

## Case

- ❖ 27-year-old female
- ❖ **PMHx:** No significant past medical history
- ❖ **Initial Visit**
  - History of Present Illness
    - Presented one day after onset of fever, sneezing, cough, body aches, and pruritic rash which started on abdomen/chest
    - Associated with swollen and erythematous eyes, though no ocular pruritis or discharge
    - Denied pain with swallowing, itchy throat, wheezing, diarrhea
    - Endorsed sick contacts
    - No history of herpes simplex virus
  - Physical Exam
    - Discrete pruritic lesions over her extensor surfaces, sub-mandibular region, and chest with palpable target lesions ranging from 0.5 to 2 cm with a central bullseye, an adjacent clearing, all surrounded by a bold erythematous ring
    - No central ulceration
    - Inconsistent scaling along the periphery
    - Periocular swelling and confluent non-raised erythema with clear demarcation. No warmth, tenderness or drainage. Conjunctiva clear
    - Oral mucosal and genitourinary sparing
- ❖ **Treatment Course**
  - Treated with prednisone 40 mg daily for 5 days
  - An influenza test was positive for influenza A
  - All lesions resolved by day 4 of prednisone
- ❖ **Follow-Up**
  - Full symptomatic resolution by day 4.
  - Physical exam with residual mild pharyngeal erythema otherwise unremarkable
- ❖ **Posttreatment recurrence:** No recurrences to date
- ❖ **Assessment**
  - 27-year-old female with erythema multiforme associated with influenza A and prodromal symptoms, with ocular and oral sparing successfully treated with quick oral prednisone taper and no recurrences to date
- ❖ **Future Plan:** Monitoring for recurrence

## Epidemiology

- ❖ Annual incidence is <1%<sup>1</sup>
- ❖ Most common age group 20-40 years old
- ❖ Slight male predominance

## Associated Triggers of Erythema Multiforme

- ❖ Viral:
  - Herpes simplex 1&2 ← cell-mediated response to viral antigens deposited in lesional skin
  - Others: Adenovirus, Varicella, Epstein-Barr, Cytomegalovirus, HIV, Parvovirus B19, COVID-19
- ❖ Bacterial/Fungal: *M. pneumoniae*, *C. psittaci*, *M. tuberculosis*, *Histoplasma capsulatum*, dermatophytes
- ❖ Medications (<10%): NSAIDs, sulfonamides, antiepileptics, penicillins

## Disease Course

### Target & Morphology

- ❖ Typical target (iris) lesions
  - Less than 3cm in diameter with central erosion on erythematous base surrounded by pale edematous rim and an erythematous peripheral halo
- ❖ Distribution: Symmetric extensor surface of extremities -> centripetal spread
  - Oral mucosal involvement (up to 70% of cases) affecting vermilion lip, buccal mucosa, gingiva, tongue<sup>2</sup>
  - Ocular mucosal involvement in an estimated 17% of cases, labial involvement estimated at 25%<sup>2</sup>
  - Systemic: fever, malaise, myalgias; cough/respiratory symptoms (*M.pneumoniae*-induced)



Figure 1. Typical iris lesions in erythema multiforme<sup>3</sup>



Figure 2. Hemorrhagic crusting and tongue ulceration in erythema multiforme<sup>4</sup>

### Diagnostic Modalities

- ❖ Laboratory: Elevated ESR, WBC, transaminitis, trigger identification (HSV PCR, *M. pneumoniae* Ag)
- ❖ Biopsy reveals basal cell vacuolar degeneration, scattered necrotic keratinocytes, lymphocytic exocytosis

**Timeline:** Lesions appear over 3-5 days (HSV-related ~8 days post-episode) and resolve within 2 weeks

## Pathogenesis of Erythema Multiforme

### Cell-mediated immune process

- ❖ Viral
  - Langerhans cell precursor-mediated viral phagocytosis & migration to epidermis via E-cadherin
  - Transfer of viral DNA fragments to epidermal keratinocytes -> dermatological viral expression
  - INF-gamma-induced inflammatory cascade -> Lysis of infected keratinocytes -> cutaneous lesion
- ❖ Drug-related: Above mechanism; exception: TNF-alpha-mediated (as opposed to INF-gamma)

## Treatment & Complications

### Recommended Treatment

- ❖ Cutaneous: Twice-daily medium-potency topical steroid (betamethasone, hydrocortisone, triamcinolone)<sup>5</sup>
- ❖ Limited oral: High-potency steroid gel (fluocinonide 0.05% gel) and Maalox mouthwash<sup>4</sup>
- ❖ Decision to admit is based on compromised oral intake and degree of pain
  - Disabling: prednisone 40-60mg, 2 to 4-week taper<sup>4</sup>

### Complications

- ❖ Keratitis, conjunctival scarring, esophagitis
- ❖ Post-inflammatory hyperpigmentation may last for months
- ❖ Approximately 25-70% recurrence cases are HSV-related<sup>2,6</sup>
  - Others: Recurrent *M.pneumoniae*, etc.

## Discussion

- ❖ Erythema multiforme without compromised oral intake can typically be managed at the outpatient level
- ❖ Topical steroids have been clinically shown to alleviate pruritis and skin discomfort<sup>3</sup>
- ❖ Patients with compromised oral intake may require hospitalization
- ❖ Patients with systemic symptoms may benefit from systemic glucocorticoids, which are not typically used in cutaneous-limited erythema multiforme
- ❖ Significance: No high-quality studies to validate efficacy of oral steroids
- ❖ Potential directions for future investigations
  - Larger-scale: Oral-prednisone treatment for cases associated with non-HSV viral-related prodromal systemic symptoms
  - Do oral steroids help prevent recurrence in patients with non-HSV viral-mediated erythema multiforme?

## References

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