Cellulitis Look-Alikes

Russell M. Petrak, M.D. [1,*]

[1] Metro Infectious Disease Consultants, Burr Ridge, IL 60527, USA
* Corresponding author: rpetrak@innovativeventures.com

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Abstract: As Infectious Disease (ID) specialists, we are frequently confronted by a clinical scenario with a broad differential diagnosis. Bacterial cellulitis usually responds rapidly to appropriate antibiotic therapy, but when it does not, alternative diagnoses must be rapidly accessed and prioritized. To accomplish this, the ID specialist needs a functional understanding of cellulitis mimics. Utilizing the intensity of illness, appearance of the eruption, and the anatomical pattern of spread, the clinician can rapidly assess, identify, and treat the appropriate malady.

Keywords: cellulitis; eruptions; dermatitis

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Bacterial Cellulitis is an infection that typically responds to appropriate antibiotics quickly. When this does not occur, rather than considering an alternative diagnosis, many patients are sent to Infectious Diseases (ID) for more aggressive antibiotic regimens. The differential diagnosis of this clinical conundrum includes multidrug-resistant pathogens, infectious complications such as abscess formation or fasciitis, and septic arthritis. In addition, non-infectious, cellulitis look-alike diagnoses must be considered, and while these diagnoses have typically been the prevue of dermatology, a patients severity of illness and lack of access to inpatient dermatology evaluations make it mandatory that an ID specialist have the ability to diagnose these maladies.

This article will review several disease entities that need to be considered when an apparent cellulitis, appropriately treated, fails to respond.

Stasis Dermatitis

Patients usually present with a history of chronic venous insufficiency and have complaints of pain, redness, drainage, and pruritus. Scaling, crusting, ulcerations and lichenification may be present (Figure 1). This may occur unilaterally or bilaterally, on the medial aspect of the lower third of the leg

and superior to the medial malleolus. Clues to the diagnosis include the chronicity of the dermatitis including hemosiderin deposits, the location of the eruption, and failure of previous antibiotic regimens. In the absence of secondary bacterial cellulitis, fever is an uncommon manifestation [1].

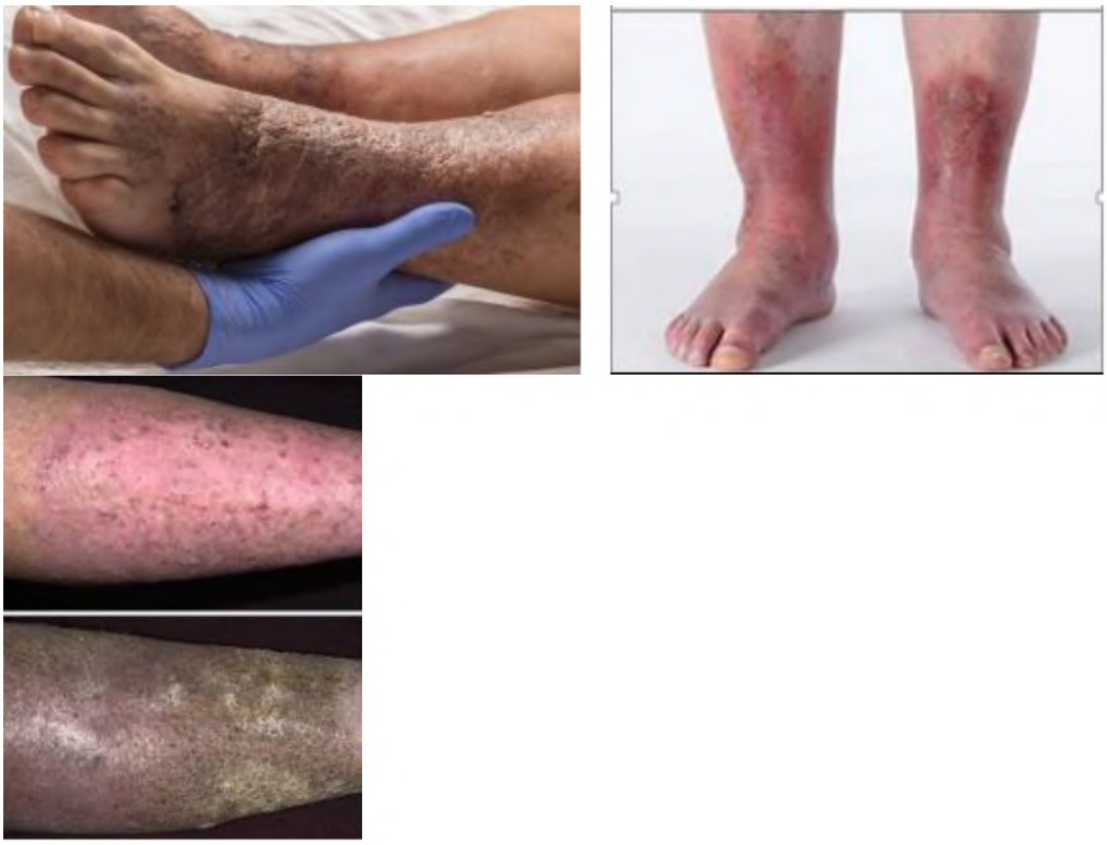

Figure 1: Stasis Dermatitis. Top Left: Reprinted with permission [2]. Top Right: Reprinted with permission from [3]. Bottom Left: Reprinted with permission [2].

Acute Febrile Neutrophilic Dermatosis (Sweet's Syndrome)

Patients present with fever and variable lesions on the extremities, face, or neck [4]. Lesions may be tender, papular, and evolve into inflammatory plaques with a pustular component. The distribution may be asymmetric. While upper-extremity lesions are the most common, lower extremity lesions may be confused with erythema nodosum (Figure 2). Triggers include pregnancy, inflammatory bowel disease, and numerous medications. Minocycline, quinolones, and trimethoprim-sulfamethoxazole are common antibiotic triggers, as well as the nucleoside analogue abacavir. Twenty percent of patients have an underlying malignancy, which is more likely to be hematologic. Sweets syndrome may precede, follow, or occur concurrently with the malignancy [5].

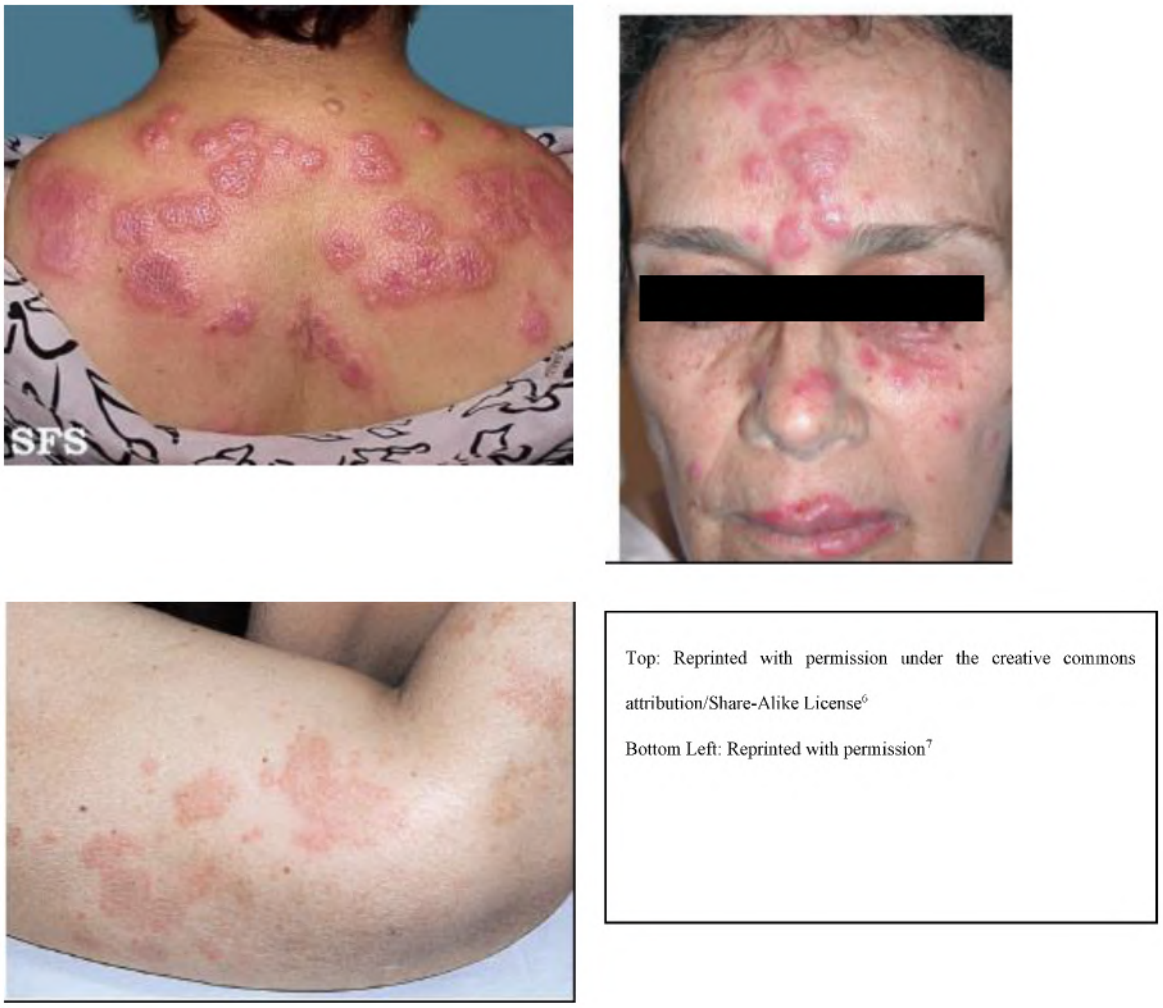

Figure 2: Acute Febrile Neutrophilic Dermatosis (Sweets Syndrome). Reprinted with permission under the creative commons attribution/Share-Alike License [6]. Bottom Left: Reprinted with permission [7].

Steven's Johnson Syndrome (SJS)

This is a potentially life-threatening disease which includes both cutaneous and mucosal involvement. Following a prodrome characterized by fever and influenza-like symptoms, the cutaneous eruptions typically begin on the face and trunk and spread in a symmetrical fashion [8]. While the scalp is spared, palms and soles may be occasionally involved. The lesions evolve from macules to the classic target lesions. These may become confluent with bullous lesions, strongly resembling a rapidly progressive bacterial cellulitis. The mucosal oral lesions include erosions and crusts and may involve any mucosal surface [9] (Figure 3).

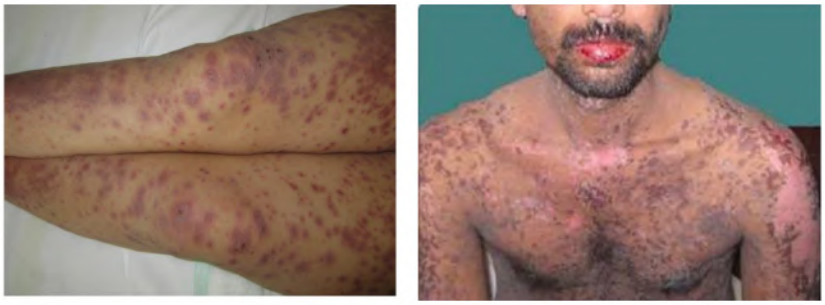

Figure 3: Stevens Johnson Syndrome. Reprinted with permission [10,11].

Acute Generalized Exanthematous Pustulosis (AGEP)

Patients present with pustules superimposed on an edematous and erythematous base. The rash usually begins on the face or intertriginous areas with rapid spread to the trunk and limbs (Figure 4). Historically, exposure to nonsteroidal anti-inflammatory agents, antibiotics, or diltiazem are the triggers for AGEP. A short incubation between 1 and 11 days prior to the eruption is a clue to the diagnosis. Mucous membrane involvement is rare. Fever, leukocytosis, and mild eosinophilia may occur [12,13].

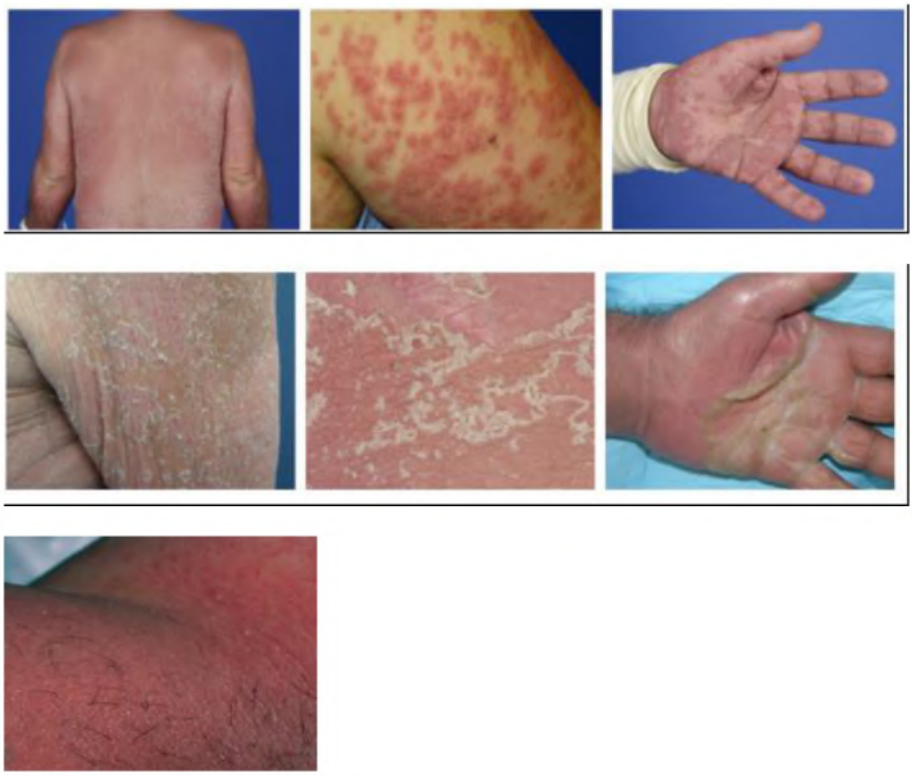

Figure 4: Acute Generalized Exanthematous Pustulosis. Reprinted with permission [14,15].

Generalized Pustular Psoriasis (GPP)

Patients typically present with an acute onset of painful, erythematous patches that rapidly become covered by numerous pustules (Figure 5). These pustules resolve over several days with residual erythema and extensive scaling. Intraoral pustulation may occasionally occur. These disease flares may reoccur, commonly upon the reintroduction of the offending agent. Triggers include withdrawal of glucocorticoids as well as exposure to numerous antibiotics, rituximab, and tumor necrosis factor inhibitors (TNFi). Other precipitating factors include pregnancy, preceding upper respiratory infections, and various viral illnesses including CMV, EBV, Varicella Zoster, and SARS-CoV-2. In contrast to AGEP, patients with GPP commonly have a history of previous psoriatic eruptions [13]. Factors favoring the dx of AGEP include the absence of a previous history of psoriasis, short incubation periods after exposure (1–11 days) to offending agents, and rapid resolution after the removal of the triggering agent. Despite the fact that TNFi have precipitated GPP, infliximab has been successfully used therapeutically [16].

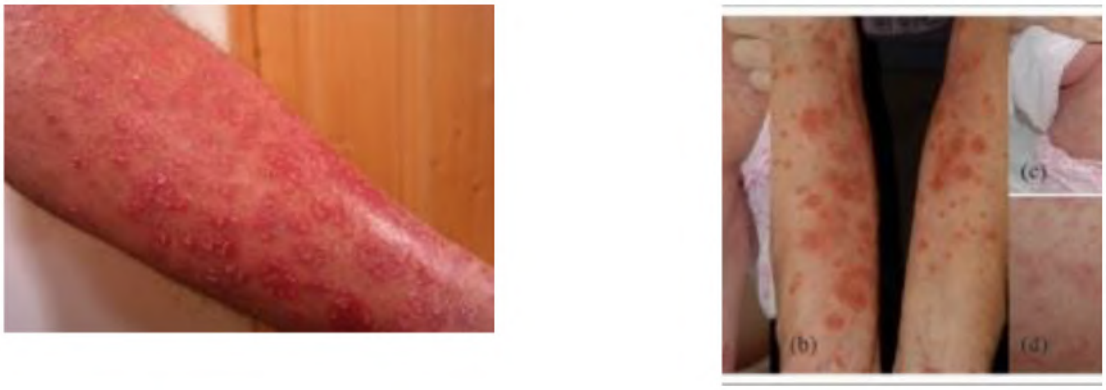

Figure 5: Generalized Pustular Psoriasis (GPP). Reprinted with permission [17,18].

DRESS Syndrome

Drug reaction with eosinophilia and systemic symptoms is a hypersensitivity syndrome characterized by a long latency phase of 2–8 weeks after exposure to an offending agent [9]. This is followed by a prodromal phase with fever and lymphadenopathy. The cutaneous eruption begins as a maculopapular eruption which progresses to a confluent erythema that may occasionally exfoliate (Figure 6). Facial edema, pruritus, and a large percentage of total body area involvement are other common findings. While mucosal involvement is common, it is not typically severe. Organ involvement is seen in over 90% of cases and may include liver, kidney, pulmonary, or cardiac involvement. Besides eosinophilia, monocytosis and atypical lymphocytes are common.

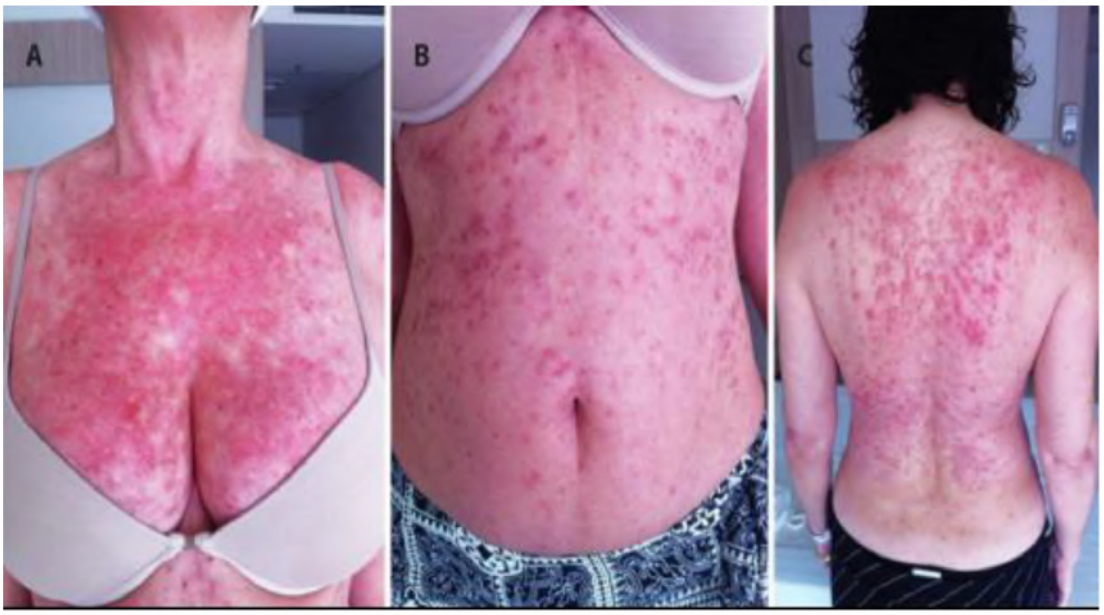

Figure 6: DRESS Syndrome. Reprinted with permission [19].

Kawasaki's Disease (KD)

Also known as mucocutaneous lymph node syndrome, KD is a common vasculitity of children which can occasionally be seen in adults. Fever and conjunctivitis are the most consistent findings, being seen in over 90% of cases. Mucositis with fissured, erythematous lips and an inflamed tongue may also be present. The rash usually begins early in the illness and can be polymorphous. Beginning as a macular eruption, the rash progresses to target-like lesions that are rarely vesicular or bullous (Figure 7) Subsequently, the dorsum of the hands and feet dominate the cutaneous clinical picture, ultimately resulting in desquamation of these areas. Cervical lymphadenopathy and cardiac manifestations may also be present [20,21].

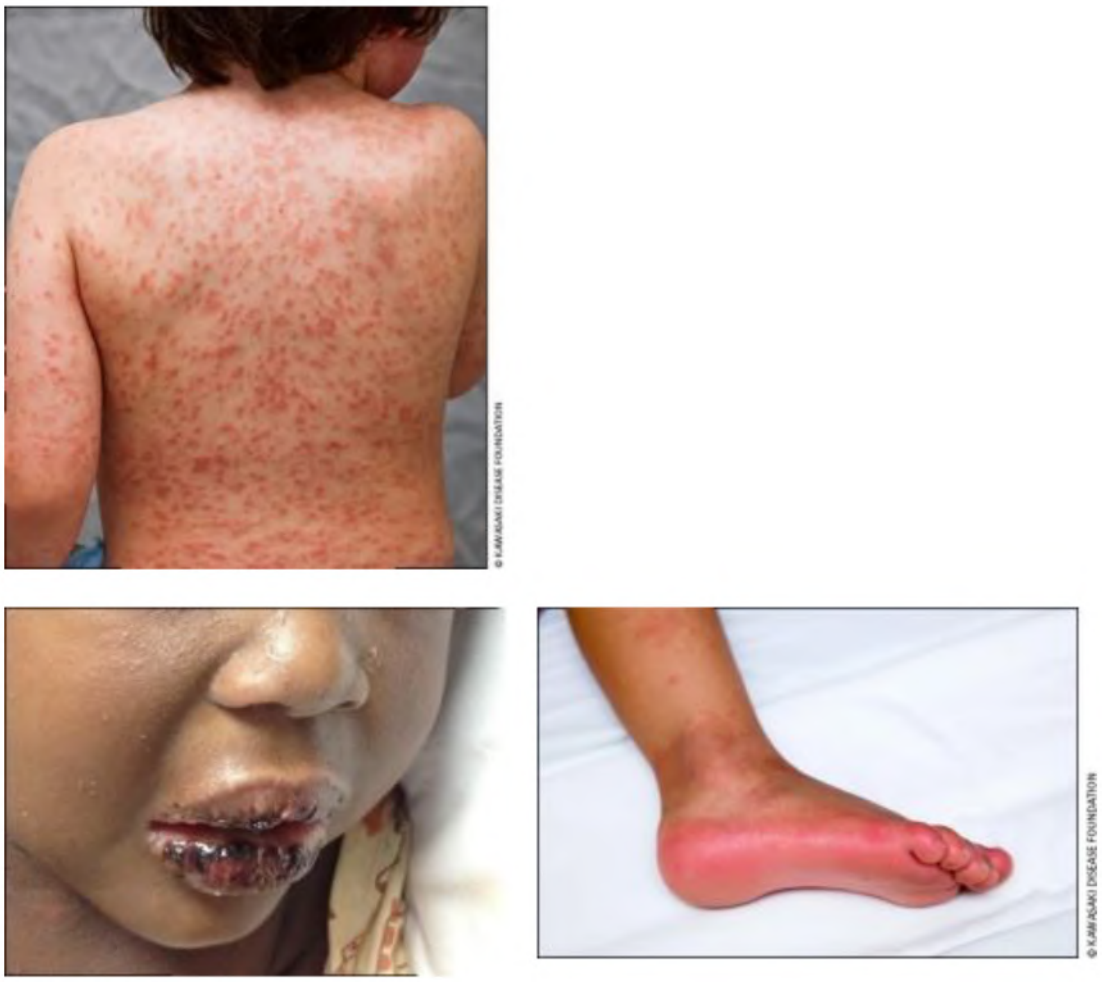

Figure 7: Kawasakis Disease. Reprinted with permission [22].

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