CELLULITIS: A mnemonic to increase accuracy of cellulitis diagnosis

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Abstract Cellulitis, a bacterial infection of the skin and subcutaneous tissue, is often misdiagnosed. Cellulitis accounts for a large number of all infectious disease-related hospitalizations in the U.S. Cellulitis can be challenging to diagnose since it lacks pathognomonic findings. We reviewed all articles on cellulitis within the last 20 years that included a statistical analysis, with odds ratios (OR), of specific clinical features of cellulitis. We then constructed a mnemonic encompassing the features with the highest odds ratios. Our mnemonic is CELLULITIS for cellulitis history, edema, local warmth, lymphangitis, unilateral, leukocytosis, injury, tender, instant onset, and systemic signs. The first characteristic has the highest OR and may be the easiest to recall: past episode(s) of cellulitis.

Keywords: lower extremity cellulitis, dermatitis, stasis dermatitis, pseudocellulitis, mnemonic

Introduction

Cellulitis, a bacterial infection of the skin and subcutaneous tissue, is often misdiagnosed [1]. Cellulitis accounts for 10% of all infectious disease-related hospitalizations in the U.S [1]. Misdiagnosis causes 50,000-130,000 needless admissions costing $195-515 million annually [1]. Each year about 44,000 patients with cellulitis mimics (pseudocellulitis) are exposed to unnecessary antibiotics [1].

Cellulitis can be challenging to diagnose since it lacks pathognomonic findings. Easy-to-remember mnemonics may be helpful for non-dermatologists in diagnosing cellulitis.

We propose a mnemonic incorporating 11 key findings, starting with the evidence-based predictive tool proposed by Raff et al. for diagnosing lower extremity cellulitis [2]. We retain the top factors of Raff's 4-component model: unilaterality, leukocytosis, and tachycardia. Our mnemonic includes three factors with strong statistical support (prior cellulitis, injury, edema) and 5 history and physical signs (instant onset, warmth, tenderness, fever, lymphangitis), [2, 3-9].

Our mnemonic is CELLULITIS. This has been developed through the authors' combined 50 years of experience consulting on inpatients with cellulitis and pseudocellulitis. **Table 1** shows odds ratios for cellulitis findings in nine studies [2, 3-9].

C – Cellulitis history

The single most important risk factor is a history of prior cellulitis, present in nearly half the cases with an odds ratio (OR) of 31, greater than any other risk factor [4].

E – Edema

Swelling (i.e. edema), pain, warmth, and erythema are four inflammatory signs typically found unilaterally in cellulitis. Preexisting lymphedema raises cellulitis risk, more than venous edema [8]. Clinically, erythema (brick-red) is the least useful

inflammatory sign in distinguishing cellulitis from mimics.

L – Local warmth
Areas of cellulitis are nearly always warmer than corresponding areas on the opposite leg. Localized warmth is often used as an inclusion criterion for diagnosing cellulitis [3, 10, 11]. A temperature difference of 0.47°C or greater between affected and unaffected skin showed 87.5% accuracy in diagnosing cellulitis [11].

L – Lymphangitis
Unlike uncomplicated dermatitis, cellulitis may present with ascending lymphangitis (continuous or interrupted tender red streaks) and sometimes, lymphadenopathy. Clinically, lymphangitis is not highly sensitive, but specific when present.

U –Unilateral
Raff et al. found asymmetry to be the most useful criterion distinguishing cellulitis from pseudocellulitis [2]. Although stasis dermatitis can present with unilateral flares, signs of stasis dermatitis are seen on the contralateral leg. Contact allergic dermatitis is seldom unilateral and has a characteristic history.

L – Leukocytosis
Leukocytosis with white blood cell count >10,000/µl is useful in asymptomatic older patients [2].

I – Injury
Trauma and ulcers allow bacterial invasion and have higher cellulitis ORs than toe-web intertrigo, which is also associated with increased cellulitis risk [3]. Local injuries and skin disruptions are more predictive of cellulitis than systemic factors such as diabetes, obesity, and smoking [3, 7].

T – Tender
Tenderness to palpation (i.e. flinching) is a more useful diagnostic factor than resting pain. In Raff's predictive model, pain *in the emergency room* had a P value versus pseudocellulitis of 0.02, whereas pain *prior to presentation* had a P value of 0.537 [2].

I – Instant onset
Patients remember the day of cellulitis onset, whereas stasis dermatitis onset is vague. Some studies require instant onset of fever and chills for inclusion [3, 8].

S - Systemic signs
Tachycardia (≥90 bmp) in the emergency department is one of Raff's predictive factors [2]. The presence of fever during cellulitis is a controversial issue. Fever is used as a cellulitis inclusion criterion in some studies, whereas in other studies fever was infrequently present [3, 8, 12-16].

Limitations: There are no case-control data validating the complete mnemonic, which includes Raff's top three factors (unilateral involvement, leukocytosis, and tachycardia), three additional independently validated factors (prior cellulitis, injury, edema), and five other history and physical findings (instant onset, warmth, tenderness, fever, lymphangitis). Furthermore, the ORs from the studies cited, with the exception of the study from Raff et al., were obtained from comparing patients with cellulitis to matched controls. This limits the applicability of using this data to diagnose cellulitis rather than differentiating cellulitis from pseudocellulitis.

Conclusion
Based on literature and the authors' collective clinical experience, the mnemonic CELLULITIS summarizes the most useful findings in diagnosing cellulitis, for cellulitis history, edema, local warmth, lymphangitis, unilateral, leukocytosis, injury, tender, instant onset, and systemic signs. The first characteristic has the highest OR and may be the easiest to recall: past episode(s) of cellulitis.

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Table 1: *CELLULITIS. Mnemonic component and adjusted odds ratios (OR) for cellulitis.*

Finding		Median OR	Source						
			Bjornsdottir[5]	Dupuy[6]	Halpern[7]	Karppelin[4]	Mokni[8]	Roujeau[9]	Njim[3]	Raff[2]
Cellulitis[&] history		31.04	31.04 (4.15-232.20)		35.15 (13.68- 90.32)			24 .0 (7.1-81.2)	2.1 (0.4-10.5)	
Edema, including lymphedema		6.77	1.51 (0.53-4.28)	leg edema 2.5 (1.2 to 5.1) lymphedema 71.2 (5.6-908)	9.69 (5.99-15.67)	11.5 (1.2-114.4)	leg edema 7.0 (1.3-38) lymphedema 19.1 (1.1-331)	4.5 (1.3-15.6)		
Local warmth[3,10,11]										
Lymphangitis										
Unilateral		8.65								8.65 (3.88-19.26)
Leukocytosis		2.43								2.43 (1.31-4.52)
Injury#	Ulcer*	12.73	11.80 (2.47-56.33)	Leg ulcer 20.6[u] (6.7 - 63.0) Pressure ulcer 6.0[u] (1.4 t - 26.0)	21.45 (8.25-55.76)		2.0[u] (0.1-31.9)	9.0 (3.7-21.8)		
	Trauma[%]	19.11		6.8[u] (4.0 - 11.7)	43.18 (22.11-84.32)	3.8[u] (1.2-11.3)	19.9 (6.7-58.8)	Cutaneous barrier disruption 22.0 (9.4-51.4)	12.4 (3.9-39.1)	
Tender										
Instant Onset[3,8]										
Systemic Signs	Heart rate ≥ 90[2]	1.94								1.94 (1.02-3.67)
	Fever[3,8,,12-16]									

§All odds ratios are adjusted for confounding factors and are multivariate except when marked u: univariate.
* Current leg ulcer only (median OR 14.88). Pressure ulcer has lower OR: 6.0.[11] History of ulcer has lower median OR: 5.06.[7,10,11,13]
# Intertrigo often included as a current injury. Median intertrigo OR was 3.81, but in Cameroon, OR was 51.4.[7-14] Environment may be confounding factor.[7-14] % Nijm limits trauma onset to ≤4 weeks before cellulitis onset.[8] Other studies do not specify.[7,9,11-13]
& Surgery and excoriating skin disease not included in history due to median ORs only 2.7[1-8] and 4.37,[2-5,7] respectively.
2 Only Raff study used ORs vs. pseudocellulitis. Age (adj. OR 2.71) included in Raff predictive model, However average age for those with cellulitis 63.2 years vs. 62.6 years without cellulitis; differences are not significant.
3 Warmth and fever > 38C or chills of instant onset (< 24 hr.) required for case inclusion.
5 Traumatic wounds included in ulcer total.
7 ORs for Halpern study obtained from Quirke.
8 Fever > 38C or chills of instant onset (< 24 hr.) required for case inclusion.