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EM CASE OF THE WEEK

BROWARD HEALTH MEDICAL CENTER: DEPARTMENT OF EMERGENCY MEDICINE

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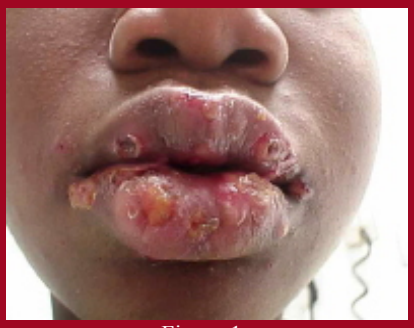

Figure 1.
Emedicine Health, 27 Feb. 2015. Web.

In the ED, it is important to have a wide differential diagnosis when a patient presents with skin lesions. Possible causes can include infectious, autoimmune, immunocompromise, allergic, or a combination of these, amongst others.

Mucocutaneous Lesions

A 33 year old male presents with oral pain, oral lesions, and pruritic skin lesions for 3 days (Figure 1). Other symptoms include subjective fever, decreased PO intake secondary to pain and cough with productive sputum. Patient denies nausea, vomiting, or weight loss. This is the first episode the patient has had like this. In addition, patient denies a history of allergies, new medications, or any significant past medical history. Vital signs include: T 101.7, RR 18, BP 113/85, HR 89, O2 Sat 97% on RA. Physical exam reveals oral ulcers, oral thrush, and inflammation, with multiple pruritic maculopapular skin lesions, and penile ulcers with associated whitish discharge. Labs include WBC 14.3, with the remainder of the CBC and CMP WNL. What is the most important treatment for this patient's likely condition?

A. PO azithromycin and doxycycline

B. IV fluconazole

C. Supportive care including but not limited to IV fluids, Motrin, Toradol, and Tylenol

D. PO prednisone

E. PO acyclovir

F. Topical bacitracin/mupirocin

G. PO levofloxacin

EM CASE OF THE WEEK

EM Case of the Week is a weekly "pop quiz" for ED staff. The goal is to educate all ED personnel by sharing common pearls and pitfalls involving the care of ED patients. We intend on providing better patient care through better education for our nurses and staff.

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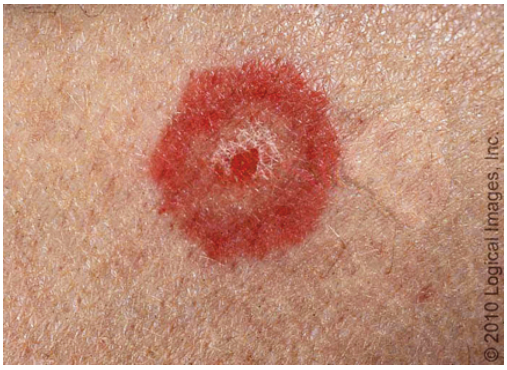

Figure 2.
UpToDate. N.p., 30 Apr. 2014. Web. 25 Nov. 2015.

Take Home Points

- Erythema Multiforme (EM) has many etiologies, including infectious, toxic, autoimmune, and many others. The most common is infectious, especially with HSV and Mycoplasma.
- EM is an immune-mediated condition. The classic "target" lesions, along with the history and remainder of the physical exam, are usually enough for diagnosis.
- It is possible for EM to look similar to many other diseases, so it is important to keep a wide differential diagnosis upon initial exam.
- Mild forms of HSV-induced EM receive symptomatic treatment.
- Severe oral/mucocutaneous forms of EM are treated with 2-3 weeks of systemic glucocorticoids.

Erythema Multiforme/HSV infection

The correct answer is D. The most likely disease process in this patient is erythema multiforme (EM) secondary to oral-genital mucocutaneous Herpes Simplex Virus infection. Treatment includes prednisone without the use of antivirals. HSV-induced EM occurs an average of 8 days after the development of HSV infection. At this point in the disease course, treatment for the HSV infection itself is no longer indicated.

Discussion:

Etiology: Many causes have been linked to the cause of EM. These include, but are not limited to: infectious, medication-induced, malignant, autoimmune, radiation-induced, sarcoidosis-related, and menstrual. The most common etiology by far is infectious, which accounts for around 90% of all causes. Infectious causes can include viral, bacterial, or fungal. HSV is the most common infectious cause of EM.

HSV-induced EM is thought to be caused by a cell-mediated immune process in which CD8+ cells target lesions in the skin that contain the HSV antigens. Subsequently, the theory is that this results in the typical "target" lesions (Figure 2).

There is debate about the association of EM with Stevens-Johnson Syndrome and Toxic Epidermal Necrolysis. However, this association is more commonly correlated with drug exposure as the inciting cause. For the purposes of this article, we will be discussing EM due to infectious causes.

Clinical Manifestations: Erythema Multiforme (EM) is an acute, immune-mediated condition in which distinct target lesions appear on cutaneous areas. Target lesions are comprised of 3 components: a central blister or ulcer surrounded by a pale area, which is then further surrounded by a dark red inflammatory zone. These lesions will often be pruritic with a burning pain. Often, patients will have associated bullae or erosions that involve the oral and genital mucosal surfaces. Oral involvement has been reported to be present in around 70% of patients with cutaneous HSV-induced EM. In the case of extensive oral lesions, patients may complain of severe odynophagia. This may lead to dehydration as patients will not be able to tolerate oral food or liquids. *cont'd next page*

Clinical Manifestations (cont'd): Patients may complain of systemic symptoms, especially in more severe cases of EM. Fever, myalgias, and malaise can be common. In cases of infectious EM due to agents that cause pneumonia, cough and other respiratory symptoms may be present.

Clinical Course: Mucocutaneous EM lesions due to HSV occur anywhere from 2 to 17 days (mean interval day is 8) after an episode of acute HSV infection. Due to the recurrence of HSV infectious manifestations, EM may recur as well. Non-HSV induced EM lesions usually appear for 3-5 days and typically will resolve within 14 days. There may be significant post-inflammatory hyperpigmentation that can remain for months.

Differential Diagnosis: The differential diagnosis for conditions causing a similar presentation to EM is very large.

Urticaria can be erythematous and edematous pruritic plaques on the skin. However, they lack the typical "target" lesion with the central bullae, ulcers, or erosions found in EM. Also, individual urticarial lesions only last for 24 hours or less and new lesions will continuously occur. In EM, the lesions will all appear within the first 72 hours of disease onset.

Stevens-Johnson syndrome lesions tend to be macular, rather that the raised, papular lesions found in EM. Medications are also the most common cause of SJS, rather than infection as occurs in EM.

Bullous pemphigoid is a chronic autoimmune disorder with bullae. Urticaria, erythematous plaques, and bullae can be present on skin and mucosal surfaces as well. "Target" lesions are rare in pemphigoid, and the epidermal necrosis seen in EM is less common. Biopsy may be required to differentiate these two.

Sweet syndrome lesions appear similar to those of EM. Biopsy will reveal neutrophilic infiltrates. Biopsy of EM will include basal cell vacuolar degeneration, necrotic keratinocytes, and lymphocyte exocytosis.

Diagnostic Work-up: History of present illness and physical exam are the most important pieces of information when considering a diagnosis of EM. It is also useful to look for other signs or symptoms of common infectious agents of EM, including HSV and Mycoplasma. For HSV, mucocutaneous ulcers can be helpful. Mycoplasma will typically also present with a dry cough for weeks.

In the cases of more severe disease and dysphagia, clinicians should assess for fluid and electrolyte imbalances. A CBC may also help to get a sense for the severity of infection. Serologic HSV testing may be considered as well.

Clinicians may order a series of labs to rule out other potential causes including gonorrhea/chlamydia, syphilis, respiratory pathogens, and HIV. Biopsy may be considered if the previous diagnostic workup is unclear. Active lesions can be sampled using direct fluorescent antibody, viral culture, Tzanck smear, or PCR studies to confirm the presence of HSV.

Treatment in Acute EM: Inciting Agents: The lesions in HSV-induced EM don't appear until approximately 8 days after the onset of disease. Oral antivirals have not been shown to affect the clinical course at this point. No formal studies have been performed on the 2nd most common cause, Mycoplasma. In general, treatment can be administered as treatment for an active infection for infectious agents other than HSV as acute infection is more common with

In patients with only cutaneous involvement or limited mucosal involvement, symptomatic relief is the only recommended therapy. Topical steroids or antihistamines may be used for pruritus.

In patients with severe oral mucosal involvement, the recommended therapy is systemic glucocorticoids, typically oral prednisone 40-60 mg/day and tapered over 2-3 weeks.

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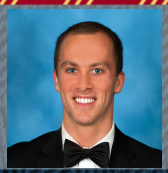

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This month's case was written by Thomas VerHage. Thomas is a 4th year medical student from NSU-COM. He did his emergency medicine rotation at BHMC in November 2015. Thomas plans on pursuing a career in Pediatric Cardiology after graduation.