Hospital Dermatology: Review of Research in 2023-2024

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PRACTICE **POINTS**

- An international Delphi study reached consensus on 93 statements regarding workup, severity assessment, and management of DRESS syndrome.
- In nursing homes, universal decolonization with chlorhexidine and nasal iodophor greatly reduced the risk for hospital transfers due to infection compared to routine care.
- Rituximab as the first-line therapy for pemphigus vulgaris is associated with long-term sustained complete remission without corticosteroid therapy.
- Dupilumab and omalizumab are emerging safe and effective treatment options for bullous pemphigoid.

Inpatient consultative dermatologists play a critical role in the care of hospitalized patients with skin disease. Our review of the 2023-2024 dermatology literature identified several areas of active investigation relevant to inpatient dermatology. In this article, we highlight advances in the understanding of severe cutaneous adverse drug reactions, diagnosis and prevention of skin and soft tissue infections, and management of autoimmune blistering diseases (AIBDs).

Inpatient consultative dermatology has advanced as a subspecialty and increasingly gained recognition in recent years. Since its founding in 2009, the Society of Dermatology Hospitalists has fostered research and education in hospital dermatology. Last year, we reviewed the 2022-2023 literature with a focus on developments in severe cutaneous adverse reactions, supportive oncodermatology, cost of inpatient services, and teledermatology.[1] In this review, we highlight 3 areas of interest from the 2023-2024 literature: severe cutaneous adverse drug reactions, skin and soft tissue infections, and autoimmune blistering diseases (AIBDs).

Severe Cutaneous Adverse Drug Reactions

Adverse drug reactions are among the most common diagnoses encountered by inpatient dermatology consultants.[2,3] Severe cutaneous adverse drug reactions are associated with substantial morbidity and mortality. Efforts to characterize these conditions and standardize their diagnosis and management continue to be a major focus of ongoing research.

A single-center retrospective analysis of 102 cases of drug reaction with eosinophilia and systemic symptoms (DRESS) syndrome evaluated differences in clinical manifestations depending on the culprit drug, offering insights into the heterogeneity of DRESS syndrome and the potential for diagnostic uncertainty.[4] The shortest median latency was observed in a case caused by penicillin and cephalosporins (12 and 18 days, respectively), while DRESS syndrome secondary to allopurinol had the longest median latency (36 days). Nonsteroidal anti-inflammatory drug–induced DRESS syndrome was associated with the shortest hospital stay (6.5 days), while cephalosporin and vancomycin cases had the highest mortality rates.[4]

In the first international Delphi consensus study on the diagnostic workup, severity assessment, and management of DRESS syndrome, 54 dermatology and/or allergy experts reached consensus on 93 statements.[5] Specific recommendations included basic evaluation with complete blood count with differential, kidney and liver function parameters, and electrocardiogram for all patients with suspected DRESS syndrome, with additional complementary workup considered in patients with evidence of specific organ damage and/or severe disease. In the proposed DRESS syndrome severity grading scheme, laboratory values that reached consensus for inclusion were hemoglobin, neutrophil, and platelet counts and creatinine, transaminases, and alkaline phosphatase levels. Although treatment of DRESS syndrome should be based on assessed

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disease severity, treatment with corticosteroids should be initiated in all patients with confirmed DRESS syndrome. Cyclosporine, antibodies interfering with the IL-5 axis, and intravenous immunoglobulins can be considered in patients with corticosteroid-refractory DRESS syndrome, and antiviral treatment can be considered in patients with a high serum cytomegalovirus viral load. Regularly following up with laboratory evaluation of involved organs; screening for autoantibodies, thyroid dysfunction, and steroid adverse effects; and offering of psychological support also were consensus recommendations.[5]

Identifying causative agents in drug hypersensitivity reactions remains challenging. A retrospective cohort study of 48 patients with Stevens-Johnson syndrome (SJS)/toxic epidermal necrolysis (TEN) highlighted the need for a systematic unbiased approach to identifying culprit drugs. Using the RegiSCAR database and algorithm for drug causality for epidermal necrolysis to analyze the cohort, more than half of causative agents were determined to be different from those initially identified by the treating physicians. Nine additional suspected culprit drugs were identified, while 43 drugs initially identified as allergens were exonerated.[6]

Etiology-associated definitions for blistering reactions in children have been proposed to replace the existing terms *Stevens-Johnson syndrome*, *toxic epidermal necrolysis*, and others.[7] Investigators in a recent study reclassified cases of SJS and TEN as reactive infectious mucocutaneous eruption (RIME) or drug-induced epidermal necrolysis (DEN), respectively. In RIME cases, *Mycoplasma pneumoniae* was the most commonly identified trigger, and in DEN cases, anticonvulsants were the most common class of culprit medications. Cases of RIME were less severe and were most often treated with antibiotics, whereas patients with DEN were more likely to receive supportive care, corticosteroids, intravenous immunoglobulins, and other immunosuppressive therapies.[7]

In addition to causing acute devastating mucocutaneous complications, SJS and TEN have long-lasting effects that require ongoing care. In a cohort of 6552 incident SJS/TEN cases over an 11-year period, survivors of SJS/TEN endured a mean loss of 9.4 years in life expectancy and excess health care expenditures of $3752 per year compared with age- and sex-matched controls. Patients with more severe disease, comorbid malignancy, diabetes, end-stage renal disease, or SJS/TEN sequelae experienced greater loss in life expectancy and lifetime health care expenditures.[8] Separately, a qualitative study investigating the psychological impact of SJS/TEN in pediatric patients described sequelae including night terrors, posttraumatic stress disorder, depression, and anxiety for many years after the acute phase. Many patients reported a desire for increased support for their physical and emotional needs following hospital discharge.[9]

Skin and Soft Tissue Infections: Diagnosis, Management, and Prevention

Dermatology consultation has been shown to be a cost-effective intervention to improve outcomes in hospitalized patients with skin and soft tissue infections.[10,11] In particular, cellulitis frequently is misdiagnosed, leading to unnecessary antibiotic use, hospitalizations, and major health care expenditures.[12] Recognizing this challenge, researchers have worked to develop objective tools to improve diagnostic accuracy. In a large prospective prognostic validation study, Pulia et al[13] found that thermal imaging alone or in combination with the ALT-70 prediction model (asymmetry, leukocytosis, tachycardia, and age ≥70 years) could be used successfully to reduce overdiagnosis of cellulitis. Both thermal imaging and the ALT-70 prediction model demonstrated robust sensitivity (93.5% and 98.8%, respectively) but low specificity (38.4% and 22.0%, respectively, and 53.9% when combined).[13]

In a systematic review, Kovacs et al[14] analyzed case reports of pseudocellulitis caused by chemotherapeutic medications. Of the 81 cases selected, 58 (71.6%) were associated with gemcitabine, with the remaining 23 (28.4%) attributed to pemetrexed. Within this group, two-thirds of the patients received antibiotic treatment prior to receiving the correct diagnosis, and 36% experienced interruptions to their oncologic therapies. In contrast to infectious cellulitis, which tends to be unilateral and associated with elevated erythrocyte sedimentation rate or C-reactive protein, most chemotherapy-induced pseudocellulitis cases occurred bilaterally on the lower extremities, while erythrocyte sedimentation rate and C-reactive protein seldom were elevated.[14]

Necrotizing soft tissue infections (NSTIs) are severe life-threatening conditions characterized by widespread tissue destruction, signs of systemic toxicity, hemodynamic collapse, organ failure, and high mortality. Surgical inspection along with intraoperative tissue culture is the gold standard for diagnosis. Early detection, prompt surgical intervention, and appropriate antibiotic treatment are essential to reduce mortality and improve outcomes.[15] A retrospective study of patients with surgically confirmed NSTIs assessed the incidence and risk factors for recurrence within 1 year following an initial NSTI of the lower extremity. Among 93 included patients, 32 (34.4%) had recurrence within 1 year, and more than half of recurrences occurred in the first 3 months (median, 66 days). The comparison of patients with and without recurrence showed similar proportions of antibiotic prophylaxis use after the first NSTI. There was significantly less compression therapy use (33.3% vs 62.3%; P=.13) and more negative pressure wound therapy use (83.3% vs 63.3%; P=.03) in the recurrence group, though the authors acknowledged that factors such as severity of pain and size of soft tissue defect may have affected the decisions for compression and negative pressure wound therapy.[16]

Residents of nursing homes are a particularly vulnerable population at high risk for health care–associated infections due to older age and a higher likelihood of having wounds, indwelling medical devices, and/or coexisting conditions.[17] One cluster-randomized trial compared universal decolonization with routine-care bathing practices

in nursing homes (N=28,956 residents). Decolonization entailed the use of chlorhexidine for all routine bathing and showering and administration of nasal povidone-iodine twice daily for the first 5 days after admission and then twice daily for 5 days every other week. Transfer to a hospital due to infection decreased from 62.9% to 52.2% with decolonization, for a difference in risk ratio of 16.6% ($P<.001$) compared with routine care. Additionally, the difference in risk ratio of the secondary end point (transfer to a hospital for any reason) was 14.6%. The number needed to treat was 9.7 to prevent 1 infection-related hospitalization and 8.9 to prevent 1 hospitalization for any reason.[17]

Autoimmune Blistering Diseases

Although rare, AIBDs are potentially life-threatening cutaneous diseases that often require inpatient management. While corticosteroids remain the mainstay of initial AIBD management, rituximab is now well recognized as the steroid-sparing treatment of choice for patients with moderate to severe pemphigus. In a long-term follow-up study of Ritux 3[18]—the trial that led to the US Food and Drug Administration approval of rituximab in the treatment of moderate to severe pemphigus vulgaris—researchers assessed the long-term efficacy and safety of rituximab as a first-line treatment in patients with pemphigus.[19] The 5- and 7-year disease-free survival rates without corticosteroid therapy for patients treated with rituximab were 76.7% and 72.1%, respectively, compared with 35.3% and 35.3% in those treated with prednisone alone ($P<.001$). Fewer serious adverse events were reported in those treated with rituximab plus prednisone compared with those treated with prednisone alone. None of the patients who maintained complete remission off corticosteroid therapy received any additional maintenance infusions of rituximab after the end of the Ritux 3 regimen (1 g of rituximab at day 0 and day 14, then 500 mg at months 12 and 18).[19]

By contrast, treatment of severe bullous pemphigoid (BP) often is less clear-cut, as no single therapeutic option has been shown to be superior to other immunomodulatory and immunosuppressive regimens, and the medical comorbidities of elderly patients with BP can be limiting. Fortunately, newer therapies with favorable safety profiles have emerged in recent years. In a multicenter retrospective study, 100 patients with BP received omalizumab after previously failing to respond to at least one alternative therapy. Disease control was obtained after a median of 10 days, and complete remission was achieved in 77% of patients in a median time of 3 months.[20] In a multicenter retrospective cohort study of 146 patients with BP treated with dupilumab following the atopic dermatitis dosing schedule (one 600-mg dose followed by 300 mg every 2 weeks), disease control was achieved in a median of 14 days, while complete remission was achieved in 35.6% of patients, with 8.9% relapsing during the observation period.[21] A retrospective case series of 30 patients with BP treated with dupilumab with maintenance dosing frequency tailored to individual patient response showed complete remission or marked response in 76.7% (23/30) of patients.[22] A phase 2/3 randomized controlled trial of dupilumab in BP is currently ongoing (ClinicalTrials.gov identifier NCT04206553).

Pemphigoid gestationis is a rare autoimmune subepidermal bullous dermatosis of pregnancy that may be difficult to distinguish clinically from polymorphic eruption of pregnancy but confers notably different maternal and fetal risks. Researchers developed and validated a scoring system using clinical factors—history of pemphigoid gestationis, primigravidae, timing of rash onset, and specific clinical examination findings—that was able to differentiate between the 2 diseases with 79% sensitivity, 95% specificity, and an area under the curve of 0.93 without the need for advanced immunologic testing.[23]

Final Thoughts

Highlights of the literature from 2023-2024 demonstrate advancements in hospital-based dermatology as well as ongoing challenges. This year's review emphasizes key developments in severe cutaneous adverse drug reactions, skin and soft tissue infections, and AIBDs. Continued expansion of knowledge in these areas and others informs patient care and demonstrates the value of dermatologic expertise in the inpatient setting.

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