FEATURE ARTICLE

CE 3.0 Contact Hours

Dermatology Emergencies

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ABSTRACT: Dermatology is primarily an outpatient specialty. However, it is important to recognize certain conditions that require referral for inpatient management as well as for healthcare professionals to appreciate the types of patients who need to be triaged appropriately in the emergency room or urgent care setting. This article will serve to summarize some of the diagnostic features and management of these patients.

Key words: Dermatology, Emergency Healthcare, Stevens–Johnson Syndrome, Toxic Epidermal Necrolysis

Dermatology is primarily an outpatient specialty, yet it is important to recognize certain conditions that require referral for inpatient management. Furthermore, healthcare professionals in the emergency room or urgent care settings need to appropriately triage patients who present with dermatological findings. This article will serve to summarize some of the diagnostic features and management of these patients.

STEVENS–JOHNSON SYNDROME AND TOXIC EPIDERMAL NECROLYSIS

Clinical Presentation and Diagnosis

Stevens–Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN) are rare but severe adverse cutaneous drug reactions characterized by erythema, hemorrhagic erosions, and separation of the epidermis, often with involvement of the mucous membranes (Harr & French, 2010; Mockenhaupt, 2014). SJS and TEN are best thought of as a single clinical entity that presents on two ends of a spectrum based on body surface area (BSA) involvement (Mockenhaupt, 2014).

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Prodromal symptoms of SJS and TEN are vague, including fever, malaise, headache, cough, stinging eyes, and conjunctivitis, making early diagnosis challenging (Harr & French, 2010; Usatine, Smith, Mayeaux, Chumley, & Tysinger, 2009). One to three days later, cutaneous findings appear, beginning on the trunk, face, palms, and soles (Harr & French, 2010). In SJS, the primary lesions are dusky red or flat atypical target lesions, usually isolated, but lesions can become confluent on the face and trunk (Harr & French, 2010). Systemic symptoms are usually present, and epidermal detachment is found on <10% of BSA (Harr & French, 2010). In SJS–TEN overlap, the primary lesions and distribution are similar to those of SJS; however, systemic symptoms are always present, and epidermal detachment affects 10%–30% of BSA (Harr & French, 2010). In TEN, the primary lesions include poorly demarcated erythematous plaques, and there is considerable confluence of lesions all over the body (Harr & French, 2010). Systemic symptoms are always present, and the involved BSA is >30% (Harr & French, 2010). More than 90% of patients with TEN develop erosions of the buccal, genital, or oral mucosa, and the respiratory and gastrointestinal tracts may be also affected (Harr & French, 2010; Revuz et al., 1987). Skin lesions can also include bullae and ulcerations, which can be extensive and affect most of the BSA (Hafermann, Barber, Dreskin, & Lindberg, 2014; Kaur & Dogra, 2013). Patients may experience ocular disease, ranging from mild conjunctival injection to corneal erosions and ulcerations (Chang et al., 2007). Additional manifestations include hypotension, renal failure, respiratory failure, seizures, and coma (Usatine & Sandy, 2010).

Diagnosis relies on clinical findings together with histological evidence of full-thickness epidermal necrolysis attributed to apoptosis of the keratinocytes (Harr & French, 2010). SJS/TEN should be in the differential for any patient showing characteristic skin lesions, and mucosal involvement should be with high suspicion for SJS/TEN and requires that a skin biopsy should be obtained (Harr & French, 2010). Direct immunofluorescence (DIF) should also be performed to rule out other autoimmune blistering diseases (Harr & French, 2010). Laboratory findings can include lymphopenia, neutropenia, thrombocytopenia, elevated erythrocyte sedimentation rate, transaminases, and blood urea nitrogen (Usatine & Sandy, 2010). The

Nikolsky sign, by which lateral pressure on erythematous skin causes blisters because of epidermal detachment, is often present but not specific for SJS or TEN (Harr & French, 2010).

Etiology

Up to 75% of cases of SJS/TEN are instigated by drugs, with the most common offenders being lamotrigine, nevirapine, allopurinol, sulfonamides, carbamazepine, phenytoin, phenobarbital, and oxicam-type nonsteroidal anti-inflammatory drugs such as meloxicam (Harr & French, 2010; Mockenhaupt, 2014; Mockenhaupt et al., 2008). In one case-control study, the median time between beginning a high-risk drug and index day was less than 4 weeks (Mockenhaupt, 2014). Infections such as mycoplasma pneumonia, influenza-like illnesses, and herpes simplex virus have also been implicated in SJS/TEN (Harr & French, 2010; Mockenhaupt, 2014). Associations have also been reported with vaccinations, radiation, sunlight exposure, pregnancy, connective tissue diseases, and neoplasms (Usatine & Sandy, 2010).

In addition, it has been known since the 1980s that there is a genetic component to developing disease (Roujeau et al., 1987). Associations have been found between sulfonamide-induced TEN with human leukocyte antigen (HLA)-A29, B12, and DR7 and oxicam-induced TEN with HLA-A2 and B12 (Roujeau et al., 1987). Recent studies in the Han Chinese population suggest an association between carbamazepine-induced SJS and HLA-B*1502 (Chung et al., 2004).

Management

Because the exact cause of SJS/TEN is unknown, treatment consists of cessation of likely causative agents, supportive care, and alleviating symptoms (Harr & French, 2012). Even after discontinuation of certain drugs, damage to the kidneys or liver, in addition to the long half-lives and reactive metabolites of certain drugs, can contribute to further morbidity (Harr & French, 2012). Most patients will require intensive care unit monitoring, with particular attention to fluids and electrolytes, nutritional requirements, wound care, and monitoring for infections. Blisters should not be debrided because their presence enhances reepithelialization (Harr & French, 2010). Erosions can be treated with chlorhexidine, octenisept, or polyhexanide and covered with nonadherent gauze; topical sulfa medications should not be used (Harr & French, 2010; Mockenhaupt, 2014). Ophthalmologic consult is necessary to prevent permanent ocular sequelae (Mockenhaupt, 2014).

Average mortality rates are 1%–5% in SJS and 25%–35% in TEN, with higher rates of death in elderly patients and those with extensive BSA involvement (Harr & French, 2010). The mortality rate of patients with TEN can be estimated using SCORTEN, a severity-of-illness score that takes into account seven independent risk factors for death: age, an underlying malignancy, tachycardia, BSA involvement, and serum urea, glucose, and bicarbonate values (Bastuji-Garin et al., 2000).

Although there are no clinical trials to support a specific therapy for SJS/TEN, several systemic drugs have been used in the literature such as systemic steroids, cyclosporine, and intravenous immunoglobulin (IVIG) to benefit patients (Harr & French, 2010; Law & Leung, 2015). An open, Phase II trial in France involving cyclosporine for SJS and TEN revealed lower death rates compared with those estimated using SCORTEN scores (Valeyrie-Allanore et al., 2010). The data regarding the use of IVIG are conflicting, with some studies showing no advantage and others reporting improvement (Chen, Wang, Zeng, & Xu, 2010; Mittmann, Chan, Knowles, Cosentino, & Shear, 2006; Stella, Clemente, Bollero, Risso, & Dalmasso, 2007). In addition, there have been several case reports describing the successful use of infliximab, plasmapheresis, hyperbaric oxygen, and cyclophosphamide for TEN (Harr & French, 2010; Mockenhaupt, 2014).

Although the skin usually heals, more than half of survivors of TEN are left with residual complications including changes to the skin, hair, nails, mucous membranes, eyes, and respiratory epithelium (Harr & French, 2010, 2012; Mockenhaupt, 2014). Skin changes include hypopigmentation or hyperpigmentation, pruritus, xerosis, and hyperhidrosis (Mockenhaupt, 2014). Hair and nail changes include reversible hair loss, onycholysis, and onychodystrophy (Mockenhaupt, 2014). In one study, 73% of patients with TEN with mucosal involvement had permanent mucosal sequelae (Oplatek et al., 2006). These mucosal changes most often affect the oral and esophageal mucosa (loss of papilla on the tongue, impaired taste, strictures of the esophagus) but can also affect the genital mucosa (adhesions in the urethra, anus, and vagina; Mockenhaupt, 2014; Oplatek et al., 2006). Ocular complications include severe dry eyes, trichiasis, symblepharon, distichiasis, ocular scarring, and blindness (Usatine & Sandy, 2010; Yip et al., 2007). The most common cause of death from TEN is septicemia, often because of central venous lines (Mockenhaupt, 2014). One of the most serious complications of TEN is damage to the tracheal and bronchial epithelium, which occurs in up to 20% of patients (Mockenhaupt, 2014).

NECROTIZING FASCIITIS

Clinical Presentation and Diagnosis

Necrotizing fasciitis (NF) is a rapidly progressive necrosis of skin, muscle, and soft tissue that spreads along fascia planes at a rate of 2–3 cm per hour (Misiakos et al., 2014). The areas most often affected are the lower extremities, abdomen, and perineum, with the latter referred to as Fournier gangrene (Usatine & Sandy, 2010).

Early signs include the triad of erythema, swelling, and tenderness, along with fever and chills (Usatine & Sandy, 2010). Anaerobic bacteria can produce gas in the

tissue that may be felt as crepitus upon palpation. Eventually, nerve destruction can lead to motor and sensory deficits (Morgan, 2010). A classic finding is increasingly severe pain out of proportion to the physical examination, because of hypoxia and swelling of the tissue, which can help rule out a differential of cellulitis (Morgan, 2010; Usatine & Sandy, 2010). The erythematous skin then develops a dusky blue hue with yellow vesicular and bullous lesions, accompanied by serosanguineous drainage (Usatine & Sandy, 2010). Four to five days later, violaceous bullae are seen, along with gangrenous skin and a "woody" feel to the tissue (James, Berger, Elston, & Odom, 2006; Misiakos et al., 2014; Usatine & Sandy, 2010). After about 10 days, eschar sloughs off (Usatine & Sandy, 2010). Those with fulminant disease present with severe septic shock and multiple organ dysfunction syndrome and rapidly deteriorate within hours (Misiakos et al., 2014; Park, Jung, Jung, Shin, & Hwang, 2009).

NF is often diagnosed clinically, although definitive diagnosis is surgical, showing "dishwater fluid" compromised of necrotic tissue and neutrophils (Misiakos et al., 2014). Suspected cases require gram staining of the drainage as well as histological examination and culture of deep tissue biopsies (Usatine & Sandy, 2010). Laboratory findings, although not specific, include white blood cell (WBC) count > 14,000 cells per mm^3, serum sodium < 135 mEq/L, and blood urea nitrogen >15 mg/dl (Usatine & Sandy, 2010). X-rays can show evidence of gas in the soft tissue, but computed tomography and magnetic resonance imaging can show with better detail the extent of infection, swelling, inflammation, and presence of gas (Misiakos et al., 2014; Morgan, 2010).

Wong, Khin, Heng, Tan, and Low (2004) created a scoring system known as LRINEC (Laboratory Risk Indicator for Necrotizing Fasciitis) to distinguish between necrotizing and nonnecrotizing soft tissue infections based on laboratory values (Wong et al., 2004). They identified six variables associated with necrotizing infections: C-reactive protein, WBC count, hemoglobin, serum sodium, creatinine, and serum glucose levels. Using this scoring system, intermediate- and high-risk patients (scoring >6/13) had a positive predictive value of 92% and negative predictive value of 96%.

Pathophysiology

Although many cases of NF are idiopathic, patients should be asked about a history of trauma including insect bites, recent surgery, skin infection, and illicit intravenous drug use (Morgan, 2010).

Type I NF accounts for 70%–80% of cases and tends to affect patients with recent trauma or surgery, those who are immunocompromised, and patients with underlying abdominal disease (Morgan, 2010; Usatine & Sandy, 2010). It is a polymicrobial infection with the most common offenders being non-group-A *Streptococci*, *Bacteroides*, *Enterobacteriaceae*, and *Peptostreptococcus* (Usatine et al., 2009). Type II NF, responsible for 20%–30% of cases, is because of infection by group A β-hemolytic strep (*Streptococcus pyogenes*) and less commonly by *Staphylocccus* (*S.*) *aureus* (Misiakos et al., 2014; Morgan, 2010). In Asia, NF can be associated with certain types of raw or undercooked seafood containing *Vibrio* spp., *Aeromonas* spp., and *Shewanella* spp. (Park et al., 2009). The rate of progression depends on the microorganisms: Type 2 NF spreads at a much faster rate than Type 1 NF (Morgan, 2010). The resulting tissue necrosis is because of damage from bacterial enzymes but also thrombosis of blood vessels in the hypodermis (Park et al., 2009).

Management

Early detection is imperative so that patients can undergo surgical debridement and receive broad-spectrum antibiotics, with the former being the most crucial component of treatment (Misiakos et al., 2014).

Early and aggressive surgical interventions are crucial; in one study, surgical delay of 24 hours increased the mortality rate of *Vibrio* spp.-induced NF from 35% to 53% (Klontz et al., 1988). Even a 12-hour delay in surgery can be fatal in patients with fulminant disease (Misiakos et al., 2014). Surgical management requires debridement, necrosectomy, and fasciotomy (Misiakos et al., 2014). After surgery, fluid losses, nutritional needs, and wound healing must be carefully monitored. The use of vacuum-assisted closure dressings aids in wound cleaning and enhances the formation of granulation tissue (Misiakos et al., 2014).

Empiric antibiotics must cover gram positives (e.g., vancomycin, linezolid, ampicillin plus gentamycin), gram negatives (e.g., quinolones), and anaerobes (e.g., clindamycin or metronidazole; Usatine & Sandy, 2010). An in vitro study found that clindamycin, either alone or with a penicillin, decreased early release of streptococcal exotoxin A compared with using a penicillin alone (Coyle, Cha, & Rybak, 2003).

For Type 1 NF, ampicillin or ampicillin–sulbactam in combination with metronidazole or clindamycin can be used (Misiakos et al., 2014). For Type 2 NF, antibiotics must cover *S. pyogenes* and *S. aureus*, which often coexist, and can include first- or second-generation cephalosporines (for methicillin-resistant *S. aureus* [MRSA]), vancomycin, daptomycin, or linezolid (Misiakos et al., 2014). Antibiotics can be tailored based on blood, wound, and tissue cultures but must be continued for at least 48 hours after patients are clinically and hemodynamically stabilized (Misiakos et al., 2014). Patients often require antibiotics for 4–6 weeks (Misiakos et al., 2014). There may be a role for adjunct hyperbaric oxygen and IVIG (especially for streptococcal toxic shock syndrome [TSS]), but further studies with these agents are required (Kaul et al., 1999; Krenk, Nielsen, & Christensen, 2007). Hyperbaric oxygen appears to reduce mortality and amputation rates for *Clostridium* spp.-associated NF by reducing α-toxin production and enhancing neutrophil activity (Escobar, Slade, Hunt, & Cianci, 2005; Morgan, 2010).

Risk factors associated with a poor prognosis are diabetes mellitus (the most common associated morbidity), chronic renal failure, liver cirrhosis, chronic alcohol abuse, and immunosuppression (Misiakos et al., 2014). Some patients require amputation of limbs if there is extensive necrosis or they are not able to tolerate the lengthy operation needed to save the limb (Misiakos et al., 2014; Tang, Ho, Fung, Yuen, & Leong, 2001). Although amputations do not reduce mortality, patients have fewer repeat operations (Wong et al., 2003). The median mortality rate for NF is 32.3%, which increases to 70% in patients with sepsis and to almost 100% without treatment (Misiakos et al., 2014; Usatine & Sandy, 2010).

ROCKY MOUNTAIN SPOTTED FEVER

Clinical Presentation and Diagnosis

The classic triad of Rocky Mountain spotted fever (RMSF) is fever, rash, and severe headache, although myalgias (especially involving the abdominal, back, and calf muscles), nausea, vomiting, abdominal pain (especially in children, which can be mistaken for appendicitis), conjunctival injection, and altered mental status can also be present (Cunha, 2008; Salinas, Greenfield, Little, & Voskuhl, 2010; Usatine & Sandy, 2010). Less commonly seen are manifestations such as periorbital edema, edema of the dorsum of the hands and feet, and hepatosplenomegaly (Cunha, 2008).

The characteristic rash of RSMF, which appears several days after the fever, starts on the wrists and ankles before spreading to the palms, soles, trunk, and extremities, often sparing the face (Salinas et al., 2010; Usatine & Sandy, 2010; Wolff & Fitzpatrick, 2005). It typically evolves from small, blanching, nonpruritic macules to maculopapular (Days 1–2) and finally petechial lesions (Days 3–5; Salinas et al., 2010; Usatine & Sandy, 2010). The petechial lesions often coalesce to form ecchymoses, resulting in a spotted appearance of the skin (Usatine et al., 2009). It is important not to miss the early pale, pink papules, especially in dark-skinned patients (Cunha, 2008). It is also possible to see skin desquamation as the disease progresses (Usatine et al., 2009).

The diagnosis is based on clinical presentation with a history favoring exposure to a tick (Salinas et al., 2010). It is helpful to ask patients about exposure to environments where ticks are found because the tick bite itself is painless and often goes unnoticed. Laboratory findings may show thrombocytopenia, hyponatremia, and elevated transaminases with a normal WBC count (Usatine & Sandy, 2010). Chest imaging can reveal interstitial pneumonitis or infiltrates because of myocarditis (Cunha, 2008; Salinas et al., 2010). Serum titers of anti-*Rickettsia* (*R.*) *rickettsi* antibodies with greater than a fourfold increase are confirmatory, but this may take up to 10 days after the onset of disease (Salinas et al., 2010; Wolff & Fitzpatrick, 2005). Punch biopsy with DIF may reveal rickettsial organisms in the endothelium of blood vessels (Salinas et al., 2010; Usatine & Sandy, 2010). Although polymerase chain reaction of skin biopsies alone is not sensitive, this method is often combined with immunohistochemical staining (Chapman et al., 2006).

Etiology

RMSF is caused by the gram-negative intracellular bacterium *R. rickettsi.* Although several ticks can transmit this disease, the two most common are the wood tick (*Dermacentor andersoni*) in the western United States and the brown dog tick (*Dermacentor variabilis*) in the eastern United States (Chapman et al., 2006; Usatine & Sandy, 2010). After the tick bites, the bacterium travels through the lymphatic system and multiplies in endothelial cells causing vascular inflammation that presents as a vasculitis (Salinas et al., 2010). Although any organ can be involved, the skin and adrenals glands are most commonly affected (Usatine & Sandy, 2010).

Management

Doxycycline 100 mg twice daily (orally or intravenously), or 2.2 mg/kg for children < 100 lbs, is the first-line treatment, with tetracycline being an alternative agent (Chapman et al., 2006). The Centers for Disease Control and Prevention recommends antibiotics for 3 days after the fever disappears and until the patient shows clinical improvement, which is usually 5–7 days (Chapman et al., 2006). In pregnancy, chloramphenicol is recommended (Yu, Merigan, & Barriere, 1999).

With a case fatality rate of 5%–10%, RMSF is the most commonly fatal rickettsial disease in the United States (Chapman et al., 2006; Salinas et al., 2010; Usatine & Sandy, 2010). The severity varies greatly with some patients being stable enough to be treated on an outpatient basis and others requiring hospitalization (Usatine & Sandy, 2010). Factors associated with more severe disease include older age, male, black race, chronic alcoholism, and glucose-6-phosphate-dehydrogenase deficiency (Walker & Raoult, 2005). Aside from severe cases, persistent fever after 48 hours of antibiotics should raise concerns regarding the diagnosis (Salinas et al., 2010). Complications of RMSF include gangrene of the digits sometimes requiring amputation, myocarditis, meningoencephalitis, meningitis, sepsis, cardiac and renal failure, hearing loss, blindness, and other neurological deficits (Archibald & Sexton, 1995; Salinas et al., 2010; Usatine & Sandy, 2010). It is imperative for healthcare professionals to report cases of RMSF to the state health department (Usatine & Sandy, 2010).

STAPHYLOCOCCAL AND STREPTOCOCCAL TSS

Clinical Presentation and Diagnosis

TSS, first described by Todd, Fishaut, Kapral, and Welch in 1978, presents with sudden-onset high fever, rash, hypotension, and multisystem organ dysfunction over the course of several hours, often in young, healthy patients

(Andrews, Parent, Barry, & Parsonnet, 2001; Silversides, Lappin, & Ferguson, 2010). A prodromal influenza-like illness usually occurs 1–2 days before patients present for medical advice (Silversides et al., 2010). The rash of TSS is often described as a sunburn-like rash, macular and erythematous, and can be widespread or localized (Reiss, 2000; Silversides et al., 2010). Mucous membrane involvement may include oropharyngeal hyperemia, strawberry tongue, and nonpurulent conjunctivitis (Reiss, 2000). Patients may display tachycardia, tachypnea, dizziness, confusion, or impaired consciousness (Silversides et al., 2010). Other manifestations may include vomiting, watery diarrhea, chills, and myalgia (Reiss, 2000). Approximately 1–2 weeks into the disease course, mild desquamation occurs over the face, trunk, and extremities, followed by full-thickness desquamation over the palms and soles (Reiss, 2000).

Although commonly associated with tampon use, TSS has also been reported with barrier contraceptives, intrauterine devices, respiratory infections, nasal packs, and various soft tissue infections including surgical wounds, infected burns, postpartum infections, and deep abscesses (Ferguson & Todd, 1990; Schwartz et al., 1989). Public education regarding the risk of TSS from tampon use has led to a decrease in menstrual-associated TSS, whereas the frequency of nonmenstrual TSS cases has remained relatively constant (Reiss, 2000). Menstrual and nonmenstrual cases, which appear the same clinically, now occur with almost the same frequency (Andrews et al., 2001; Reingold, Hargrett, Dan, et al., 1982). The former is classically seen in White women of childbearing age, whereas the latter is seen equally in men and women (Reiss, 2000).

Diagnosis can be challenging when patients have other comorbidities. There are several case definitions from the Centers for Disease Control and Prevention, but many times, the diagnosis rests upon clinical presentation, abnormal laboratory values, and culture results (Reingold, Hargrett, Shands, et al., 1982; Silversides et al., 2010). Patients with risk factors (postoperative patients, menstruating women) should be viewed with a high level of suspicion (Silversides et al., 2010). In all suspected cases, it is imperative to obtain cultures and gram staining of potential sites of infection (Silversides et al., 2010). Blood cultures tend to be positive in streptococcal TSS but not staphylococcus TSS (Silversides et al., 2010). Chest imaging may show evidence of acute respiratory distress syndrome (ARDS) and be helpful in excluding alternative diagnoses (Silversides et al., 2010). Polymerase-chain-reaction-based tests for the superantigen genes, anti-TSS-toxin-1 (TSST-1) antibody assays, and flow cytometry for T-cell analysis may also be helpful (Ferry et al., 2008; Granger et al., 2010; Javid Khojasteh, Rogan, Edwards-Jones, & Foster, 2003).

Etiology

Menstrual-associated TSS is caused by *S. aureus*, whereas nonmenstrual TSS is attributable to both *S. aureus* and *Streptococcus pyogenes* (Reiss, 2000). Both bacteria are part of the normal flora of the skin and mucous membranes; however, certain strains produce toxins that generate an overwhelming immune response resulting in a cytokine storm (Andrews et al., 2001; Silversides et al., 2010). Staphylococcal TSST-1 and enterotoxins and streptococcal exotoxins are "superantigens" that activate excessive numbers of T cells and enhance the release of proinflammatory cytokines such as interleukin (IL)-2, tumor necrosis factor α, IL-6, IL-12, and interferon γ, resulting in the clinical signs and symptoms of TSS (Andrews et al., 2001; Fast, Schlievert, & Nelson, 1989; Parsonnet & Gillis, 1988; Parsonnet, Gillis, & Pier, 1986; Reiss, 2000; Silversides et al., 2010). Most adults have antibodies to TSST-1; disease occurs only when a person lacks the neutralizing antibody, suggesting that intrinsic host factors play an important role in the development of disease (Reiss, 2000; Silversides et al., 2010).

Management

With a mortality rate of 4%–22% for staphylococcal TSS and up to 85% for streptococcal TSS, early identification and treatment are paramount (Madhusudhan, Sambamurthy, Williams, & Smith, 2007; Silversides et al., 2010). The three components of managing TSS include identifying the source of infection, providing supportive care, and administering antibiotics.

A thorough physical examination is necessary to look for and remove foreign bodies that might be instigating the infection, to debride infected wounds, or to drain abscesses (Reiss, 2000). The main priority for patients with TSS is supportive care similar to that for septic shock, which usually warrants admission to the intensive care unit (Silversides et al., 2010). Most patients require massive fluid resuscitation and vasopressors because of resistant hypotension and sometimes intubation and ventilation (Reiss, 2000; Silversides et al., 2010). Other supportive measures include hydrocortisone, glycemic control, blood products, and parenteral nutrition (Silversides et al., 2010). The third component of treatment is antibiotic therapy, which ideally should be started after blood cultures are taken (Silversides et al., 2010). For staphylococcal TSS, nafcillin, cloxacillin, or flucloxacillin are used alone or with an aminoglycoside, whereas vancomycin is reserved for MRSA strains (Silversides et al., 2010). For streptococcal TSS, clindamycin is used together with penicillin (Madhusudhan et al., 2007).

Interestingly, antibiotics are not used to shorten the duration of disease but rather to reduce the risk of recurrence; up to one third of patients with menstrual TSS who are not treated with antibiotics will experience recurrent disease (Davis, Chesney, Wand, & LaVenture, 1980; Davis et al., 1982). Those at risk are likely colonized with a virulent strain of *S. aureus* and lack the neutralizing antibody that normally protects adults from the toxin (Andrews et al., 2001). Patients treated with

antistaphylococcal antibiotics appear to decrease their risk of recurrent disease (Andrews et al., 2001; Davis et al., 1980, 1982). Recurrent nonmenstrual TSS is far less common, although cases have been reported (Andrews et al., 2001). Further evaluation is required to determine the appropriate duration of therapy to eliminate toxigenic carriage, but previous studies suggest that a 2-week course is sufficient (Andrews et al., 2001). IVIG might play a role for patients with severe streptococcal disease, but there are insufficient data to recommend a particular dosing regimen (Darenberg et al., 2003; Schlievert, 2001; Silversides et al., 2010).

Complications of TSS include coagulation abnormalities such as disseminated intravascular coagulation, sepsis, acute tubular necrosis, acute kidney injury, ARDS, hepatic dysfunction, splitting of the nails, reversible hair and nail loss, cardiac dysfunction, and central nervous system complications (Reiss, 2000; Silversides et al., 2010).

CHILD ABUSE

Most children experiencing physical abuse have cutaneous findings. We will briefly review dermatological findings of the more commonly seen abuse patterns and mention several cultural practices that are often mistaken for signs of child abuse.

Bruises are a very common finding in children, especially over the knees, anterior tibia, and bony prominences (Carpenter, 1999; Chadwick, 1992). Bruises of varying ages in uncommon areas, such as the upper arms, medial and posterior thigh, hands, trunk, cheeks, ears, neck, genitalia, and buttocks, should raise suspicion (Ermertcan & Ertan, 2010). Bruises in infants who are not yet mobile, especially under 9 months old, are a red flag (Labbé & Caouette, 2001). The shape of the bruise can sometimes give an indication to the type of object used to harm the child (Ermertcan & Ertan, 2010; Kos & Shwayder, 2006).

Ecchymoses, abrasions, or lesions in an oval or elliptical pattern should raise suspicion for a bite mark, with human bite marks typically more superficial than animal bites (Ermertcan & Ertan, 2010). All bite marks should prompt a full skin examination for other signs of abuse; they can pose a concern regarding infection (Kos & Shwayder, 2006). The shape, color, and diameter must be recorded; photographs should be taken; and the bite should be swabbed with a sterile cotton swab and sent to a forensic laboratory (Ermertcan & Ertan, 2010; Kini & Lazoritz, 1998).

Burn abuse commonly affects children under 3 years old and can be caused by flames, cigarettes, electrical/chemical burns, and exposure to household appliances (Ermertcan & Ertan, 2010). Cigarette burns typically present as well-demarcated, 7- to 10-mm, circular lesions with a deep crater, often grouped over the face, hands, and feet (Ermertcan & Ertan, 2010). Children forcibly lowered into hot bathwater have symmetrical burns over the buttocks, perineum, and lower extremities with uniform depth and well-demarcated borders, often referred to as tidemarks (Stratman & Melski, 2002; Yeoh, Nixon, Dickson, Kemp, & Sibert, 1994). Stocking and glove burns result from forced immersion of the hands and feet (Ermertcan & Ertan, 2010; Stratman & Melski, 2002). Children submerged in hot water tend to have sparing of the flexural creases, resulting in zebra stripes (Ermertcan & Ertan, 2010).

The oral cavity is frequently injured in child abuse victims so a thorough examination is necessary. Injuries can include contusions, burns, and lacerations of the tongue, lips, buccal mucosa, palate, and gums. Children can experience fractured or displaced teeth, facial bone and jaw fractures, and tears of the frenulum or labia (Ermertcan & Ertan, 2010). A torn frenulum is almost always pathognomonic of abuse (Kos & Shwayder, 2006). Erythema or petechiae of the palate, especially the junction of the soft and hard palate, is sometimes suggestive of oral sexual abuse (Ermertcan & Ertan, 2010).

Several other findings are also concerning for child abuse. Traumatic alopecia may be accompanied by petechiae at the pulled hair root or a boggy scalp because of subgaleal hemorrhage (Ermertcan & Ertan, 2010; Kos & Shwayder, 2006). The differential diagnosis includes tinea capitis, traction alopecia, trichotillomania, loose anagen syndrome, and alopecia areata (Ermertcan & Ertan, 2010). Findings of sexual abuse include abrasions and lacerations of the genitalia and bite marks on the inner thighs of genitalia (Ermertcan & Ertan, 2010). Finally, children can present with signs of neglect such as severe dermatitis, subcutaneous wasting, and scaly skin because of malnutrition and poor hygiene (Ermertcan & Ertan, 2010).

There are several cultural practices that are important for us to be aware of because their manifestations can mimic those of child abuse (Ermertcan & Ertan, 2010). Cao gio, also known as coin rubbing or coining, is a well-known practice in Southeast Asia whereby a coin is rubbed repeatedly over pre-oiled or lubricated skin to treat many different illnesses (Yeatman & Dang, 1980). It can result in linear erythematous marks, petechiae, purpura, and burns, most often on the back, neck, head, shoulders, and chest (Davis, 2000; Ermertcan & Ertan, 2010; Yeatman & Dang, 1980). A practice known as cupping creates areas of lower air pressure and suction next to the skin, resulting in circular ecchymoses, hyperpigmentation, hematomas, and lacerations (Ravanfar & Dinulos, 2010). Oils are often placed on the skin, to which children can develop a contact dermatitis with erythema, blisters, and scaling (Ravanfar & Dinulos, 2010). Moxibustion, a component of traditional Chinese medicine, burns herbs that are placed on the skin via acupuncture needles, either directly or via a moxa stick, sometimes resulting in burns and scars (Ravanfar & Dinulos, 2010). Salting is a practice in Turkey whereby neonates are scrubbed with salt for an hour, which can lead to epidermolysis, severe hypernatremia, and scalded skin (Ravanfar & Dinulos, 2010). Gridding, originating from Russian culture,

consists of painting a grid-like pattern on the back of a child with iodine to help with respiratory illnesses (Ravanfar & Dinulos, 2010).

THE ERYTHRODERMIC PATIENT: MANAGEMENT APPROACH

Clinical Presentation and Diagnosis

Erythroderma, also known as exfoliative dermatitis, is a dermatological emergency most commonly seen in patients 41–61 years old, with a male-to-female ratio of 2:1–4:1 (Bruno & Grewal, 2009; Rothe, Bernstein, & Grant-Kels, 2005). It is characterized by diffuse erythema and scaling of the skin, often affecting more than 90% of BSA, but sometimes sparing the nose and paranasal areas (Okoduwa et al., 2009). Cutaneous findings often begin as erythematous patches that grow in size, coalesce, and spread over the body (Okoduwa et al., 2009). White and yellow scales develop, and the skin eventually appears bright red, dry, scaly, and warm upon touch (Okoduwa et al., 2009). Chronic erythroderma is often characterized by lichenfication, diffuse alopecia, nail dystrophy, keratoderma, and ectropion (Rothe et al., 2005). Nail changes include thick, dry, and brittle nails; nail shedding; subungual hyperkeratosis; distal onycholysis; and ridging of the nail plate (Okoduwa et al., 2009). Patients can also report fever, malaise, fatigue, pruritus, gynecomastia, and peripheral or periorbital edema (Okoduwa et al., 2009; Rothe et al., 2005).

Etiology

The most common causes are psoriasis, spongiotic dermatitis, drug eruptions, and cutaneous T-cell lymphoma (Rothe et al., 2005). However, etiologies include exacerbation of underlying dermatoses (psoriasis, atopic dermatitis, seborrheic dermatitis, pityriasis rubra pilaris), infections, systemic diseases, hematologic diseases (cutaneous T-cell lymphoma), and solid tumor malignancies (Rothe et al., 2005). In many cases, no underlying cause can be found, and the condition is labeled as idiopathic. In one study analyzing 64 cases of erythroderma, the two most common causes were underlying dermatoses (58%) and drugs (16%), with 16% of cases labeled as idiopathic (Eugster, Kissling, & Brand, 2001). The most common drug triggers include antiepileptics, antibiotics, antihypertensives, calcium channel blockers, cimetidine, lithium, and other topical agents (Akhyani, Ghodsi, Toosi, & Dabbaghian, 2005; Okoduwa et al., 2009). As the etiologies are numerous, here, we will focus on a general approach for the management of erythrodermic patients, which is common to all etiologies.

Management

The first step in the management of erythroderma is obtaining a detailed history, paying particular attention to all systemic and topical medications. Vital signs must be taken to ensure that patients are stable and do not require immediate admission to hospital (Rothe et al., 2005). Next, patients need a thorough skin examination, with special focus on the nails, mucous membranes, and lymph nodes and the presence or absence of hepatosplenomegaly (Rothe et al., 2005). Certain physical findings can suggest the underlying etiology, for example, psoriatic erythroderma (psoriasiform plaques), pityriasis rubra pilaris (islands of spared skin, orange palmoplantar keratoderma, hyperkeratotic follicular plaques on extensor surfaces), lichen planus (violaceous papules and buccal mucosal lesions), erythrodermic dermatomyositis (Gottron's papules, heliotrope rash, periungual telangiectasias, poikiloderma), immunobullous diseases (blisters and erosions), Sézary syndrome (severe pruritus, lagophthalmos, alopecia, lymphadenopathy, hepatosplenomegaly, fissured keratoderma, onychodystrophy, and leonine facies from skin infiltration), and scabies (burrows, especially along the flexural wrist surfaces; Okoduwa et al., 2009; Rothe et al., 2005; Yamashita, Abbade, Marques, & Marques, 2012).

Laboratory changes, although often not specific, include leukocytosis with eosinophilia, anemia, decreased albumin, elevated uric acid, erythrocyte sedimentation rate, and immunoglobulin E (Okoduwa et al., 2009; Rothe et al., 2005; Yamashita et al., 2012). Sézary cell count > 20% of circulating lymphocytes and a CD4–CD8 ratio > 10 are suspicious for Sézary syndrome (Yamashita et al., 2012). Biopsies are often nonspecific, illustrating hyperkeratosis, parakeratosis, acanthosis, and perivascular inflammatory infiltrates (Okoduwa et al., 2009). Retrospective studies show that the correlation between pathological diagnosis and clinical diagnosis ranges from 48% to 66%; multiple punch biopsies are usually required to establish a diagnosis (Rothe et al., 2005; Walsh et al., 1994; Zip, Murray, & Walsh, 1993). The use of special stains, gene rearrangement tests (to rule out lymphoproliferative disease), and DIF (helpful for ruling out autoimmune blistering diseases) can also facilitate diagnosis (Rothe et al., 2005). Patch testing can help rule out allergic contact dermatitis, and biopsies of abnormal lymph nodes may reveal underlying malignancies (Rothe et al., 2005). If no etiology is found, a systemic disease should be considered, and the patient should be surveilled appropriately (Rothe et al., 2005).

Patients should stop taking all unnecessary medications, especially those that are known to be possible triggers. They often require supportive care with focus on fluid and electrolyte requirements, nutrition, and wound care (Rothe et al., 2005). Protein loss from scaling of the skin requires an increase in daily protein by 25%–30% in psoriatic erythroderma and 10%–15% for other causes; deficits cause edema, muscle wasting, and hypoalbuminemia (Kanthraj et al., 1999). For weeping or crusted lesions, emollients and low-potency topical corticosteroids can be applied, covered by wet dressings or the use of oatmeal baths (Rothe et al., 2005). Caution is advised with topical immunomodulators such as tacrolimus as one patient with

generalized leukemic erythroderma developed elevated blood levels of tacrolimus, posing a risk for nephrotoxicity (Teshima et al., 2003). Other supportive measures include the use of air humidifiers to help moisturize the skin and prevent hypothermia and oral antihistamines to relieve pruritus (Chang et al., 2007; Rothe et al., 2005). Systemic treatment options include corticosteroids, methotrexate, cyclosporine, mycophenolate mofetil, and acitretin (Rothe et al., 2005). Patients with signs of secondary infection require systemic antibiotics, and those with edema may benefit from a diuretic (Rothe et al., 2005).

Patients are at high risk for thermoregulatory dysfunction, fluid and electrolyte imbalances, high-output cardiac failure, ARDS, secondary infection, and sepsis (Rothe et al., 2005). The most common causes of death are pneumonia, septicemia, and heart failure (Okoduwa et al., 2009). Although drug-induced erythroderma will resolve after cessation of the offending drug, the prognosis for other cases of generalized erythema depends on the underlying cause.

DRUG REACTION WITH EOSINOPHILIA AND SYSTEMIC SYMPTOMS SYNDROME

Clinical Presentation and Diagnosis

Drug reaction with eosinophilia and systemic symptoms (DRESS) syndrome is a severe drug reaction that typically occurs 2–8 weeks after exposure to the causative agent and can present with a variety of features (Choudhary, McLeod, Torchia, & Romanelli, 2013). Certain patterns are more commonly associated with specific drugs. However, most patients have fever, cutaneous manifestations, and systemic findings such as lymphadenopathy, leukocytosis with eosinophilia, and abnormal liver function tests (Choudhary et al., 2013).

In one study analyzing retrospective data from 216 patients with cutaneous drug reactions and systemic symptoms, 73%–100% had cutaneous findings, with the most common patterns being a diffuse maculopapular rash and erythroderma (Peyrière et al., 2006). However, lichenoid dermatitis, urticaria, vesicles, bullae, pustules, purpura, erythema multiforme lesions, facial edema, and cheilitis can also be present (Chiou et al., 2008; Choudhary et al., 2013; Peyrière et al., 2006). Other systemic symptoms include hematological abnormalities such as anemia, thrombocytopenia, and neutropenia; gastrointestinal symptoms; renal dysfunction (especially when associated with allopurinol); lung involvement (most commonly associated with minocycline); and heart abnormalities (also commonly associated with minocycline; Peyrière et al., 2006).

DRESS is a clinical diagnosis for which various diagnostic criteria have been created to try to standardize diagnosis (Choudhary et al., 2013). Santiago, Gonçalo, Vieira, Coelho, and Figueiredo, (2010) reported on the benefits of patch testing as a method to identify the culprit drug, but this was limited to DRESS induced by antiepileptics (Santiago et al., 2010).

Etiology

Common drug triggers include antiepileptics (the predominant cause of DRESS), allopurinol, sulfonamides, and antibiotic metabolites (Chiou et al., 2008; Choudhary et al., 2013; Eshki et al., 2009). Although the exact etiology is unknown, DRESS is most likely multifactorial. There is a genetic component characterized by a deficit in enzymes that break down drug metabolites (Choudhary et al., 2013). In addition, there are probably associations with certain HLA subtypes, such as has been described with HLA-B*1052 and carbamazepine-induced SJS (Chung et al., 2004). Finally, certain drugs might trigger reactivation of a virus, such as has been observed for the Epstein–Barr virus (Kano & Shiohara, 2004).

Management

Treatment of DRESS involves cessation of the offending agent and supportive measures. Systemic corticosteroids are often used although the data are insufficient (Zuliani, Zwahlen, Gilliet, & Marone, 2005). There are successful reports involving immunosuppressive agents such as cyclophosphamide and cyclosporine (Laban et al., 2010; Zuliani et al., 2005).

Visceral involvement can lead to pneumonitis, hepatitis, renal failure, colitis, encephalitis, myocarditis, pericarditis, cardiac failure, and pancytopenia, causing multiorgan failure (Choudhary et al., 2013; Eshki et al., 2009). Although most patients recover after cessation of the causative agent, the mortality rate is often reported at 10% (Chiou et al., 2008; Eshki et al., 2009).

CONCLUSION

Although dermatology may have fewer emergencies compared with other specialties, the mortality rates of those diseases can be profound. In addition, it can be challenging to pinpoint the diagnosis. Many of the diagnoses are made on clinical grounds without the benefit of standardized diagnostic criteria. Several of the conditions described above can present with a variety of different symptoms. Furthermore, the clinical presentations can change based on disease progress. Finally, patients can have comorbid conditions that exacerbate or mask their clinical presentation.

Although there are many other examples of diseases of the skin that require immediate attention, we have attempted to describe some of the more common states for practitioners to be aware of. As with most conditions, early intervention and diagnostic acumen are important for long-term success in managing these patients. ■

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