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The prognostic values of soft tissue sonography for adult cellulitis without pus or abscess formation

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Abstract

The current practice for cellulitis in diagnosis and treatment is mainly based on subjective clinical judgement without validated objective guidance. For patients with non-purulent cellulitis needing intravenous antibiotic treatment in hospital, we found soft tissue sonography performed around 4 days after initiation of antibiotics might have prognostic values. The patients with soft tissue sonographic pattern of subcutaneous thickening alone had shorter duration of antibiotic treatment and higher rate of early treatment response to antibiotics than those with the pattern of cobblestone appearance. Larger-scale research may be warranted to validate the prognostic roles of sonography in cellulitis management.

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Cellulitis is defined as an acute bacterial infection involving dermis and subcutaneous tissue, mostly caused by streptococci and *Staphylococcus aureus* in immunocompetent adults.¹ The diagnosis and treatment for cellulitis are typically based on physician's judgement on physical findings and suggestive history.² However, such a subjective approach cannot always be unequivocal and thus, looking for an appropriate objective tool to facilitate the disease management would be important for clinical practice. Because of its discernible imaging features of cellulitis,^{3,4} soft tissue sonography can potentially play some clinical roles in cellulitis management. There are

four distinct soft tissue sonographic patterns of cellulitis described in the literature.^{3–6} For convenience, we arbitrarily designated them as follows: pattern 1, subcutaneous thickening alone (Fig. 1a); pattern 2, subcutaneous disarray without pus accumulation (cobblestone pattern) (Fig. 1b); pattern 3, subcutaneous disarray with pus accumulation (Fig. 1c) and pattern 4, subcutaneous distortion with abscess formation (Fig. 1d). Pus or abscess formation in cellulitis, revealed in sonography as pattern 3 or 4, is known to prolong antibiotic treatment.² Several studies have demonstrated the effectiveness of soft tissue sonography to facilitate identification and drainage of pus or abscess formed in severe cellulitis.^{3,5,7–10} However, for cellulitis without pus or abscess formation as reflected sonographically in patterns 1 and 2, the clinical values of soft tissue sonography are still not appreciated.^{3,9}

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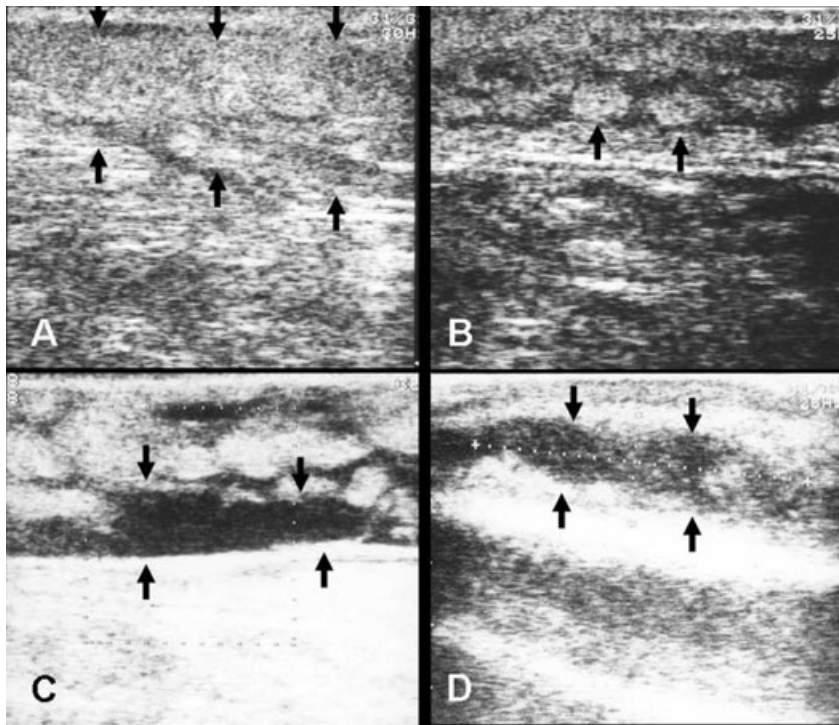


Figure 1 (A) Increased subcutaneous thickness and echogenicity (arrows). (B) Disarray of subcutaneous tissue forming a cobblestone pattern (arrows). (C) Disarray of subcutaneous tissue with a residual cobblestone pattern and pus accumulation (arrows). (D) Frank abscess formation enclosed by distorted subcutaneous tissue (arrows) without typical cobblestone pattern. The patterns in (A) and (B) were designated as pattern 1 and pattern 2 respectively in this study.

We hypothesized patients with cellulitis in sonographic patterns 1 and 2 might have different clinical outcomes. To test our hypothesis, we prospectively followed 34 patients randomly selected from a cohort of 120 consecutive patients with cellulitis admitted to our hospital for intravenous antibiotic treatment. All the selected patients were examined by a single experienced physician for soft tissue sonography after admission. The diagnosis of cellulitis was based on clinical history and physical examination. All the clinical data were retrieved at the time of sonographic examination. The attending physicians of individual patients were unaware of sonographic patterns of cellulitis if there was no identifiable pus or abscess formation by sonography. Three out of the 34 followed patients were excluded from analysis because of pus or abscess formation confirmed by sonography during the follow-up period, which was known to complicate the treatment course.² Finally, 31 patients with either sonographic pattern 1 or 2, but no progression to pattern 3 or 4, were qualified for the analysis.

Soft tissue sonography was performed with a 7.5-MHz linear transducer (Aloka Co., Ltd., Tokyo, Japan) on an ALOKA SSD-2000 ultrasound system. All the involved areas of cellulitis were scanned and compared with the opposite normal areas to determine the sonographic abnormality. When both sonographic pattern 1 and pattern 2 developed in an individual patient, only pattern 2 was recorded. The clinical characteristics and outcomes

we recorded for analysis are shown in Table 1. We defined total antibiotic days as treatment duration of both intravenous and oral antibiotics. The early antibiotic response was defined as symptomatic improvement in the involved skin areas within 3 days after antibiotic treatment.

The treatment is based on routine clinical practice for cellulitis.^{2,11,12} For those patients with diabetes mellitus (DM), broad coverage antibiotics were considered first if mixed Gram-positive and Gram-negative bacterial infection was highly suspected.^{2,12,13} Antibiotic therapy was only initiated after the diagnosis was confirmed by the attending physicians. The necessity for switching to another antibiotic, changing the route of drug administration, or the decision to stop treatment was judged by the attending physicians. The total duration of antibiotic treatment, including both oral and intravenous therapy, was at least for 7 days.^{2,12}

Discrete data were presented as frequencies and percentages and continuous variables as mean or median and standard deviation (SD). Data that were not distributed normally were logarithmically transformed to approximate normal distribution before analysis. Differences of clinical characteristics between patients with two sonographic patterns were assessed using independent *t*-test or Fisher's exact test. Multiple linear regression or logistic regression was used to estimate the differences of clinical outcomes between two groups with or without

Table 1 Clinical characteristics and outcomes for cellulitis in patients with different sonographic patterns

	Sonographic pattern		Total	P
	Pattern 1	Pattern 2		
Number of patients	11	20	31	
Clinical characteristics				
Age (mean \pm SD), years	71.2 \pm 14.1	61.3 \pm 16.4	64.8 \pm 16.1	0.10
Sex (female : male)	7:4	5:15	12:19	0.06
Body mass index (median \pm SD)	23.8 \pm 3.4	23.9 \pm 5.3	23.8 \pm 4.6	0.84
Smoking (%)	18	25	22.6	1.0
Diabetes mellitus (%)	36	40	38.7	1.0
Hypertension (%)	73	45	54.8	0.26
Malignancy (%)	27	10	16.1	0.32
History of surgical operation† (%)	45	25	32.3	0.42
Fever (body temperature > 38°C) (%)	55	50	51.6	1.0
Time from abx initiation to echo exam (median \pm SD), days	3.0 \pm 4.3	4.0 \pm 5.9	4.00 \pm 5.5	0.25
Initial abx as cephalosporin class (%)	45	30	35.5	0.45
Initial abx as penicillin class‡ (%)	55	65	61.3	0.71
Concurrent local wounds (%)	27	50	41.9	0.28
Concurrent tinea on extremities (%)	18	55	41.9	0.07
Location of cellulitis (U : L : H)	2:8:1	3:17:0	5:25:1	0.45
Peripheral leucocyte count (mean \pm SD)	11577 \pm 6412/ μ L	10067 \pm 5417/ μ L	10603 \pm 5730/ μ L	0.52
Hemoglobin (mean \pm SD)	12.29 \pm 3.31 g/dl	12.03 \pm 2.28 g/dL	12.11 \pm 2.64 g/dL	0.82
Platelet (mean \pm SD)	202.8 \pm 95.4K/ μ L	216.9 \pm 91.4K/ μ L	211.9 \pm 91.49K/ μ L	0.64
C-reactive protein (median \pm SD)	5.00 \pm 5.24 mg/dL	3.04 \pm 7.31 mg/dL	3.26 \pm 6.54 mg/dL	0.97
Blood culture positive rate (%)	10	11	10.7	1.0
Clinical outcomes§				
Early abx response rate (%)	91	45	61	0.002
Total abx days (median \pm SD)	16.0 \pm 6.0	23.5 \pm 38.7	21.0 \pm 32.5	0.04
Total IV abx days (median \pm SD)	12.0 \pm 4.4	14.0 \pm 13.0	14.0 \pm 10.9	0.04
Total hospitalization days (median \pm SD)	15.0 \pm 6.8	16.0 \pm 13.6	15.0 \pm 11.7	0.10

†In corresponding extremities of cellulitis. ‡Penicillinase-resistant. §The *P*-values are adjusted for age, sex, diabetes, malignancy, smoking and initial antibiotics. Abx, antibiotics; IV, intravenous; SD, standard deviation; U : L : H, upper extremities : lower extremities : head.

adjustment for covariates. Small datasets (less than 10 samples with a given group) were corrected with exact tests. A two-tailed *P*-value of <0.05 was considered as statistically significant.

Of a total of 31 patients, 11 patients had sonographic pattern 1 and 20 had pattern 2. No significant difference was noted in clinical characteristics for patients with sonographic patterns 1 and 2 (Table 1). The mean age of our patients was 64.8 years and 19 of them were men. The prevalence of DM, hypertension, malignancy and surgical history was 38.7%, 54.8%, 16.1% and 32.3% respectively. The laboratory data revealed mild peripheral leucocytosis and slightly elevated C-reactive protein level. As for the clinical outcomes, we found the patients with the sonographic pattern 2 had lower early response rate to antibiotics and longer duration of total antibiotic treatment than those with pattern 1 (Table 1). The early antibiotic response rate was 91% in pattern 1 and 45% in pattern 2 (*P* = 0.002). The median total duration of antibiotic treatment in pattern 1 and in pattern 2 was 16 days

and 23.5 days respectively (*P* = 0.04). The median duration of hospitalization was 15 days in our patients without difference between the two patterns.

Although soft tissue sonography was generally considered of little clinical use for cellulitis without pus or abscess formation,^{3,9} our data suggested that soft tissue sonography might be an independent prognostic indicator in this situation. In addition to early antibiotic response, the sonographic patterns in cellulitis without pus or abscess formation also correlated with total antibiotic treatment duration, indicating their potential values in prognosis and treatment planning. Compared with the patients with sonographic pattern 1 (subcutaneous thickening alone), the patients with pattern 2 (cobblestone) responded less to antibiotic treatment within 3 days and exhibited prolonged antibiotic treatment by about 1 week (Table 1). In addition, as we found no difference in potential clinical confounding factors between patients with patterns 1 and 2 (Table 1), we suggested the sonographic patterns of cellulitis

without pus or abscess formation might independently influence the duration of antibiotic treatment and correlate with early antibiotic response. Because most cases of cellulitis do not progress to pus or abscess formation, our results may be applicable in a majority of patients with cellulitis.

The sonographic pattern of cellulitis can be dynamic during the disease course.^{3,4,9} For paediatric cellulitis, it was suggested the timing of soft tissue sonography relative to the disease onset might influence the sonographic patterns.⁵ However, it is quite difficult to determine the exact onset time of cellulitis in the clinical setting. Therefore, in the current study, we defined the timing of sonography as the 'time from antibiotic initiation to echo examination', which would be rather precise in daily clinical practice (Table 1). Based on this definition, the median examination timing of soft tissue sonography in our patients was 4 days after initiation of antibiotic treatment without difference between patients with patterns 1 and 2 (Table 1). Therefore, it is suggested that the appropriate examination timing should be around day 4 of antibiotic treatment.

The patients in our study population were of relatively advanced age with high prevalence of chronic illnesses and surgical history. This clinical profile may result from physicians' tendency to admit patients with adverse factors to develop complicated disease courses, such as DM, infected local wound and surgical procedures.^{2,12-14} As there is no indisputable guideline for cellulitis admission,^{2,11,12,15} the clinical characteristics in our patients may be a good approximation to that in usual clinical setting.

There are limitations in the current study. First, because the examination timing for sonography was around 4 days after initiation of antibiotic treatment when most of the patients were recovering from the disease, it would be possible that the sonographic patterns were actually associated with cellulitis at different resolving pace without prognostic power. Second, although we found no difference in aetiologies of cellulitis, such as local wounds and tinea, between the two sonographic patterns, the data from our small-sized study could not completely exclude the possibility that different aetiologies could also explain for different disease courses. A larger-scale study would be warranted to address these possibilities and clarify the clinical roles of soft tissue sonography in cellulitis.

In conclusion, our data suggested soft tissue sonographic patterns correlated with early antibiotic response and antibiotic treatment duration for cellulitis without pus or abscess formation, implying a potential prognostic value. Larger-scale studies are warranted to further

evaluate clinical applicability of soft tissue sonography in cellulitis management.

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