Our Dermatology Online

Continuing Medical Education

Dermatologic Emergencies CME Part II: Infections and infection-related complications

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ABSTRACT

This section covers the strategies for managing the dermatologic infectious diseases and how they present in emergency and acute settings. In order to keep the staff and patients safe, emergency physicians should be able to limit the nosocomial infection spread.

Key words: *Necrotizing fasciitis; Purpura fulminans; Meningococcemia; Toxin-mediated Staphylococcal diseases; Leprosy reactions*

• NECROTIZING FASCIITIS

Necrotizing fasciitis (NF) is classified into four types according to the causative microorganism (Table 1). Trauma is the most identifiable etiology and includes external injuries and surgeries. However, cryptogenic (spontaneous) infections may occur deep within tissues without a portal of entry. Risk factors include immunosuppression, especially diabetes, malignancy, obesity, and alcoholism [1].

The early cutaneous changes of NF can mimic cellulitis (severe tenderness, erythema, warmth, and swelling that does not respond to antibiotics), progressing into severe pain out of proportion to clinical findings that may be followed by anesthesia as cutaneous nerves are destroyed. The erythema evolves to a dusky grayish color with rapidly spreading woody edema and malodorous watery discharge [2]. If not diagnosed early, systemic manifestations of shock or organ dysfunction may follow [3].

Fournier gangrene is an NF subtype localized to the genitalia, perineum, anus, and, occasionally, the skin of the lower abdomen that commonly occurs in adults with significant underlying comorbidities, especially diabetes [4,5].

Physicians should be aware of the potential pitfalls that may delay the early diagnosis of NF (Table 2).

Diagnosis is usually based on a combination of local and systemic clinical findings, radiological imaging, histology, and Gram staining with a microbial culture of tissue biopsies [6].

Treatment

Any delay in the diagnosis could prove to be fatal; early and extensive surgical debridement (fasciotomy) is the mainstay treatment (Fig. 1) in addition to broad-spectrum antibiotics (including gram-positive, gram-negative, and anaerobic coverage) and hemodynamic support. Survival significantly increases with early surgical intervention, preferably within 24 hours of hospital admission [7-9]. The role of hyperbaric oxygen and intravenous immunoglobulin (IVIg) is controversial [10,11].

• MENINGOCOCCEMIA

Meningococcemia is a rare, severe form of infection caused by Neisseria meningitidis, an aerobic gram-negative diplococcus. Complement deficiency and drugs that inhibit the complement pathway,

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Practical pearls:

- Non-responsive skin infection with disproportionate pain, pain that extends beyond the apparent infection margins, and/or hypoesthesia or anesthesia should raise the suspicion of necrotizing fasciitis
- Surgical therapy should be sought once the diagnosis of NF is clinically suspected and should not be delayed by diagnostic imaging. Delayed diagnosis is associated with increased risk of morbidity and mortality

Table 1: Types of necrotizing fasciitis [12]

type 1	Polymicrobial infection involving aerobic and anaerobic organisms. it is usually seen in older adults and those with underlying comorbidities
type 2	Monomicrobial infection mainly including group A Streptococcus followed by MRSA*.it may occur in any age group and those without any underlying illness
Type 3	Gram-negative marine organisms due to trauma in seawater (V. vulnificus) or freshwater (Aeromonas)
Type 4	Fungal infection, mainly Candida spp. and Zygomycetes and is typically seen in immunocompromised patients

* Methicillin-resistant Staphylococcus aureus

Table 2: Pitfalls in the diagnosis of NF [13]

- Absence of fever due to NSAIDs use
- Delay in the development of cutaneous manifestations in spontaneous NF (without a history of trauma)
- Attributing severe pain to injury or procedure
- Nonspecific imaging tests findings
- Attributing the associated systemic manifestations to other causes like food poisoning or viral illness
- Despite being positive in 20-60% of the patients, blood culture may not reflect all organisms involved in polymicrobial NF.

such as eculizumab, are well-known risk factors for meningococcemia [14,15]. Early manifestations are often nonspecific, such as fever, headache, malaise, and nausea/vomiting. Although the characteristic petechial rash is a more specific finding, it is only observed in 45% to 65% of cases [16,17]. The petechial or purpuric eruption with an irregular outline and central gunmetal gray color may progress to purpura fulminans with severe DIC. Subsequently, the patient may show signs of sepsis and septic shock, with the rapid onset of hypotension, pericarditis, cardiac tamponade, acute adrenal insufficiency due to hemorrhage (Waterhouse–Frederickson syndrome), and multi-organ failure [18,19]. Meningococcal septicemia occurs in 20% of cases and is associated with poor outcomes. Meningiococcimeia is a clinical diagnosis that can be confirmed with blood culture; however, investigations should not delay treatment initiation [20,21].

Treatment

Antibiotics can dramatically improve patient outcomes. Third-generation cephalosporin, cefotaxime 2g qds or ceftriaxone 2 g bd IV is recommended as soon as meningococcemia is suspected. Patients with a history of anaphylaxis to cephalosporins should consider chloramphenicol and quinolones as alternatives. Antibiotics should be administered alongside fluid resuscitation and supportive measures for sepsis, as indicated [22,23] (Fig. 2). For close contacts, rifampicin and ciprofloxacin can be used as chemoprophylaxis [24].

Practical pearls

- Meningiococcimeia should be suspected in any patient with febrile illness and petechial rash
- No investigation should delay antibiotic administration
- If intravenous access cannot be obtained within 15 minutes, intramuscular or intraosseous ceftriaxone/cefotaxime or penicillin should be used.

• STAPHYLOCOCCAL SCALDED SKIN SYNDROME (RITTER'S DISEASE)

Staphylococcal scalded skin syndrome (SSSS) is a potentially life-threatening disorder. It is caused by hematogenous dissemination of the exfoliative toxins (ETA and ETB) of phage group II strains (e.g. types 55 and 71) of S. aureus [25,26] (Fig. 3). It occurs primarily in infants and adults with chronic renal insufficiency or immunodeficiency [27,28].

Prodromal symptoms often include fever, irritability, and poor oral intake with **skin tenderness**, which can be so severe that the infant will refuse to lie down or allow anyone to hold them. Erythema typically starts on the face and intertriginous sites with characteristic periorificial crusting and radial fissuring. Within 1 to 2 days, the rash progresses into superficial blistering and desquamation with a positive Nikolsky sign [29]. Complications of SSSS include sepsis, pneumonia, dehydration, electrolyte imbalance, and hypothermia [30].

Diagnosis is mainly based on the clinical findings. This can be confirmed by culturing *S. aureus* from any suspected primary focus of infection, such as the nasopharynx, conjunctiva, umbilicus, and diaper area [31,32]. Skin biopsies usually show intra-epidermal cleavage at the level of the granular layer [33].

Treatment

Patients with SSSS are preferably treated in burn or intensive care units. Immediate empiric treatment with intravenous anti-staphylococcal antibiotics such as nafcillin, oxacillin, or flucloxacillin is recommended in most patients for a minimum of 1 week [34,35]. If MRSA is suspected, antibiotics with MRSA coverage (*e.g.*, vancomycin or linezolid) are indicated [36]. Clindamycin can be used as an adjunct therapy to inhibit the production of exotoxins [37]. Supportive care is a critical component of management, including skin and wound care and the management of potential fluid and electrolyte abnormalities [38,39].

Practical pearls

- Unlike pediatric patients, adults with SSSS usually have underlying morbidities like chronic renal disease or immunosuppression. Hence every adult patient with SSSS should be screened for an underlying predisposing risk factor
- SSSS can be differentiated from other similar blistering disorders by the lack of mucosal involvement and more superficial epidermal involvement on histological examination

• TOXIC SHOCK SYNDROME (TSS)

Toxic shock syndrome is an acute life-threatening illness caused by Staphylococcus aureus or group A Strep superantigen exotoxins (Fig. 4). TSS toxin 1 (TSST-1) is responsible for most menstrual TSS cases and about half of the non-menstrual TSS, where staphylococcal enterotoxins are also implicated [40]. Non-menstrual TSS can occur in the settings of soft tissues and respiratory infections, post-surgical and postpartum wound infections, burns, barrier contraceptive use, and retained foreign bodies such as nasal packing [41]. TSS is characterized by rapid onset of fever, hypotension, multi-organ system involvement, diffuse macular erythroderma and desquamation 1 to 2 weeks after the onset of illness, typically involving the palms and soles [42,43].

In contrast to staphylococcal TSS, streptococcal TSS is more likely to cause respiratory symptoms, is less likely to cause a typical cutaneous reaction and is associated with a poorer prognosis. Mortality associated with streptococcal TSS is 5%–10% in children compared to 30%–80% in adults [44].

The diagnosis of staphylococcal TSS can be established based on the CDC clinical and laboratory criteria (Table 3).

Treatment

Early recognition and institution of therapy are essential to avoid a fulminant course. Hemodynamic stabilization with intravenous fluids and/or vasopressor agents is the most crucial aspect of treatment. Parental beta-lactamase-resistant antistaphylococcal antibiotics are needed to eradicate bacteria and prevent recurrence [45]. Adjunctive therapeutic measures include clindamycin [46,47] to suppress toxin production, intravenous immunoglobulin (IVIG) to neutralize the toxin- [48,49], and surgical removal of the foreign bodies.

Practical pearls

- A high index of suspicion is required while making the diagnosis of TSS; CDC based definition criteria are mainly for research purposes, some of the criteria can only be established in a retrospective manner, and most importantly, not all the cases of TSS meet the CDC criteria
- The presentation of non-menstrual TSS is identical to the menstrual one, but it can occur in both sex in more comprehensive clinical settings, and it is associated with a higher mortality rate
- The seven Rs can be used to guide the management of TSS [50]
    - Recognition
    - Resuscitation
    - Removal of infection source
    - Rational choice of antibiotics
    - Role of adjuvant therapy
    - Review progression
    - Reduction of secondary infection in close contacts

• PURPURA FULMINANS

Purpura fulminans (PF) is a rapidly progressive, highly thrombotic disorder that mainly affects neonates and children that accompany bacterial, and more rarely, viral infections. PF is characterized by a high mortality rate caused by disseminated thrombosis and subsequent multi-organ failure [52]. The clinical picture of PF is often dominated by shock with

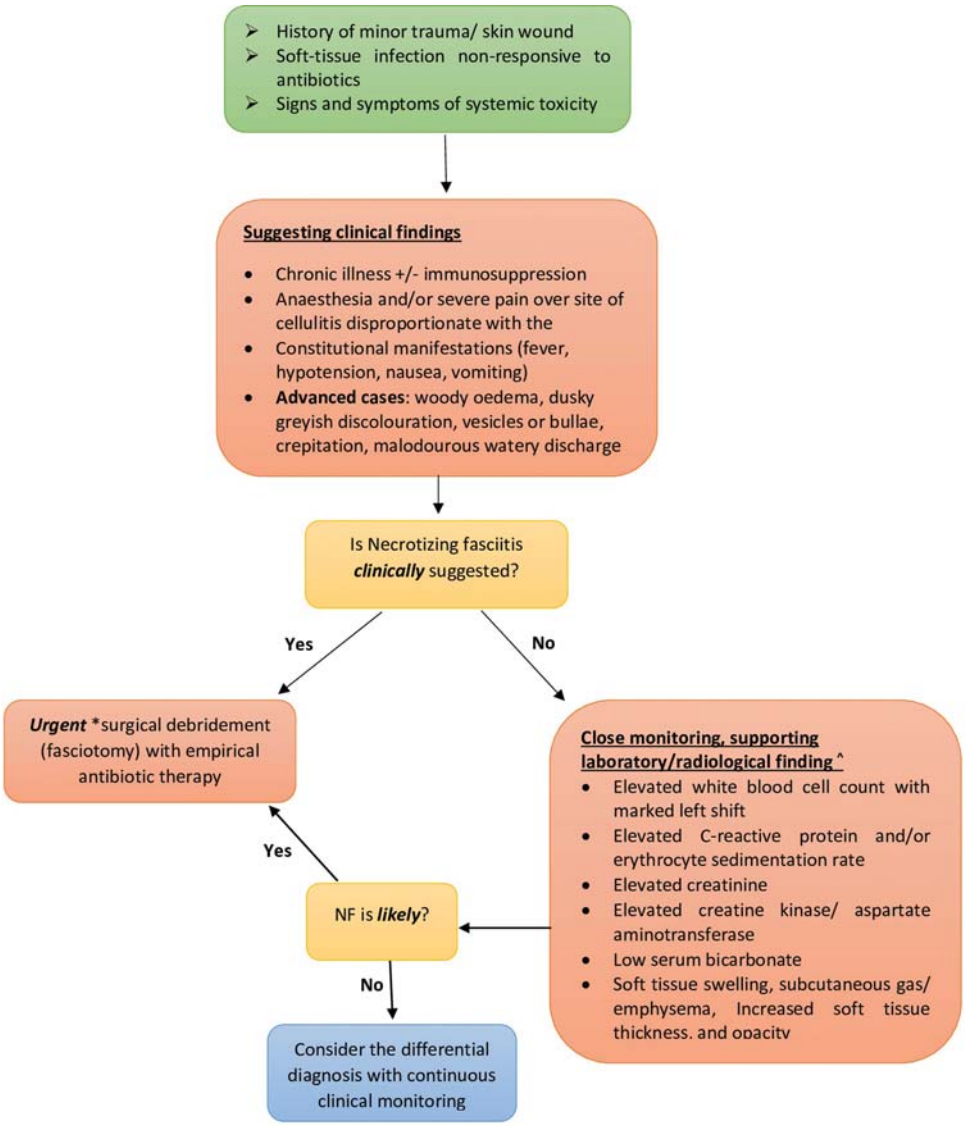

Figure 1: Necrotizing fasciitis. Flowchart of the suggested clinical, laboratory and radiological findings of NF. Fasciotomy is the mainstay treatment of necrotizing fasciitis. ^Laboratory investigations should not delay the urgent surgical debridement. *delayed surgical debridement (> 12 hours) associated with poor outcome.

hypotension and hypovolemia. The cutaneous lesions are marked by vascular occlusion features, including retiform, branching purpuric patches that rapidly evolve into hemorrhagic necrosis, and are sometimes preceded by bulla formation [53,54]. In the acute phase, the laboratory findings of PF are those of the associated DIC, including thrombocytopenia, hypofibrinogenemia, increased fibrin degradation products (FDP), and prolonged prothrombin (PT) and activated partial thromboplastin (aPTT) times. Measurements of protein C (PC) and S (PS) are additional essential investigations that should be performed at presentation [55]. The most important underlying triggers and patho-mechanisms of PF are presented in Table 4.

Treatment

PF of any cause requires urgent intervention to avoid a rapidly progressive multi-organ thrombotic injury. Most patients require complete supportive care and urgent broad-spectrum antimicrobial therapies (for sepsis). PF with DIC also requires urgent FFP (10–20 ml/kg every 8–12 h) to replace the consumed pro-coagulant and anticoagulant plasma proteins. Additional platelet concentrates (10–15 ml/kg) and cryoprecipitate (5 ml/kg) may be necessary for significant thrombocytopenia and hyperfibrinogenemia, respectively [56]. PC concentrates are licensed for cases with severe heritable PC deficiencies [57,58]. Anticoagulants can be used cautiously for PF complicated by large-

vessel venous thrombosis or central venous catheter thrombosis [59,60].

Practical pearls

- Mortality in PF is mainly caused by overwhelming thrombosis, and survivors may suffer from significant scarring and limbs amputation
- After few weeks of clearing the infection, death may occur due to thrombi obstructing small/medium blood vessels. Hence physicians should be vigilant to thrombotic complications while treating the underlying septic trigger.
- Due to overlapping causes and lack of pathognomonic characteristics, the diagnose of purpura fulminans may be challenging.
- If the diagnosis of purpura fulminans is suspected, it should be assumed to be related to acute infection until proven otherwise

• ECTHYMA GANGRENOSUM (EG)

Ecthyma gangrenosum is an uncommon, fulminant cutaneous infection classically associated with Pseudomonas aeruginosa bacteremia; however, other causative pathogens can produce clinically indistinguishable lesions [62-64]. The cutaneous manifestations of EG result from occlusion of the subcutaneous blood vessels by proliferating organisms in the media and adventitia layers. Infection typically occurs in critically ill or immunocompromised patients with severe neutropenia, representing a major predisposing factor [65]. Several case reports have described EG in previously healthy immunocompetent individuals without underlying identifiable causes [66].

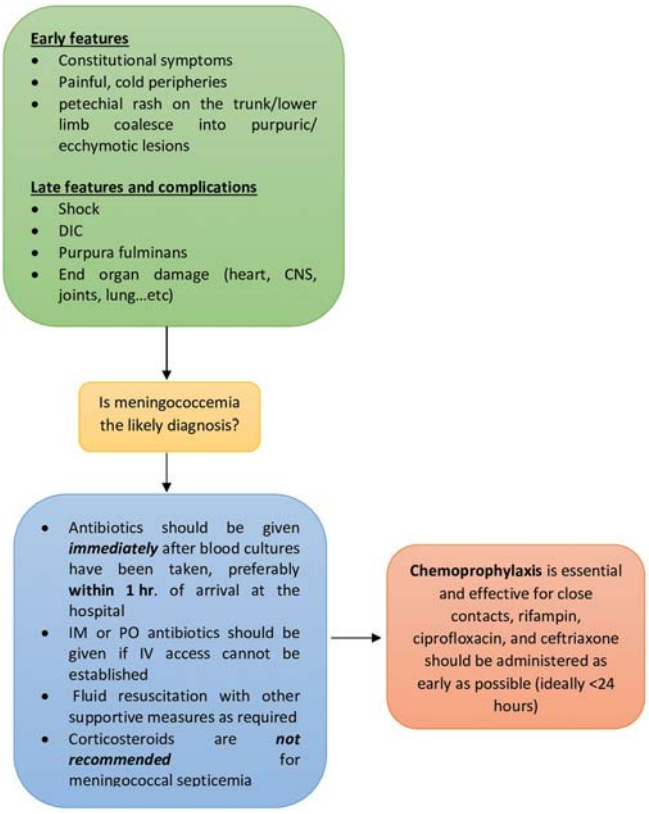

Figure 2: Meningococcemia. Key points in the management of meningococcemia include antibiotics, supportive measures and chemoprophylaxis for close contacts.

Cutaneous lesions of EG initially appear as painless, erythematous macules that rapidly evolve into hemorrhagic pustules and/or bullae with an erythematous border. Ultimately the lesions progress to necrotic ulcers with surrounding erythema and a central black Eschar. While EG can occur at any anatomical location, the anogenital area and extremities are most commonly involved, followed by the trunk and face [67,68].

Urgent diagnosis should be made based on the clinical characteristics of the lesion, supported by blood and wound bacteriologic cultures and tissue biopsy. Biopsy of the EG lesion typically shows perivascular hemorrhage and infiltration of neutrophilic granulocytes with central necrosis. The diagnosis of EG should alert the physician to the possibility of an underlying Pseudomonas bacteremia [69]. The unfavorable prognosis in EG is linked to several factors presented in Table 5.

Treatment

Although the usual outcome of EG is poor, rapid and aggressive appropriate systemic treatment can lead to a better prognosis. Empiric antimicrobial therapy typically includes antipseudomonal beta-lactams, aminoglycosides, and/or fluoroquinolones alone or in combination. Once the causative organism and its antibiotic sensitivity are known, directed therapy can be tailored to these results. Surgical excision and debridement under antibiotic cover are indicated for progressive lesions [70,71].

Practical pearls

- Undermined ulcerative skin lesion in an immunosuppressed patient should raise the suspicion of ecthyma gangrenosum
- The presence of these lesions should increase the possibility of bacteremia/sepsis, especially with *P. aeruginosa*, and should encourage blood culture collection.
- Early initiation of appropriate antibiotic therapy is imperative as it can change the prognosis

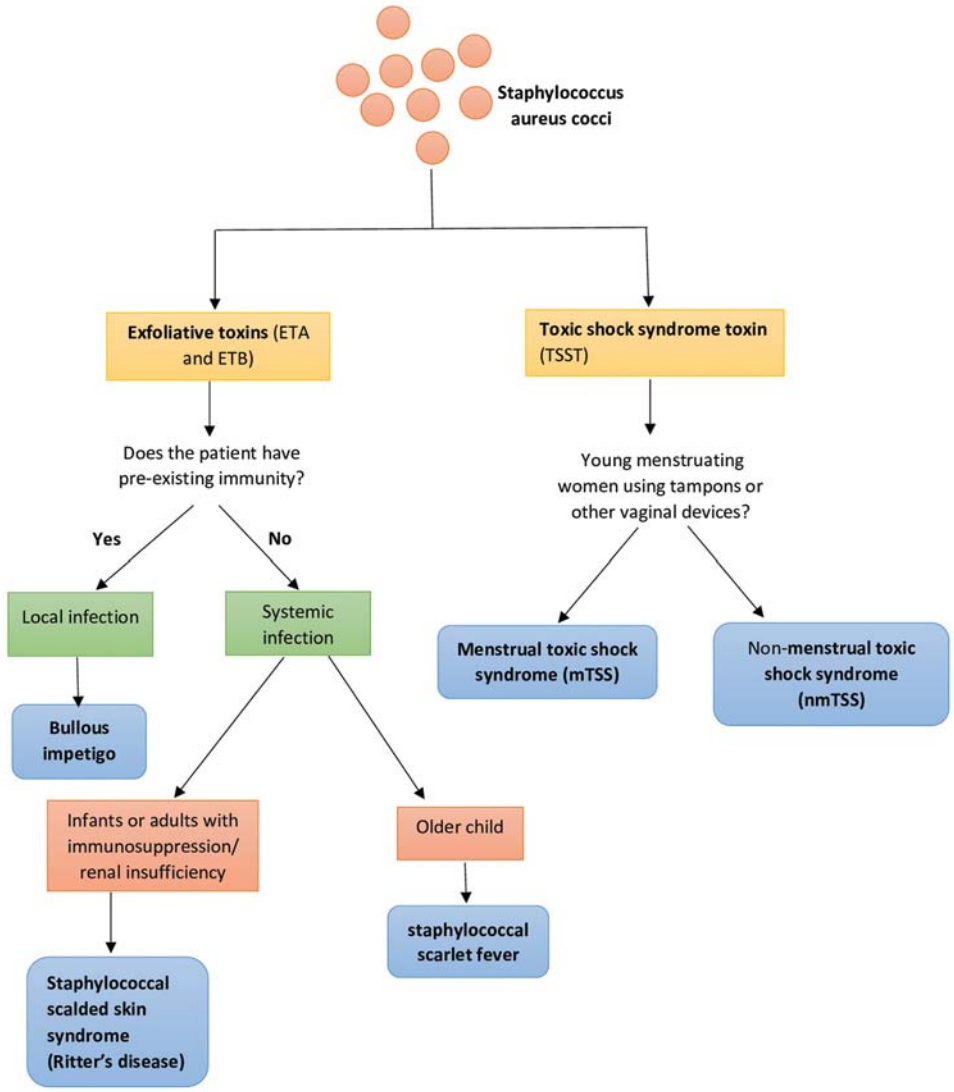

Figure 3: Staphylococcal scaldeWd skin syndrome and toxic shock syndrome. Spectrum of toxin-mediated Staphylococcal diseases.

• CUTANEOUS ANTHRAX (WOOL SORTER'S DISEASE)

Anthrax is primarily a zoonotic disease. The main route of transmission is contact with, or inhalation of Bacillus anthracis, a gram-positive bacillus. Most cases are due to occupational exposure to infected animals or their products[72,73]. Anthrax remains a global concern because it can potentially be used as a biological weapon [74-76].

The disease occurs primarily in three forms: cutaneous, respiratory, and gastrointestinal, with cutaneous anthrax accounting for 95% of the cases globally.

With proper treatment, cutaneous anthrax can be self-limiting without complications in 80%—90% of cases. Rarely, extensive edema, septic shock, and meningitis can result from the lymphohematogenous spread of infection [77].

Bacillus anthracis is usually introduced at the site of a cut or abrasion, on exposed areas such as the arms, face, or neck. Mild cutaneous anthrax usually starts as a painless purpuric macule or papule resembling an insect or spider bite evolving into a vesicle filled with clear or serosanguineous fluid. The vesicle usually ruptures and ulcerates, leaving a painless black necrotic eschar. The eschar is often surrounded by striking, non-pitting edema and may be accompanied by lymphadenopathy. Over the next 1–2 weeks, eschar dries and sloughs with no permanent scarring [78,79]. Severe cutaneous anthrax is defined by the presence of a large

cutaneous lesion with a bullous reaction, extensive edema and systemic symptoms, including fever, tachycardia, and tachypnea. Without antibiotic treatment, mortality may be as high as 20%, usually due to septicemia [80,81].

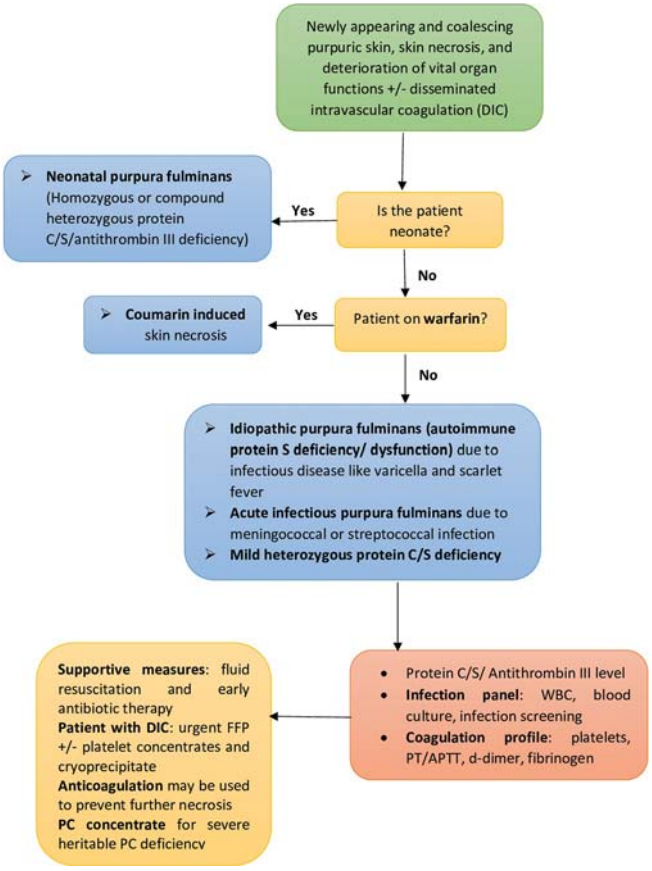

Figure 4: Purpura fulminans. Flowchart of approach to the patient presented with PF [61].

Table 3: CDC case definition for staphylococcal TSS [51]

Clinical criteria
Fever: temperature ≥38.9°C (102.0°F)
Rash: diffuse macular erythroderma
Desquamation: 1 to 2 weeks after onset of rash
Hypotension: for adults: systolic blood pressure ≤90 mmHg; for children <16 years of age: systolic blood pressure less than 5th percentile by age
Multisystem involvement (3 or more of the following organ systems): gastrointestinal, muscular, mucous membranes, renal, hepatic, hematologic, central nervous system
Laboratory criteria
Negative blood or cerebrospinal fluid cultures for alternative pathogens (blood cultures may be positive for *Staphylococcus aureus*)
Negative serologies for Rocky Mountain spotted fever, leptospirosis, or measles
Case classification
Probable case: A case that meets the laboratory criteria and four of the five clinical criteria Confirmed case: A case that meets the laboratory criteria and all five of the clinical criteria, including desquamation (unless the patient dies before desquamation occurs)

Treatment

If the cutaneous anthrax is associated with a concomitant inhalational exposure, the CDC recommended antibiotics for at least 60 days, compared to a 7–10-day course for a purely cutaneous exposure, quinolones and doxycycline are first-line agents [82].

Practical pearls

- "Malignant pustule" is an abandoned misnomer of cutaneous anthrax as pustules are rarely present, and their presence decreases the likelihood of anthrax diagnosis

• ECZEMA HERPETICUM (KAPOSI VARICELLIFORM ERUPTION)

Eczema herpeticum is a life-threatening viral infection that presents as a background to other dermatological conditions. It is mainly caused by herpes simplex virus type1 (HSV1), although HSV2, Coxsackie A16, smallpox, and vaccinia have all been implicated [83,84]. The majority of EH cases occur in infants/children more than adults with pre-existing atopic dermatitis; however, it can occur in other conditions with impaired skin barrier such as Darier disease, Hailey–Hailey disease, various bullous diseases, burns, ICD, mycosis fungoides, Sézary syndrome, and ichthyoses [85].

Eczema herpeticum is characterized by clusters of umbilicated, dome-shaped vesicles that quickly progress to monomorphic, punched-out erosions with hemorrhagic crusts. The patient may generally feel unwell, commonly with fever and lymphadenopathy. Rarely EH may result in the hematogenous spread of HSV with hepatic,

Table 4: underlying causes and pathogenesis of PF

1-Severe sepsis DIC and consumptive coagulopathy caused by severe sepsis such as meningococcal septicaemia, streptococcus, Haemophilus, and staphylococcus sepsis
2-Postinfectious (autoimmune) purpura fulminans 7-10 days after infection due to acquired autoimmune antibodies against protein S and C, most commonly associated with Varicella and Streptococcus infections
3-Heritable PC pathway defects Severe protein C and rarely protein S deficiency due to homozygous mutations in the *PROC* and *PROS1* genes, respectively

Table 5: Factors associated with higher EG mortality

• Neutropenia
• Septic shock
• Inappropriate or delayed antibiotic therapy
• Resistant microorganisms

pulmonary, ocular, and CNS manifestations [86-89]. If not treated promptly, the mortality rate of EH can be 6%–10%, primarily due to bacterial superinfection. EH is a clinical diagnosis and can be confirmed by scraping the blister for viral culture, direct fluorescent antibody staining, PCR sequencing, or Tankz smear [90].

Treatment

Early diagnosis and antiviral treatment can prove lifesaving. Systemic antiviral chemotherapy such as a 7-day course of intravenous acyclovir (5-10 mg/kg per dose administered intravenously) three times daily which may be prolonged according to the clinical course of the disease [91,92].

Practical pearls

- Eczema herpeticum can be easily misdiagnosed as an acute exacerbation of atopic dermatitis, signs that encourage the diagnosis of eczema herpeticum in children with atopic dermatitis include [93]:
  - Areas of rapidly worsening, painful eczema
  - Clustered blisters consistent with early-stage cold sores
  - Punched-out erosions (circular, depressed, ulcerated lesions) usually 1–3 mm that are uniform in appearance (these may coalesce to form larger areas of erosion with crusting)
  - Possible fever, lethargy, or distress.

• LEPROSY REACTIONS

Leprosy reactions are a significant cause of hospitalization and disability. They occur primarily in patients with lepromatous and borderline leprosy due to immune-mediated inflammation involving the skin, nerves, eyes, and other body organs (Fig. 5). These reactions may occur before diagnosis, during treatment, or after treatment completion [94,95]. Leprosy-related conditions requiring urgent referral for assessment and treatment are summarized in Table 6.

Type 1 reaction (reversal or upgrading reaction)

Type 1 reaction (T1R) is a Th1 mediated delayed-type hypersensitivity reaction to *M. leprae* antigens. T1R occurs primarily in patients with borderline leprosy (BT, BB, BL) with immunological recovery during or after treatment, which causes a sudden increase in cell-mediated immunity and a shift toward the polar tuberculoid end of the Ridley-Jopling leprosy spectrum [97,98]. It is characterized by increased inflammation of established skin lesions, and the emergence of new skin lesions with acute neuritis. Neuritis causes loss of sensory and muscle function, which is generally associated with nerve pain, but in some cases without pain or nerve tenderness (silent neuritis) [99]. In clinical practice, type 1 reactions can't be diagnosed using laboratory tests and the diagnosis is usually made based on clinical manifestations [100].

Type 2 reaction (erythema nodosum leprosum)

Erythema nodosum leprosum (ENL) is a systemic inflammatory condition caused by cutaneous and systemic small-vessel vasculitis. It is characterized by Th2 mediated excessive immune complex formation and deposition that occurs primarily in patients with LL and BL [101,102]. ENL is characterized by the sudden onset of nodular skin lesions associated with features of systemic vasculitis including, iridocyclitis, lymphadenitis, hepatosplenomegaly, orchitis, glomerulonephritis, joint swelling, and dactylitis (Table 7). The main risk factor for ENL is lepromatous leprosy with skin infiltration, high bacterial load, and an age of less than 40 years [103]. The diagnosis of ENL is primarily based on clinical findings. Skin biopsy may be helpful when the diagnosis is unclear [104].

Lucio phenomenon (erythema necroticans)

The lucio phenomenon is an uncommon immunological reaction that occurs in patients with diffuse non-nodular lepromatous leprosy, mainly in western Mexico [106]. It is characterized by irregular purpuric macules, especially below the knees that evolve into bullous lesions that rapidly ulcerate. This severe reaction primarily occurs in patients who have not received treatment, and it may coincide with ENL [107,108].

Treatment

Lepra reactions require urgent treatment as they can lead to irreversible deformities. Thus, early diagnosis and timely initiation of anti-inflammatory measures are crucial. Multidrug therapy (MDT) should be continued or initiated (in those who first present with T1R). Aspirin or paracetamol should be administered to reduce pain and fever, and rest is essential. Corticosteroids are the cornerstones of type 1 reactions and acute neuritis therapy. The dose may be adjusted according to neurological function

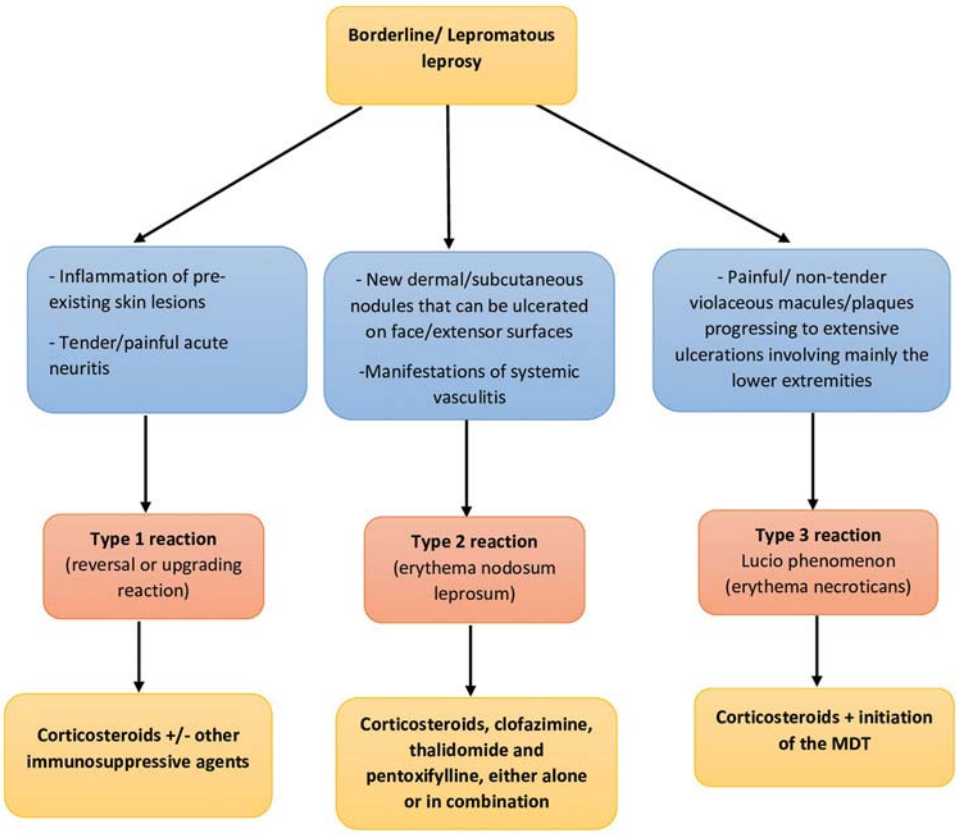

Figure 5: Leprosy reactions. Leprosy reactions include type 1 reaction (reversal or upgrading reaction), type 2 reaction (erythema nodosum leprosum) and type 3 reaction (Lucio phenomenon, erythema necroticans).

Table 6: Indications of urgent referral for assessment and treatment in leprosy [96]

• Severe leprosy reactions, including: – Severe reversal reactions – Reversal reactions overlying a major nerve trunk – Neuritis, including silent neuritis – Erythema Nodosum Leprosum (ENL) reactions
• Severe infection of the hand or foot (usually related to an ulcer with foul-smelling discharge); the hand or foot will be hot, red, swollen, and probably painful.
• Eye involvement in leprosy – four specific problems that need urgent referral: – Recent loss of visual acuity – A painful red eye – Recent inability to close the eye (lagophthalmos) – A reaction in a leprosy skin patch on the face
• Serious adverse drug reactions

assessment [109,110]. Alternative immunosuppressive agents, including azathioprine, cyclosporine, and methotrexate, may play a role in the management of severe T1R non-responsive to corticosteroids [111-113].

ENL is often recurrent, chronic, and a significant health problem in countries where leprosy is endemic. Therefore, treatment is often prolonged and requires several months to years of therapy. Treatment for ENL aims to resolve skin lesions, relieve pain, and reduce and prevent complications by reducing systemic and neural inflammation. Limited high-quality clinical data are available to guide drug choice, dosing, and duration. However, corticosteroids, clofazimine, thalidomide, and pentoxifylline, either alone or in combination, are the most commonly used drugs to treat ENL [114,115]. Because of its well-known teratogenic side effects, the WHO does not support the use of thalidomide [105]. Patients with Lucio's Phenomenon usually respond well to the initiation of MDT alone or in combination with corticosteroids [116].

Practical pearls

- Reversal reaction is one of the presentations of immune reconstitution inflammatory syndrome (IRIS) in HIV patients after commencing the HAART; hence patients with reversal reaction should be screened for HIV co-infection as a triggering factor
- In order to prevent or alleviate the nerve damage and its complications, long-term follow-up is critical for patients who developed leprosy reactions
- Unlike the erythema nodosum, ENL mainly affects the face and extensors of the upper and lower extremities

Table 7: WHO criteria of severe ENL [105]

• Numerous ENL nodules with high fever
• ENL nodules and neuritis
• Ulcerating and pustular ENL
• Recurrent episodes of ENL
• Involvement of other organs (e.g. eyes, testes, lymph nodes, joints).

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