaining of visual blurring, pain and discharge.<sup>2</sup> Careful monitoring of the patient must be performed for symptoms

concerning for central HSV infection such as headache or confusion. If left untreated, infection can become disseminated or develop a secondary bacterial infection which leads to death.<sup>11</sup>

In this case, confirmation of HSV-1 was made via viral polymerase chain reaction. The patient was treated with a course of acyclovir for seven days and the rash resolved within a week. Upon further questioning her baseline eczema had been worsened by her recent increase in water exposure after joining the local aquatic center, likely predisposing her to infection. The patient now is more vigilant and more consistently uses moisturizer to avoid future eczema exacerbations.

## AUTHOR DISCLOSURES:

No relevant financial affiliations.

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