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Clinical Review

CLINICAL MIMICS: AN EMERGENCY MEDICINE-FOCUSED REVIEW OF CELLULITIS MIMICS

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☐ **Abstract—Background: Cellulitis is a common clinical condition with low rates of morbidity and mortality if treated appropriately. Mimics of cellulitis presenting with erythema, edema, warmth, and pain can be associated with grave morbidity and mortality if misdiagnosed. Objective: This review investigates the signs and symptoms of cellulitis, mimics of cellulitis, and an approach to the management of both cellulitis and its mimics. Discussion: The current emergency medicine definition of cellulitis includes erythema, induration, warmth, and swelling. Given the common pathophysiologic pathways, cellulitis mimics often present in an analogous manner. These conditions include septic bursitis, septic joint, deep vein thrombosis, phlegmasia cerulea dolens, necrotizing fasciitis, flexor tenosynovitis, fight bite (closed fist injury), orbital cellulitis, toxic shock syndrome, erysipelas, abscess, felon, paronychia, and gouty arthritis. Many of these diseases have high morbidity and mortality if missed by the emergency physician. Differentiating these mimics from cellulitis can be difficult in the fast-paced emergency setting. A combination of history, physical examination, and focused diagnostic assessment may assist in correctly identifying the underlying etiology. For many of the high mortality cellulitis mimics, surgical intervention is necessary. Conclusion: Cellulitis and its mimics present similarly due to the same physiologic responses to skin and soft tissue infections. A combination of history, physical examination, and diagnostic assessment will help the emergency physician differentiate cellulitis from mimics. Surgical intervention is frequently needed for high morbidity and mortality mimics. Published by Elsevier Inc.**

☐ **Keywords—mimics; cellulitis; septic bursitis; septic joint; deep vein thrombosis; phlegmasia cerulea dolens; necrotizing fasciitis; flexor tenosynovitis; fight bite; orbital cellulitis; toxic shock syndrome; erysipelas; abscess; felon; paronychia; gout**

INTRODUCTION

Cellulitis is a common condition managed in the emergency department (ED), with 2.3 million ED visits annually in the United States (1). The rate of admission has been steadily increasing by 73% from 1997 to 2011, with 330,000 admissions in 1997 to 652,000 admissions in 2011 (2,3). Patients with cellulitis commonly present with nonspecific physical examination findings of inflammation including erythema (rubor), edema (tumor), warmth (calor), and pain (dolor) that develop over days (3–6). However, of the 652,000 patients admitted to the hospital every year, approximately 30% are misdiagnosed by emergency physicians (1,3,7,8).

There are several definitions of cellulitis, often leading to confusion (Table 1). Per the Infectious Diseases Society of America (IDSA) 2014 guidelines on skin and soft

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tissue infections, cellulitis "refer[s] to diffuse, superficial spreading skin infection … [the definition of cellulitis] is not appropriate for cutaneous inflammation associated with collections of pus such as septic bursitis, furuncles, or skin abscesses (6)." Classic signs of cellulitis include rubor, tumor, calor, and dolor. However, these findings were initially used to describe inflammation (9). Additional physical examination findings may include edematous skin. This may result in peau d'orange, which is skin resembling an orange peel. Painful regional lymphadenopathy may also be noted (3). Cellulitis is nearly always unilateral (10). Bilateral cellulitis is unusual, as are chronic findings lasting over several months, or pruritus (10). These findings suggest another condition. Laboratory findings may include elevated white blood cell count in 34–50%, elevated erythrocyte sedimentation rate in 59–91%, and elevated C-reactive protein in 77–97% (3,11,12). Blood cultures are low yield and not recommended, except in patients who are immunocompromised, neutropenic, and seriously ill (including septic shock) (6). These physical examination and laboratory findings are highly nonspecific and are often present with cellulitis mimics. These nonspecific findings account for why many patients are misdiagnosed and fail outpatient treatment of cellulitis.

Fortunately, many of the cellulitis mimics are benign if missed: venous stasis, lymphedema, gout, paronychia, and contact dermatitis (3). Although nonemergent cellulitis mimics have been discussed in the literature, there is a lack of focus on emergent diagnoses (3). This article seeks to illustrate diagnoses that emergency physician should not miss when considering cellulitis on the differential diagnosis.

METHODS

Authors conducted a literature search of Medline, EBSCO, and Google Scholar for search terms including mimics, cellulitis, septic bursitis, septic joint, deep vein thrombosis, phlegmasia cerulea dolens, necrotizing fasciitis, flexor tenosynovitis, fight bite, orbital cellulitis, toxic shock syndrome, erysipelas, abscess, felon, paronychia, and gouty arthritis. Guidelines on cellulitis were included. Articles in English were included. Authors agreed on articles to include by consensus.

DISCUSSION

Why Does Erythema, Induration, Warmth, and Swelling Occur in Cellulitis?

Cellulitis is characterized by erythema, warmth, edema, and pain due to the underlying pathophysiology. A nidus of inflammation, such as bacteria penetrating through the skin, triggers immune system response. Histamine, prostaglandins, and bradykinins are released into the soft tissue, causing vasodilation with subsequent erythema and warmth. Histamine also acts on endothelial cells, resulting in leakage of plasma into the interstitium and tissue space, leading to edema (9). Increased pain at the site of cellulitis is due to sensitization of sensory nerve endings by bradykinin and prostaglandin E2 (PGE2). Lastly, systemic symptoms such as fever can occur due to the release of interleukin-1 and tumor necrosis factor from macrophages. Release of these cytokines stimulates cyclooxygenase activity and the release of PGE2. Elevated levels of PGE2 act on the hypothalamus to increase the set point temperature of the body, resulting in fever (15).

Table 1. Definitions of Cellulitis from Various Sources

Society	Definition
IDSA 2014	Diffuse, superficial spreading skin infection. The cellulitis definition is not appropriate for cutaneous inflammation associated with collections of pus such as septic bursitis, furuncles, or skin abscesses (6).
*Journal of the American Academy of Dermat*ology	Clinicians should use the term "cellulitis" for superficial spreading skin infections without an underlying collection of pus (4).
Tintinalli's Emergency Medicine: A Comprehensive Study Guide	*Cellulitis* is an infection of the dermis and subcutaneous tissues of the skin. Cellulitis is divided clinically as *purulent* or *nonpurulent,* and management of the two types is different. Purulent cellulitis is cellulitis with an abscess, or cellulitis with drainage or exudate in the absence of a drainable abscess. Nonpurulent cellulitis has no purulent drainage or exudate and no associated abscess (5).
Rosen's Emergency Medicine Concepts and Clinical Practice (13)	Cellulitis is an infection of the skin tissue denoted by erythema, swelling, and local tenderness. Unfortunately, the literature on soft tissue infections is often confusing with respect to definition and therapy, in part because the nomenclature has been based on individual names, anatomic areas, or events (e.g., postsurgical gangrene).
Harrison's Principles of Internal Medicine (14)	Cellulitis is an acute inflammatory condition of the skin that is characterized by localized pain, erythema, swelling, and heat.

IDSA = Infectious Diseases Society of America.

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