Erythema Multiforme following Smallpox Vaccination

22 yo Female previously healthy ER clerk S/P smallpox returns for a take check on day 7 post-vaccination. She complains of 2 days of subjective fever, mild headache, fatigue, myalgias and regional lymphadenopathy. She reports that she has bed-bound due to constitutional symptoms for the preceding 3 days.

On exam she is mildly ill-appearing.
Temp 100.7F, B/P 110/70, P112. and delayed cap refill.

HEENT: Dry mucous membranes
Lungs: clear
CV: No gallop
Abd: soft, no tenderness to palpation
Back: Right costovertebral angle tenderness
Ext: delayed cap refill
Skin: Right deltoid 1cm pustule on erythematous base at vaccination site

UA: sp grav 1.020, WBC TNTC
CBC: 12K WBC with left shift
Urine Cx Pending
Blood Cx Pending

Assessment:
1. Pyelonephritis
2. Major reaction s/p smallpox vaccination

Plan:
1. S/P bolus of 1L normal saline
2. Ceftriaxone 1gm IV
3. Sulfa-Trim 500mg BID x 10 days
4. Return to clinic 3 days, sooner for worsening of symptoms

3 days later she presents for follow-up.
Overall she is feeling better but notes new onset pruritic rash x 24 hours for which she has been taking benadryl prn.

Exam reveals a healing vaccination site with early eschar formation. Diffuse symmetrical erythematous macular lesions patches on the trunk, extensor surfaces, palms and soles. Upon closer inspection, the lesions are noted to have a dull red to dusky sharply demarcated wheal, with a central papule and surrounding halo of clearing. Mucosal membranes are intact.

She is diagnosed with Erythema Multiforme, the state health official contacted and a VAERS form filled out.

1. **What features in the history and physical support this diagnosis?**

   - *The hallmark "iris" or "targetoid" lesion.*

2. **What do you think was the etiology for the EM?**

   - *Onset interval of symptom is consistent with post-vaccinial EM (day 10). Drug hypersensitivity, food, systemic disease and infection (e.g., HSV or mycoplasma) are other potential etiologies of EM. Patients presenting with hypersensitivity rashes should be evaluated for non-vaccinial etiologies, as well.*

3. **What is the expected time course from onset to resolution?**

   - *[description of EM following other infectious organisms] The evolution and resolution of individual lesions can last a week. However, lesions may continue to appear in crops for as long as 2-3 weeks. Overall the rash can last less than 4 weeks from initial onset of symptoms to resolution.*

4. **What do you want to watch this patient closely for over the next few days?**

   - *Stevens-Johnson (Erythema Multiforme Major): involvement of 2 mucosal surfaces or >10% of body surface area.*

5. **How do you treat this illness?**

   - *Supportive care with antipruritics. VIG is not indicated. Consider discontinuation of sulfa drug.*

6. **What infection control precautions should be used in this case?**

   - Routine care of vaccination site. No special precautions for the generalized rash of EM, because virus is not thought to be present in the lesions.

7. **Any special considerations for handling the blood and urine cultures that have been obtained?**

   - *No. The vaccinia virus is not viable in media that is used for routine bacterial culture. If, at time of diagnostic evaluation, vaccinia virus is suspected, a viral culture may be obtained. Prior to collecting the viral culture, you must ensure that your laboratory is certified as a BSL 2 (biosafety lab level 2) and that the laboratorians have been appropriately vaccinated with vaccinia.*

- *The diagnoses of smallpox vaccine adverse events are based on clinical evaluation and history. Currently diagnostic vaccinia testing is not approved for clinical decision-making.*

- *Check out the following link for instructions on how to collect specimens for vaccinia:*

- *http://www.bt.cdc.gov/agent/smallpox/vaccination/vaccinia-specimen-collection.asp*

8. **How soon should the VAERS form be submitted?**

- *Within one week. Recall:*

  - *<u>Serious/unexpected requiring CDC consultation or request for VIG/CDV release</u> – DO NOT DELAY IN SEEKING ASSISTANCE. Contact State Health Department or CDC to obtain clinical consultation or to request IND therapeutics. The CDC will assist in filling out a VAERS form*
  - *<u>Serious but does not require CDC consultation / request for IND therapeutics</u> – 48 hours*
  - *<u>All others</u> – within one week*

9. Can she be revaccinated with smallpox vaccine?

- *According to Goldstein JA, Neff JM, Lane JM, Koplan JP. Smallpox vaccination reactions, prophylaxis, and therapy of complications. Pediatrics 1975;55(3):342-347, this patient would not have had a contraindication to revaccination during the era of routine childhood vaccination.*

  ……..revaccination of children with a history of inadvertent inoculation or erythematous or urticarial rashes presents no known or theoretical risk. Revaccination of children who have had eczema vaccinatum is not contraindicated; individuals with a history of post-vaccinial central nervous system disease (PVE/PVEM) should not be revaccinated.

DISCUSSION POINTS:

1. Some individuals feel sufficiently ill that they fail to maintain proper hydration.

2. Name some features that help distinguish the spectrum of rashes that are associated with smallpox vaccination.

    a. **Nonspecific rashes:** Erythematous rash +/- papules with absence of vesicles or pustules (onset ~10 days post-vaccination)

    b. **Erythema multiforme:** hallmark targetoid lesion (onset ~10 days post-vaccination)

    c. **Generalized vaccinia:** Vesicular or pustular lesions. When significant erythema is present, might be confused with EM. (onset 6-9 days post-vaccination)

    d. **Eczema vaccinatum:** Vesicular or pustular lesions that might be confluent with/without umbilication (predilection for site of atopic dermatitis eruptions). Tends to occur in persons with history of eczema or atopic dermatitis, but has been described less frequently in persons with other dermatologic conditions.

GOALS:

1. Describe the spectrum of nonspecific rashes occurring after smallpox vaccination.
2. Review infection control precautions in hypersensitivity reactions.
3. Review laboratory requirements for handling vaccinia testing.
4. Review timeline for VAERS submission.