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ELSEVIER

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The rash that leads to eschar formation

Carly Dunn, BA, Ted Rosen, MD*

Department of Dermatology, Baylor College of Medicine, Houston, Texas, USA

Abstract When confronted with an existent or evolving eschar, the history is often the most important factor used to put the lesion into proper context. Determining whether the patient has a past medical history of significance, such as renal failure or diabetes mellitus, exposure to dead or live wildlife, or underwent a recent surgical procedure, can help differentiate between many etiologies of eschars. Similarly, the patient's overall clinical condition and the presence or absence of fever can allow infectious processes to be differentiated from other causes. This contribution is intended to help dermatologists identify and manage these various dermatologic conditions, as well as provide an algorithm that can be utilized when approaching a patient presenting with an eschar.

Introduction

To constitute an emergency, a condition should be acute at onset, associated with clinical manifestations, have risk of morbidity or mortality, and require a timely diagnosis to avoid these consequences. One such dermatologic emergency is the eschar. The eschar is cutaneous necrosis, which is characterized by the formation of a thick, black, adherent crust. Although an eschar may be localized at the time of presentation, this cutaneous manifestation often represents a systemic disorder or the potential for developing a systemic disorder. Often an eschar is infectious in etiology; however, it may be toxic, embolic, or vasculitic in nature. The clinical context is key when assessing a patient for proper management and therapeutic decision making.

This contribution is intended to help dermatologists and other providers identify and describe dermatologic conditions that progress to an eschar so that clinicians are better able to recognize key sign and symptom patterns which signify an emergency (Table 1). A basic diagnostic algorithm is shown in Figure 1 for the workup of a patient presenting with an eschar.

Flap necrosis

Obtaining an ideal outcome for skin reconstruction has long been a challenge for dermatologists, as well as for plastic and other surgeons. One complication of skin grafts and flaps is flap necrosis. Patients present with a focal area of necrosis in the region of their flap or graft during the postoperative period.[1] One study of reverse sural artery flaps found that partial flap necrosis occurred in 11.2% of the 179 flaps,[2] and a prospective study of flap necrosis after 606 mastectomies with immediate reconstruction found a rate of flap necrosis of 14%.[3] In regard to predisposing risk factors, these studies reported conflicting conclusions as to whether body mass index, diabetes, surgical technique, and flap variables contributed to the risk of developing flap necrosis.[2,3] In dermatologic surgery,

* Corresponding author. Tel.:+1 713 794 7129.
E-mail addresses: vampireted@aol.com, rosen@bcm.edu (T. Rosen).

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Table 1 Major causes of eschar

Disease/Etiology	Age	Number of lesions	Presence of fever	Additional notes
Flap necrosis	Adults	One area	No	Postoperative
Embolic	Adults	Few	No	Cardiovascular history
Mucormycosis	Adults	One area	Yes	Diabetes mellitus
Fungal sepsis	Any	Few	Yes	History
Bacterial sepsis (EG)	Any	Few	Yes	History
Miscellaneous infections: anthrax, tularemia scrub typhus, plague	Any	One to many	Usually	Travel history
Anticoagulant	Adults	One	No	History
Calciphylaxis	Adults	One to few	No	Renal disease
Necrotizing fasciitis or Fournier gangrene	Older adults	Large area	Yes	Recent trauma or GI/GU procedure
Snake or spider bite	Any	One	Maybe	History

EG, ecthyma gangrenosum; GI, gastrointestinal; GU, genitourinary.

reported rates of flap necrosis are lower. A recent retrospective evaluation of the safety of large skin flaps or grafts and interpolation flap surgery reported postoperative necrosis rates of 3% out of 331 reconstruction procedures.[4] This is similar to previous reports, which ranged from 1.4% to 4.8%.[5–8]

One clear risk factor for development of tissue necrosis after a tissue flap or graft is use of tobacco products. Heavy smokers, those consuming one or more packs per day, develop flap or graft necrosis three times more often compared with nonsmokers, light smokers, and former smokers.[7] For patients with risk factors for flap necrosis, such as heavy smokers or patients with vascular compromise, limiting tissue dissection and undermining or using a delay phenomenon can improve flap viability.[9–11] Use of phosphodiesterase type 5 inhibitors, such as tadalafil or sildenafil, have been shown in animal models to decrease the rate of flap necrosis.[12,13] In the case of flap necrosis, management should include local wound care. Maintaining a moist environment and using an antimicrobial ointment that penetrates the eschar can prevent infection and promote separation, facilitating reepithelialization and healing.[14] In a letter to the editor, five patients with flap necrosis were described, each of whom had received conservative treatment while being followed 6 weeks postoperatively by in-office debridement to remove the superficial necrosis.[15]

Embolic

Cholesterol emboli are the result of shearing forces causing atherosclerotic plaque rupture. These emboli can be either iatrogenic or spontaneous. For this reason, there is often a history of cardiovascular disease in patients who experience this phenomenon. Presentation can include a variety of findings such as livedo reticularis, purpura, cyanosis, blue toes, digital gangrene (eschar formation), painful subcutaneous nodules, and renal failure. A skin biopsy of the lesion will characteristically show biconvex needle-like clefts in vessels in approximately 92% of patients; therefore, this finding is considered a specific sign for cholesterol emboli. Treatment involves withdrawal of anticoagulants if possible, optimization of nutritional status, initiation of a statin to stabilize plaques, and systemic corticosteroids if there is evidence of recurrent cholesterol emboli or inflammation.[16]

Arterial emboli are commonly seen in patients who have had surgery and patients in intensive care, with additional risk factors of advanced age, hypercoagulability, cardiac abnormalities, and atherosclerotic disease. Common manifestations include stroke and lower limb ischemia. Management of arterial emboli involves immediately restoring blood flow, initiating anticoagulation if the source is cardiac, and optimizing therapy of any comorbid conditions.[17]

Septic emboli can present similarly to cholesterol emboli as either palpable purpura, petechiae, hemorrhagic plaques, pustules, nodules, cyanosis, or livedo reticularis. The most common causes of septic emboli are bacterial endocarditis, infected endovascular devices, and infected pseudoaneurysms after endovascular procedures. Skin biopsy of these lesions will show thrombi of neutrophils in the dermal blood vessels. Once a diagnosis of septic emboli is made, treatment includes empiric antimicrobial therapy and imaging to localize the primary focus of infection.[18]

Mucormycosis

Mucormycosis is a life-threatening fungal infection that is most commonly seen in diabetic or immunocompromised patients. It often begins with acute onset of pain and swelling on or near the eye or nose that later develops ischemia, followed by a well-defined eschar. Mucormycosis is due to one of several nonseptate fungi, notably *Mucor, Rhizopus,* or *Absidia*.[19,20] (Note the genus *Absidia* is also known as *Lichtheimia.*) Diagnosis is based on history, as well as direct microscopy of a wound exudate, histologic evaluation of a biopsy specimen, and the result of a fungal culture. Another aid in diagnosing mucormycosis is the use of molecular assays, such as polymerase chain reaction, to identify the responsible organisms.[21] Depending on the site of infection, treatment consists of vigorous surgical debridement in conjunction with

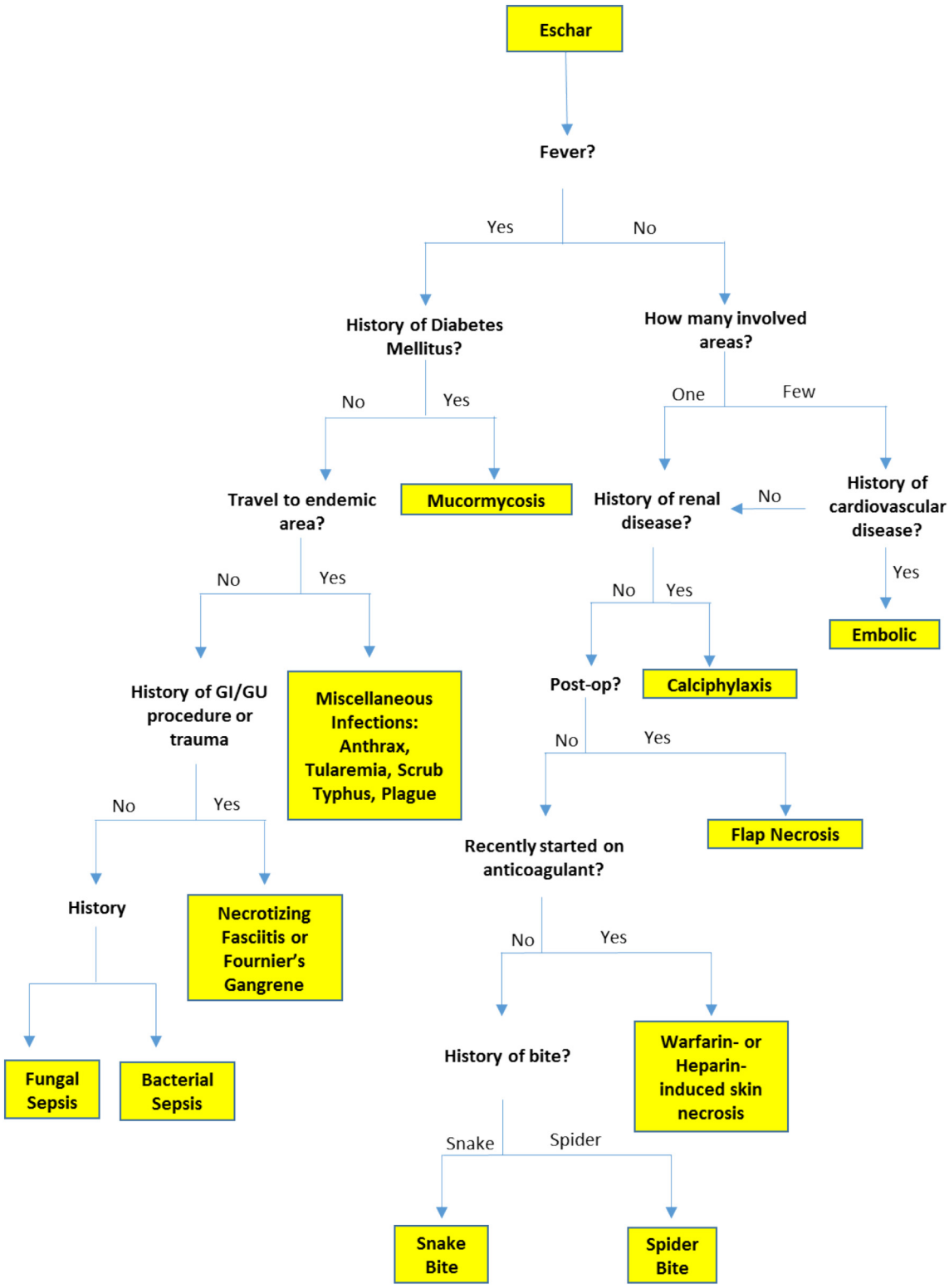

Fig. 1 Diagnostic algorithm for an eschar.

the administration of an antifungal agent, such as lipid-based amphotericin B (first line), posaconazole, or isavuconazole.[19,20] Even with adequate treatment, mortality is approximately 40%.[19] One uncommon variant of this fungal illness is posttraumatic mucormycosis. This differs from other forms by increased frequency of cutaneous localization, rarity of an underlying condition such as diabetes mellitus, and involvement of different species (*Apophysomyces elegans* complex

and *Saksenaea vasiformis*). These patients will have a history of trauma, often from traffic accidents (37%), domestic violence (15.1%), or natural disasters (13.4%). Posttraumatic mucormycosis also commonly requires surgical intervention (extensive debridement) but is associated with a better survival than other forms of cutaneous mucormycosis.[22]

Fungal sepsis

Invasive fungal diseases are difficult infectious disorders to recognize clinically, particularly among patients in intensive care units.[23] In recent years, the incidence of invasive fungal diseases has increased. These infections are associated with a high mortality rate, even with the development of multiple new antifungal drugs. Invasive aspergillosis and invasive candidosis represent the majority of invasive fungal infections, and the mortality rate for these mycoses is as high as 30% to 40% (Figure 2).[24] Conditions that can indicate an invasive fungal disease include clinical manifestations consistent with pneumonia, sino-nasal disease that can present with an ulcer followed by an eschar, and disease of the central nervous system. Comorbid patient factors include neutropenia, chronic obstructive pulmonary disease, hepatic cirrhosis, HIV infection, nonlymphoma cancer, steroid use, solid organ transplantation, and a prolonged stay in an intensive care unit.[23] Diagnosis of invasive fungal diseases can be made by various methods, the full extent of which are beyond the scope of this review; however, one such method is the serum 1,3-beta-D-glucan assay which detects a polysaccharide of the fungal cell wall that is released into the bloodstream. A recent meta-analysis assessed the diagnostic accuracy of 1,3-beta-D-glucan assay for diagnosis of invasive fungal infections.[24] The results of this study found that >80 pg/mL of 1,3-beta-D-glucan can be used to distinguish patients with invasive fungal infections from those without, with an indeterminate level between 60 to 80 pg/mL. This highly sensitive (98% to 100%) and specific (97% to 98%) assay detects *Candida* species, *Acremonium, Aspergillus, Fusarium, Histoplasmosis, Coccidioidomycosis,* and *Sporothrix schenckii,* but does not detect *Cryptococcus, Blastomyces dermatitidis,* or *Zygomycetes*.[24] Management should include removal of central venous catheters or implanted devices, performing a fundoscopic examination to rule out endocular infection, and antifungal therapy.[25] Broad spectrum antifungals are initially used and can be narrowed once the precise fungal species is identified. Documented candidosis should be treated with an echinocandin, per the Infectious Diseases Society of America's 2016 update; fluconazole and amphotericin B, or its lipid formulation, are alternative therapies.[26] For *Aspergillus,* voriconazole is first line, with amphotericin B, azoles, and echinocandins as alternatives. Amphotericin B is first line for mucormycosis. Duration of treatment ultimately depends on the extent of disease, clinical response, status of the patient's immune system, and precise fungal species.[25]

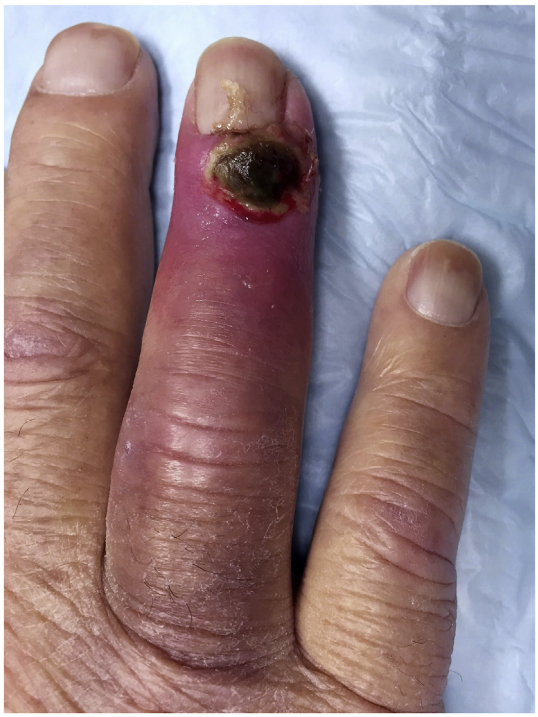

Fig. 2 Tender eschar as a sign of candidemia in a febrile patient.

Bacterial sepsis

One classic manifestation of bacterial sepsis is ecthyma gangrenosum. This condition is most often caused by *Pseudomonas aeruginosa* but may also be seen in conjunction with septicemia due to *Klebsiella spp, Escherichia coli, Serratia,* and rarely *Staphylococcus aureus.* Ecthyma gangrenosum starts as a solitary, painless, red swelling, possibly develops a fragile bulla, and then progresses rapidly to a painless eschar-covered ulcer (Figure 3). This whole progression of the lesions typically occurs within 12 to 24 hours. Patients will be toxic-appearing and febrile, and they often are immuno-

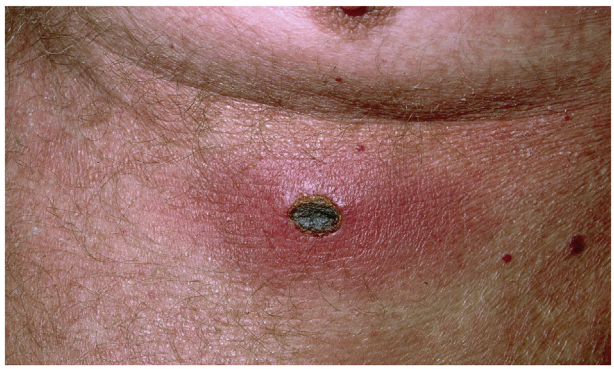

Fig. 3 Painless, solitary ecthyma gangrenosum in a neutropenic patient.

compromised or neutropenic.[27,28] A meta-analysis of 167 cases in the literature from 1975 to 2014 showed the responsible organism was most commonly *P. aeruginosa* (73.65%), followed by other bacteria in 17.35%, and fungi in 9% of patients. This review also revealed that up to 33% of patients were sick but not immunocompromised, and up to 4.2% were previously healthy.[29] At least one case report has documented an instance where ecthyma gangrenosum occurred in a previously healthy 3-month-old infant.[30] Management should include blood and skin cultures, survey for the focus of infection, and initial treatment with appropriate intravenous antimicrobials for presumed *P. aeruginosa*.[28] After confirmation of the diagnosis of ecthyma gangrenosum, aggressive antimicrobial or antifungal therapy should be started, based on culture and sensitivity results. An additional component of treatment often includes surgical debridement or even excision for management of the necrotic skin lesions.[30]

Vibrio vulnificus

Vibrio vulnificus can be a deadly pathogen. Ingestion of raw or undercooked seafood can lead to septicemia; whereas, the skin infection caused by *Vibrio vulnificus* is from exposure to contaminated water or related to an injury by contaminated marine life, such as shrimp or fish.[31] Clinically, wound-related infections present with hemorrhagic bullae, fever, and a history of wound exposure to contaminated water. The infection can progress rapidly to necrotizing fasciitis with the risk of limb loss. The most common time of the year for this infection is during the summer months.[32] One risk factor for this condition is liver insufficiency, which is thought to be related to the elevated serum ferritin, percentage of transferrin iron saturation, and disrupted iron physiology leading to enhanced bacterial growth and decreased phagocytosis.[31] After diagnosis, treatment involves antimicrobials and debridement of necrotic tissue.[32] Antimicrobial resistance has become more prevalent, leading to alteration in the current recommended treatment regimen to include ceftriaxone and concomitant doxycycline or minocycline.[32,33] Even with antimicrobial therapy, fatality rates are approximately 20% for wound-related *Vibrio vulnificus* infections.[32]

Anthrax

Anthrax is a zoonotic infection caused by the gram-positive rod *Bacillus anthracis.* Transmission of cutaneous anthrax (which accounts for approximately 95% of cases), is via the introduction of spores through breaks in exposed skin.[34,35] Although anthrax infections are rare in developed countries, the 2001 bioterrorism attack in the United States and the anthrax outbreak among intravenous drug abusers in Europe in 2009 and 2010 have demonstrated the importance of being aware of and being able to recognize this infection.[35] Clinically, anthrax presents as a pruritic painless papule, similar to a bug bite, that progresses to an ulcerated lesion with a central eschar.[34] Fever and regional lymphadenopathy may also be present. Shock is rare in cutaneous anthrax, being more commonly associated with inhalational disease. When anthrax is suspected, diagnosis can be made with Gram stain and culture, polymerase chain reaction, or immunohistochemistry. Treatment involves antimicrobial administration, pending confirmatory tests.[35] Anthrax is susceptible to multiple antimicrobials, including intravenous penicillin G, chloramphenicol, tetracycline, erythromycin, streptomycin, fluoroquinolones, and cefazolin.[34,35] Based on case reports, glucocorticoids may be entertained as an adjunctive therapy in cutaneous anthrax.[36] Estimated mortality for cutaneous anthrax infection is less than 1%.[35]

Tularemia

Tularemia is an often serious, rare disease caused by a gram-negative coccobacillus, *Francisella tularensis,* which is found in the northern hemisphere.[37] Approximately 125 to 200 cases are reported annually in the United States, mostly in the south central region, the Pacific Northwest, and parts of Massachusetts.[38] Patients range in age, and the most common clinical presentations are respiratory disease, ulceroglandular or glandular lesions with lymphadenopathy, and a febrile illness without localizing signs. The cutaneous form of tularemia is caused by direct contact with infected animals, such as rabbits, cats, and coyotes, or arthropod bites (eg, ticks or deerflies).[39] Case mortality ranges from 2% to 24%. Diagnosis can be made with culture or by polymerase chain reaction from skin lesions, lymph nodes, or a blood sample. Serologic studies would show a four-fold increase in immunoglobulin G titers from patients in the acute and convalescent stages of infection. First-line treatment is with streptomycin; gentamicin, doxycycline, and ciprofloxacin are second-line therapies. In Western states, where tularemia is more common, a higher suspicion for this rare infection is required in patients with compatible signs and symptoms.[37]

Scrub typhus

This rickettsial infection, transmitted by the bite of the trombiculid mite (chigger), is caused by *Orientia tsutsugamushi.* Clinically, patients present with a high fever, headaches, myalgias, and occasionally a maculopapular rash; however, the pathognomonic rash is an eschar which occurs at the site of the insect bite.[40] This infection should be included in the differential diagnosis in any sick traveler from an endemic area (which extends from Japan and Russia, to Australia, to Pakistan, and is prevalent in India) presenting with these features, meningoencephalitis, or hepatorenal failure.[40,41] In the case of suspected scrub typhus, the patient should be started on empiric doxycycline while awaiting confirmatory tests.[40]

Plague

The plague is a rare, highly contagious, life-threatening, flea-borne zoonosis caused by *Yersinia pestis.* From 2001 to 2017, the annual number of reported cases ranged from 1 to 17 with a median of three cases. Transmission to humans occurs through the bite of infected fleas, direct contact with infected tissues or body fluids, or inhalation of respiratory droplets from ill contacts or animals. Nonspecific clinical manifestations of the plague include fever, malaise, abdominal pain, nausea, and vomiting. Bubonic plague, which accounts for 80% to 85% of cases, presents with a painful swelling of one or more lymph nodes. In addition, the skin may turn black and form an eschar, especially on the fingers, toes, or nose, resulting in this disease being associated with the term "The Black Death." Streptomycin or gentamicin are first-line therapies, which can be switched to tetracycline or doxycycline, once the patient becomes afebrile.[42] An alternative antimicrobial class that can be used is the fluoroquinolone group. Anttimicrobial prophylaxis after contact with rodents in an endemic area is accomplished with either levofloxacin or doxycycline. Although there is no licensed vaccine currently available in the United States, a subunit vaccine is in development.[43] With the advent of antimicrobials, mortality has been reduced to approximately 16%.[44]

Anticoagulant skin necrosis

Warfarin-induced skin necrosis is an unusual complication of use of this anticoagulant, occurring in approximately 1 out of every 10,000 patients who receive the drug. Lesions commonly occur within 10 days of warfarin initiation and are found on the buttock, breast, abdomen, or thigh because of the reduced blood supply to adipose tissue.[45,46] Clinically, it appears as painful petechiae which develop into hemorrhagic bullae before progressing to an eschar. Typical patients include middle-aged women (with a women-to-men ratio of 9:1.3), persons who are obese, and those who are hospitalized for an acute illness that requires initiation of an anticoagulant.[45] Underlying risk factors also include deficiency of protein C, protein S or factor V Leiden, hyperhomocysteinemia, antithrombin III, and antiphospholipid antibodies.[46] A patient's complaint of pain or discomfort in susceptible areas of the body should arouse suspicion, and diagnosis is clinical, as neither protein C nor S levels are sensitive nor specific.[45,46] Therapy of warfarin-induced skin necrosis is to reverse the effect of warfarin. This is done by discontinuing the drug and initiating heparin for anticoagulation,[45] as well as administering 10 mg intravenous vitamin K, 10 mL/kg fresh frozen plasma (1 unit of fresh frozen plasma is approximately 200 mL), or prothrombin complex concentrate.[47] Wound treatment includes debridement and topical therapy with either local antimicrobials or special dressings.[45] Warfarin can later be reintroduced with continuation of heparin until the international normalized ratio is within the normal range.[46]

Heparin-induced thrombocytopenic necrosis is an uncommon immune-related phenomenon in which antibodies bind to a heparin-containing antigen complex causing thrombosis. Risk factors are the same as in warfarin-induced skin necrosis, and rare cases of heparin-induced skin necrosis have been described in patients who are pregnant.[48] Typically, this condition presents around 5 to 7 days after initiating heparin. Lesions may begin as bruises that progresses to necrosis and cyanosis.[45] Because clinically this is similar to skin necrosis related to other causes, a detailed medical history is necessary, when heparin-induced skin necrosis is suspected.[49] The presence of antibodies and a platelet count drop by 50% can confirm the diagnosis of heparin-induced skin necrosis. Treatment involves immediate cessation of heparin and initiation of a different anticoagulant. In certain cases, thrombolytic therapy and thrombectomy are performed to allow for reperfusion of the affected area. Wound care is similar to that for warfarin-induced skin necrosis; however, unlike in warfarin-induced skin necrosis, heparin should not be restarted as this condition is immune-related and will recur. Even with treatment, mortality rates are as high as 25%.[45]

Calciphylaxis

Calciphylaxis is the sudden development of tender, violaceous, and reticulate lesions that progress to necrotic, exceptionally painful eschar-covered ulcers (Figure 4). This condition is due to occlusion of microvessels by calcification in areas with thick adipose tissue. Patients affected classically

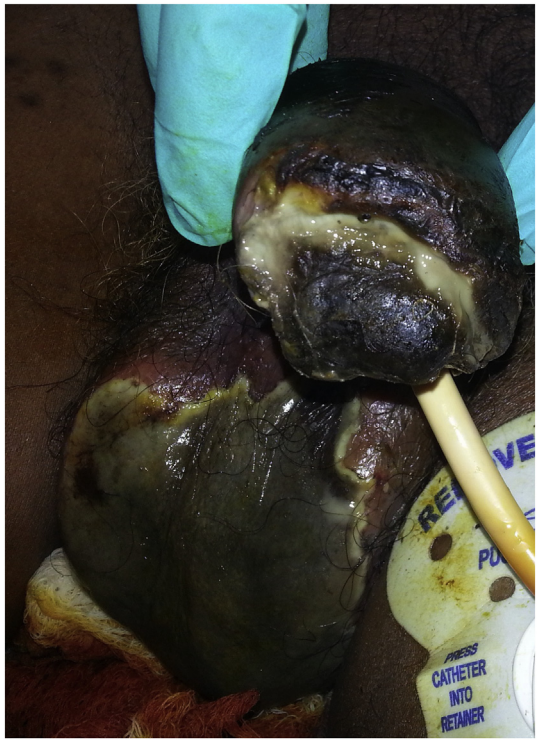

Fig. 4 Calciphylaxis, with both penile and scrotal eschars.

have renal failure and are on chronic hemodialysis, with an annual incidence in the United States of approximately 35 cases per 10,000 patients.[50] Other risk factors include obesity, diabetes mellitus, liver disease, systemic corticosteroid use, female sex, and an elevated calcium phosphorus product.[16,50] There is one case report of calciphylaxis due to recurrent pancreatitis, with no underlying renal failure; however, this is exceedingly rare.[51] Diagnosis is clinical, and the medical provider must have a high index of suspicion for this condition.[51] Skin biopsy is not required, as the findings can be difficult to identify; however, in patients without end-stage renal disease or in cases of early or atypical lesions, a biopsy should be strongly considered. Biopsies are contraindicated for acral, penile, or infected calciphylaxis lesions.[50] Histologically, calcification of the media and intima of vessel walls is seen, and this calcification leads to thrombosis and infarction of the skin. Additionally, the findings of superficial vascular calcifications on radiographic imaging can be sensitive for the diagnosis of calciphylaxis. Arteriolar calcification is described as having a "railroad," "tram track," or "pipestem" pattern.[52] One study found that out of 10 patients with biopsy-confirmed calciphylaxis, nine had radiographic imaging demonstrating moderate-to-severe vascular calcification in the area of the biopsy.[53]

Treatment is mainly supportive, with analgesics, local wound care, and normalization of any calcium homeostasis imbalances. Additional therapy with bisphosphonates, cinacalcet, and sodium thiosulfate have been utilized to help improve pain and wound healing.[16] Sodium thiosulfate is beneficial, as it increases the solubility of calcium deposits, and it can be used in both uremic and nonuremic calciphylaxis. To help prevent episodes in the future, supplemental calcium, vitamin D, and other medications that may trigger calciphylaxis should be avoided.[51] Prognosis is generally poor, with a 1-year mortality rate of 45% to 80% in patients who have end-stage renal disease.[50]

Necrotizing fasciitis

Necrotizing fasciitis is a life-threatening deep soft tissue infection, including the fascia. Differentiating necrotizing fasciitis from other soft tissue infections is critical, as necrotizing fasciitis is a surgical emergency that requires timely diagnosis followed by aggressive surgical debridement.[54] Predisposing factors include diabetes mellitus, alcoholism, immunosuppression, smoking, and sedentary lifestyle.[55] Classically, this infection is caused by group A *Streptococcus* and may develop into shock and multiple organ failure, known as streptococcal toxic shock syndrome. In the early stages, necrotizing fasciitis resembles cellulitis and erysipelas, with nonspecific signs such as swelling, tenderness or pain, and erythema at the site. This then can rapidly progress over 24 to 72 hours to dusky, bullous lesions.[56] The cardinal sign is crescendo or abrupt pain that is out of proportion to examination findings; however, pain may be absent or attenuated in patients who have received analgesics, including nonsteroidal antiinflammatory drugs. Patients are usually tachycardic (59%), and other signs may also be present such as fever (44%), tachypnea (26%), and hypotension (21%).[54,55] *Streptococcus pyogenes* can gain entry into the skin through breaches due to insect bites, penetrating trauma, drug injections, chicken pox, surgical incisions, or childbirth; however, as many as 50% of cases start in the deep tissues, such as after a muscle strain or bruise.[56]

When necrotizing fasciitis is suspected, broad spectrum antibiotics should be started to cover the commonly suspected organisms and can later be narrowed based on culture results. The mainstay of treatment is prompt, wide and deep surgical debridement. Studies have shown that debridement of tissue improves mortality compared with cases where surgery is delayed for even a few hours.[54] One adjunctive therapy is hyperbaric oxygen, which might reduce morbidity and mortality by inhibiting bacterial growth; however, the effectiveness of hyperbaric oxygen remains controversial, as studies have conflicting outcomes.[55,56] The mortality for necrotizing fasciitis ranges from 30% to 80%,[56] with better outcomes in patients who are diagnosed early and receive prompt surgical intervention and appropriate antimicrobial coverage.

Fournier gangrene

This is a polymicrobial necrotizing fasciitis of the genital or perineal skin and soft tissues due to an infection after trauma or instrumentation. The basic pathophysiology involves vascular thrombosis and tissue necrosis. Clinically, this condition presents initially as swelling, with progression to purulence, then ischemia, then eschar formation, then tissue sloughing. The source of the infection is most commonly from the lower gastrointestinal tract, followed by the skin, then the urogenital tract.[57,58] Different case studies from Greece and from Brazil found that the most common organisms associated with Fournier gangrene are *Escherichia coli, Staphylococcus aureus, Streptococcal* species, and *Pseudomonas aeruginosa*.[59,60] Fournier gangrene is seen most commonly in diabetic patients aged 50 to 60 years old, with a man to woman ratio of 10-25:1. Other risk factors include alcoholism, cancer, and HIV-positivity. In men, the most common sites in descending order are the scrotum, penile shaft or perineum, and abdomen. In women, the vulva is more common than the perineum. Treatment involves aggressive debridement of necrotic tissue and antimicrobial administration based on culture results, with delayed surgical repair as needed. Case reports have found benefit with adjunctive wound care measures, such as hyperbaric oxygen and negative pressure wound therapy.[61,62]

Snake bite

Snake bites can cause local tissue damage, resulting in pain, edema, necrosis, and coagulopathy. In North America, coral

snakes and pit vipers, which include rattlesnakes, cottonmouth snakes (also called water moccasins), and copperheads, are the most common groups of venomous snakes.[63] Many vipers, pit vipers, and cobras are known to cause tissue necrosis, sloughing, and eschars.[64] For diagnosis, a history of a snake bite is key. Initially, tight jewelry or clothing that might be constrictive should be removed, and the use of tourniquets, wraps, incision, suction, cooling, electric shocks, and the like should be avoided.[63,65] During transportation to the hospital, the extremity should be elevated and immobilized for comfort. Identification of the species of snake is important so that the appropriate antivenom can be given; however, capture or killing of the snake is not necessarily advised. Pain control should be accomplished with acetaminophen or opioids instead of nonsteroidal antiinflammatory drugs due to their antiplatelet effects.[63] A more detailed description of snake bites and their management is beyond the scope of this contribution; however, more information regarding snake bites, their clinical manifestations, and treatments can be found in the chapter entitled, "Overview of Venomous Snakes of the World," in *Medical Toxicology*,[64] this review[66] on North American snake envenomation, the World Health Organization's database on snakes and antivenom, or the database created by the University of Adelaide, Australia, which is available at http://www.toxinology.com.

Spider bite: Brown recluse

Loxoceles reclusa, known as the brown recluse spider, and related species are found in the Midwestern and Southern United States but not on the East Coast, and have a painless bite that can result in dermonecrosis and, less commonly, a systemic illness that can be deadly.[67–69] Within 8 hours, pain, erythema, and swelling develop which progresses first to ischemia and then to overt eschar formation (Figure 5). The latter usually sloughs off to form a deep ulcer. The majority of cases (67% to 90%) remain a localized phenomenon; however, 10% to 30% of cases develop into a viscerocutaneous form. In this form, sequential signs and symptoms begin 2 to 4 days after the bite. First, a morbilliform rash, fever, nausea, and vomiting appear, followed by hemolysis, thrombocytopenia, and hematuria. Lastly, the patient can develop shock, disseminated intravascular coagulation, acute renal failure, and ultimately death.[70] History of a spider or bug bite is important in the diagnosis of this condition; and the standard of diagnosis includes collecting and properly identifying the spider responsible. There is no proven effective treatment for *Loxosceles* bites, and proper treatment remains controversial. Therapeutic intervention typically includes rest, elevation of the affected area, and ice application; nonsteroidal antiinflammatory drugs can be utilized to relieve pain and swelling. Additional therapies may include a nitroglycerin patch, systemic steroids in severe cases, dapsone (this may prolong healing time and worsen scar formation), and antivenom. All have been used with variable results.[70]

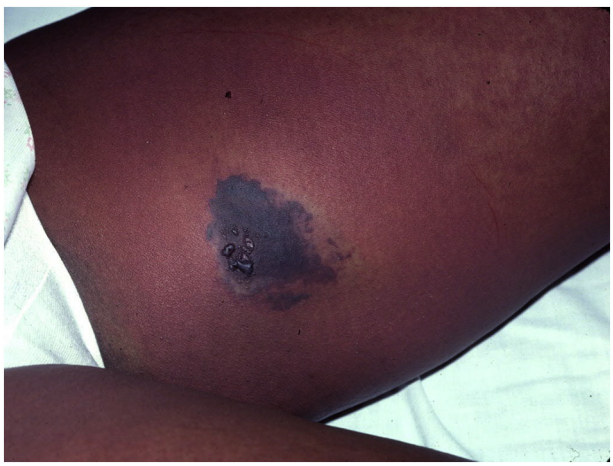

Fig. 5 Typical eschar from verified brown recluse spider bite.

Context

When confronted with an existent or evolving eschar, it is important to put the lesion into proper context:

- History is often important, including enumeration of recent travels and exposure to living or dead wildlife.
- Past medical history may be critical, including the presence of diabetes, kidney disease, neutropenia, cancer, and atherosclerosis.
- Recent medical interventions, such as cystoscopy and vascular cannulation, must be noted.
- Is the patient febrile? The latter suggests an infectious etiology, although an afebrile patient may have an eschar due to calciphylaxis or cholesterol emboli.
- Is the eschar painful? Lesions due to calciphylaxis are usually associated with exquisite pain, early mucormycosis is tender, and ecthyma gangrenosum characteristically painless.

The algorithm in Figure 1 helps organize contextual diagnostic clues.

Conclusions

Although there are many potential causes of an eschar, it is important to differentiate between them, as many etiologies can be life-threatening. This review is intended to provide clinicians with an algorithm in working up a patient with an eschar to ensure that patients receive prompt management and therapy.

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