Risky Rashes: A Review of Dermatologic Emergencies

Presenter: Anne Wildermuth, MMS, PA-C, EM CAQ, RD
Assistant Professor, Division of Physician Assistant Education
University of Nebraska Medical Center

Stevens - Johnson Syndrome (SJS) & Toxic Epidermal Necrolysis (TEN)

1) Overview
   a) Severe mucocutaneous reaction resulting in necrosis and detachment of the epidermis
   b) SJS & TEN are variants of same disease continuum
   c) Typically triggered by medications; onset within 8 weeks of starting medication
      i) Anticonvulsants, allopurinol, sulfonamides, nevirapine, and –oxicam NSAIDS most frequently implicated
2) Presentation
   a) "Influenza-like" prodrome 1-3 days prior to skin changes
   b) Exanthematous rash may be initial symptom
   c) Cutaneous findings:
      i) Painful, coalescing, erythematous/purpuric macules or diffuse erythema; macules may have targetoid appearance
      ii) Face and thorax first → widespread
      iii) Vesicles and bullae form → skin sloughing
      iv) Nikolsky sign: epidermal sloughing with lateral pressure on unblistered skin
   d) Mucosal lesions:
      i) Seen in majority of cases
      ii) Can precede or follow the skin eruption
      iii) Oral, ocular, and urogenital are most commonly involved locations
3) Diagnosis
   a) Clinical
   b) Laboratory abnormalities may include anemia, lymphopenia, elevated LFTs, hypoalbuminemia, electrolyte imbalance, elevated BUN, hyperglycemia
   c) Skin biopsy may be beneficial for appropriate management and disposition
4) Management
   a) Remove causative drug
   b) Stabilize with supportive care; maintain normal body temperature; treat infection only if present
   c) Admit all cases; most will require treatment in an ICU or burn unit
   d) Consider treatment with cyclosporine early in the course of illness
   e) Recurrence is possible; educate patient on avoiding causative drug for life.

Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS) Syndrome

1) Overview
    a) Drug-induced hypersensitivity reaction
        i) Typically occurs 2-8 weeks after drug exposure
        ii) Allopurinol, anticonvulsants, sulfonamides, vancomycin, minocycline, and dapsone most frequently implicated
    b) Potentially life-threatening because of internal organ failure and/or epidermal sloughing
    c) Prolonged course with frequent relapses is common
2) Presentation
    a) Prodrome – fevers, malaise, lymphadenopathy
    b) Mucous membrane pain without ulceration
    c) Morbilliform rash → diffuse, infiltrated erythema with follicular accentuation
    d) DRESS suggested when eruption is ≥50 percent of the BSA and/or includes 2+ of:
        i) Facial edema
        ii) Infiltrated lesions
        iii) Scaling
        iv) Purpura
    e) Exfoliative dermatitis & desquamation of palms/soles possible
    f) Internal organ involvement in majority of patients
        i) Liver, kidneys, and lungs are most commonly involved, but other organs may be affected
3) Diagnosis
    a) High clinical suspicion
    b) Lab evaluation to confirm diagnosis and evaluate visceral involvement
        i) Eosinophilia on CBC differential & peripheral smear
        ii) Skin biopsy: perivascular eosinophils and lymphocytes
        iii) Obtain a CMP (possible LFT increase), UA (possible nephritic syndrome or eosinophils in sediment), EKG & troponin (evaluate for myocarditis)
4) Management
    a) Remove causative drug
    b) Admission – ICU or burn unit preferred
    c) Systemic corticosteroids
        i) Taper over 3-6 months to prevent relapse
    d) Treat cutaneous lesions with high or super-high potency steroids
    e) Cases may persist for months with relapses and remissions
    f) Patients may develop autoimmune endocrine diseases months or years after resolution

Necrotizing Fasciitis

1) Overview
    a) Deep tissue infection causing progressive destruction of muscle fascia and overlying subcutaneous fat
    b) Systemic toxicity develops rapidly
    c) Associated with significant mortality
    d) Risk factors: diabetes, drug use, obesity, immunosuppression, recent surgery, traumatic wounds
2) Pathophysiology
    a) Type I
        i) Mixed infection – aerobic and anaerobic
        ii) Risk factors: diabetes, peripheral vascular disease, immunocompromised, recent procedure or surgery
    b) Type II
        i) Group A *Streptococcus* (GAS) or other beta-hemolytic streptococci
        ii) *A. hydrophila* or *V. vulnificus* infection in a seawater-exposed injury
        iii) Affects all ages and without specific past medical history
        iv) Risk factors: skin injury, blunt trauma, recent surgery, childbirth, injection drug use, varicella
3) Presentation
    a) Initially overlying tissue can appear unaffected
    b) Early skin changes:
        i) Erythema, warm, shiny
        ii) Edema, induration
        iii) Exquisitely tender with pain out of proportion to exam
    c) Later skin changes:
        i) Patches of red-purple to blue-gray
        ii) Skin breakdown, bullae (pink/purple fluid), gangrene
        iii) Skin becomes anesthetic
    d) Subcutaneous gas may result in palpable crepitus
    e) Triad of warning signs: rapid progression, pain out of proportion to exam, crepitus
4) Diagnosis
    a) Have a low threshold for consideration of diagnosis
    b) Diagnosis only confirmed with surgical exploration
    c) Do not delay surgical debridement for diagnostics
    d) Laboratory studies:
        i) Laboratory studies alone are not predictive
        ii) CBC with differential, CMP, ESR and/or CRP, CK, Lactic Acid, Blood Cultures x 2 sets, Gram Stain & Culture in OR
    e) Imaging
        i) Radiographs or noncontrast CT can accurately identify soft tissue gas

5) Treatment
    a) Surgical emergency – immediate surgical consult
    b) IV antibiotics
        i) Initial antibiotic regimen:
            (1) A carbapenem or beta-lactam-beta-lactamase inhibitor *plus*
            (2) *MRSA* coverage - Vancomycin, daptomycin, linezolid, etc. *plus*
            (3) Consider adding clindamycin for antitoxin effects
    c) Hemodynamic support
    d) Treat sepsis per guidelines
    e) Early surgical exploration and debridement of necrotic tissue
        i) "Dishwater" fluid drainage & necrotic fascia are classic findings
        ii) Aggressive debridement until only viable tissue remains
        iii) Surgical site left open & regularly debrided in OR until necrosis ceases
    f) Antibiotic therapy alone is insufficient for treatment and is associated with high mortality
    g) Tailor antibiotics to gram stain, culture, and sensitivities when available
    h) Confirmed GAS treatment: Penicillin G & Clindamycin
    i) IV immune globulin in GAS complicated by toxic shock syndrome
    j) Continue antibiotics until no further debridement and hemodynamics normalized

Presentation & Handout References:

1. Goldsmith LA, et al. *Fitzpatrick's Dermatology in General Medicine, 8th ed.* United States: McGraw-Hill, 2012.
2. Knoop KJ, Stack LB, Storrow AB, et al. *The Atlas of Emergency Medicine, 4e.* United States: McGraw-Hill, 2018.
3. Papadakis MA, McPhee SJ, et al. *Current Medical Diagnosis & Treatment 2018*. United States: McGraw-Hill, 2018.
4. Puvanendran R, Meng Huey JC, Pasupathy S. Necrotizing Fasciitis. *Can Fam Physician*. 2009 Oct; 55(10): 981–987.
5. High WA, Roujeau JC. Stevens-Johnson syndrome and toxic epidermal necrolysis: Pathogenesis, clinical manifestations, and diagnosis. In: Up To Date. Adkinson NF, Levy ML, Mockenhaupt M (Ed). UpToDate, Waltham, MA, 2017.
6. High WA, Roujeau JC. Stevens-Johnson syndrome and toxic epidermal necrolysis: Management, prognosis, and long-term sequelae. In: Up To Date. Adkinson NF, Levy ML, Mockenhaupt M (Ed). UpToDate, Waltham, MA, 2017.
7. Roujeau JC. Drug reaction with eosinophilia and systemic symptoms (DRESS). In: Up To Date. Mockenhaupt M, Corona R (Ed). UpToDate, Waltham, MA, 2017.
8. Stevens DL, Baddour LM. Necrotizing soft tissue infections. In: Up To Date. Sexton DJ, Edwards MS (Ed). UpToDate, Waltham, MA, 2018.
9. Husain Z, Reddy BY, Schwartz RA. DRESS Syndrome: Part II. Management and therapeutics. *J Am Acad Dermatol*. 2013 May;68(5):709.e1-9; quiz 718-20. doi: 10.1016/j.jaad.2013.01.032.
10. Stevens DL, Bisno AL, Chambers HF, et al. Practice guidelines for the diagnosis and management of skin and soft tissue infections: 2014 update by the Infectious Diseases Society of America. *Clin Infect Dis*. 2014 Jul 15; 59(2):e10-52. doi: 10.1093/cid/ciu444.
11. Creamer D, Walsh SA, Dziewulski P, et al. UK Guidelines for the management of Stevens-Johnson syndrome/toxic epidermal necrolysis in adults 2016. *J Plast Reconstr Aesthet Surg*. 2016 Jun;69(6):e119-e153. doi: 10.1016/j.bjps.2016.01.034.
12. Chan HL, Stern RS, Arndt KA, et al. The incidence of erythema multiforme, Stevens-Johnson syndrome, and toxic epidermal necrolysis. A population-based study with particular reference to reactions caused by drugs among outpatients. *Arch Dermato*l. 1990 Jan;126(1):43-7.
13. Schopf E, Stuhmer A, Rzany B, et al. Toxic epidermal necrolysis and Stevens-Johnson syndrome. An epidemiologic study from West German. *Arch Dermatol*. 1991 Jun;127(6):839-42.
14. Finklestein Y, Macdonald EM, Li P. Recurrence and Mortality Following Severe Cutaneous Adverse Reactions. *JAMA*. 2014;311(21):2231-2232. doi:10.1001/jama.2014.839.
15. Gonzalez-Herrada C, Rodriguez-Martin S, Cachafeiro L, et al. Cyclosporine Use in Epidermal Necrolysis Is Associated with an Important Mortality Reduction: Evidence

from Three Different Approaches. *J Invest Dermatol*. 2017 Oct; 137(10):2092-2100. doi: 10.1016/j.jid.2017.05.022.
16. Gilbert M, Scherrer LA. Efficacy and safety of cyclosporine in Stevens-Johnson syndrome and toxic epidermal necrolysis. *Dermatol Ther.* 2019 Jan;32(1):e12758. doi: 10.1111/dth.12758.
17. Fouchard N, Bertocchi M, Roujeau JC, et al. SCORTEN: A Severity-of-Illness Score for Toxic Epidermal Necrolysis. *J Invest Dermatol*. 2000 Aug;115(2):149-53.
18. Lim VM, Do A, Berger TG, et al. A Decade of Burn Unit Experience with Stevens-Johnson Syndrome/Toxic Epidermal Necrolysis: Clinical pathological diagnosis and risk factor awareness. Burns. 2016 Jun;42(4):836-43. doi: 10.1016/j.burns.2016.01.014.
19. Assier H, Bastuji-Garin S, Revuz J, et al. Erythema multiforme with mucous membrane involvement and Stevens-Johnson syndrome are clinically different disorders with distinct causes. *Arch Dermatol*. 1995 May;131(5):539-43.
20. Kim DH, Koh YI. Comparison of diagnostic criteria and determination of prognostic factors for drug reaction with eosinophilia and systemic symptoms syndrome. *Allergy Asthma Immunol Res*. 2014 May;6(3):216-21. doi: 10.4168/aair.2014.6.3.216.
21. Smuszkiewicz P, Trojanowska I, Tomczak H. Late diagnosed necrotizing fasciitis as a cause of multiorgan dysfunction syndrome: A case report. *Cases Journal* 2008, 1:125. doi:10.1186/1757-1626-1-125. Copyright license: https://creativecommons.org/licenses/by/2.0/legalcode.
22. Lim VM, Do A, Berger TG, et al. A Decade of Burn Unit Experience with Stevens-Johnson Syndrome/Toxic Epidermal Necrolysis: Clinical pathological diagnosis and risk factor awareness. Burns. 2016 Jun; 42(4): 836-43. doi: 10.1016/j.burns.2016.01.014.
23. Assier H, Bastuji-Garin S, Revuz J, et al. Erythema multiforme with mucous membrane involvement and Stevens-Johnson syndrome are clinically different disorders with distinct causes. *Arch Dermatol*. 1995 May; 131(5):539-43.
24. Kim DH, Koh YI. Comparison of diagnostic criteria and determination of prognostic factors for drug reaction with eosinophilia and systemic symptoms syndrome. *Allergy Asthma Immunol Res*. 2014 May;6(3):216-21. doi: 10.4168/aair.2014.6.3.216.
25. Wong CH, Chang HC, Pasupathy S, et al. Necrotizing fasciitis: clinical presentation, microbiology, and determinants of mortality. *J Bone Joint Surg Am*. 2003;85-A(8):1454.
26. Kaul R, McGeer A, Low DE, et al. Population-based surveillance for group A streptococcal necrotizing fasciitis: Clinical features, prognostic indicators, and microbiologic analysis of seventy-seven cases. Ontario Group A Streptococcal Study. *Am J Med*. 1997;103(1):18.
27. Darenberg J, Luca-Harari B, Jasir A, et al. Molecular and clinical characteristics of invasive group A streptococcal infection in Sweden. *Clin Infect Dis*. 2007;45(4):450.
28. Hietbrink F, Bode LG, Riddez L, et al. Triple diagnostics for early detection of ambivalent necrotizing fasciitis. *World J Emerg Surg*. 2016 Oct 11; 11:51.