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Original article

Cutaneous infections, good use of antibiotics and diagnostic accuracy

Infections cutanées, bon usage antibiotique et pertinence diagnostique

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Abstract

The medical dashboard (DB) recording our clinical practices indicated on one hand the use of two different diagnosis terms, acute dermohypodermitis (ADH) or cellulitis, and on the other hand, an important antibiotic prescription heterogeneity. Our aim was to define these two diagnosis groups and to document compliance to our antibiotic therapy protocol.

Method. – ADH and cellulitis were selected in our medical DB that records all patient data. Our local antibiotic therapy protocol was designed in April 2009; the prescription of recommended antibiotic agents defined the compliance to recommendations. The patient files indicating non-consensual therapy were analyzed to determine the reasons for inappropriate prescription.

Results. – Three hundred and four cases of ADH and 82 of cellulitis were diagnosed over 6.5 years. ADH was associated with older age ($P = 0.007$), a higher frequency of venous insufficiency ($P = 0.015$), a lower frequency of cancer ($P = 0.007$), and was more often located on lower limbs ($P < 0.001$), compared to cellulitis. The diagnosis of ADH was associated with higher compliance to our antibiotic therapy protocol, compared to cellulitis: 68% versus (vs.) 24%, $P < 0.001$, and after April 2009: 53% vs. 64%, $P = 0.033$. Among the 162 inappropriate antibiotic prescriptions (42%), 75 were deemed justified after analyzing the patient file, but less frequently for ADH compared to cellulitis: 49% vs. 11,5%, $P < 0.001$.

Conclusion. – ADH presents different clinical characteristics compared to cellulitis. The antibiotic therapy protocol for ADH cannot be applied to cellulitis.

Keywords: Acute dermohypodermitis; Erysipelas; Cellulitis; Evaluation of professional practices

Résumé

Le tableau de bord (TB) d'infectiologie montrait d'une part, l'utilisation de deux termes diagnostiques, dermo-hypodermites aiguës (DHA) ou cellulites, en conclusion de la prise en charge des infections cutanées et, d'autre part, une hétérogénéité thérapeutique. Notre objectif était de caractériser ces deux groupes diagnostiques et de connaître l'observance de notre protocole d'antibiothérapie.

Patients et méthode. – Les DHA et les cellulites étaient sélectionnés à partir du TB répertoriant chaque patient hospitalisé. Le protocole thérapeutique était discuté en avril 2009, l'utilisation des molécules proposées définissant la bonne observance. Les dossiers des patients bénéficiant d'une antibiothérapie non consensuelle était analysés afin d'en déterminer les motifs.

Résultats. – En 6,5 ans, 304 DHA et 82 cellulites étaient diagnostiquées. Les DHA étaient associées à un plus grand âge ($p = 0{,}007$), une plus grande fréquence d'insuffisance veineuse ($p = 0{,}015$), une moindre fréquence de cancers ($p = 0{,}007$), et étaient plus souvent aux membres inférieurs ($p < 0{,}001$), comparativement aux cellulites. Le diagnostic de DHA était associé à une meilleure observance du consensus comparativement aux cellulites : 68 % versus (vs) 24 %, $p < 0{,}001$, et après avril 2009 : 53 % vs 64 %, $p = 0{,}033$. Parmi les 162 antibiothérapies ne respectant pas le protocole (42 %), 75 étaient justifiées à la lecture du dossier, moins fréquemment en cas de DHA : 49 % vs 11,5 %, $p < 0{,}001$.

Conclusion. – Les DHA présentent des caractéristiques cliniques différentes des cellulites. Le consensus thérapeutique des DHA paraît inadapté à la prise en charge des cellulites.

Mots clés : Dermo-hypodermite aiguë ; Érysipèle ; Cellulite ; Évaluation des pratiques professionnelles

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Cutaneous infections constitute a heterogeneous nosological group, the French 2000 consensus on erysipelas had spread the concept of acute dermohypodermitis (ADH) [1]. Even if this term is well defined, there are still clinical cases in which the term "cellulitis" is adequate [2]. In daily practice, according to medical experience, these two terms are probably used synonymously, even though a previous study revealed that some clinical parameters (age, localization) identified two different diagnoses [2].

The continuous professional development (CPD) includes the principles of professional practice assessment (PPA), recording medical practices, analyzing them, taking corrective measures based on the drafting of a decisional protocol/algorithm, then on the assessment of its application [3]. We set up a dashboard (DB) of medical activity in our unit allowing a rapid PPA [4]. The consecutive analyses made with this DB contribute to real time evaluation of our therapeutic practices [5].

Concerning cutaneous infections due to pyogenes bacteria, the DB identified the two previously mentioned terms, ADH (or erysipelas) and cellulitis [6]. The reasons for using these two semantic entities by senior infectious diseases physicians remain unknown, as well as their therapeutic impact. Our objectives were to define ADH and cellulitis on a diagnostic and therapeutic level, and to evaluate observance of the antibiotic therapy protocol for cutaneous infections, implemented in 2009.

1. Patients and method

Each hospitalized patient is recorded in our DB spreadsheet with 28 items to be documented. The required data comes from hospitalization reports, which were systematized according to a consensual pattern. The exact definition of hospitalization causes and final diagnosis, extracted from these reports, validated by the senior infectious diseases specialist managing the patient, is classified in categories defined by site of the infection, constituting as many homogeneous groups of hospital stay [4].

ADH (or erysipelas) and cellulitis were selected in the DB, dental or pharyngeal origin and nosocomial origin were exclusion criteria.

The therapeutic protocol was initiated in April 2009, and included all the propositions made during the 2000 consensus conference [1]. Protocol observance was defined as use of recommended agents, without taking into account doses or modes of administration. The prescriptions of antibiotic therapy outside of the protocol justified a complete reviewing of the medical file so as to determine the four essential motivations:

- adaptation to bacteriological results;
- antibiotic therapy adapted to the associated infection;
- antibiotic therapy modified because of an adverse evolution;
- antibiotic therapy adapted to specific comorbidities.

The analysis of the protocol impact relied on the measure of hospitalization duration and on patient outcome. The latter was defined as adverse when the patient needed to be transferred to surgery for abscess drainage or removal of necrotic tissues, to the ICU, or in case of death.

The DB variables were collected with the Statview® software. The associations between qualitative data were assessed with the Chi^2 test for a theoretical population superior to 5. The comparisons of averages were made with Mann and Whitney's non-parametric test. The differences were considered significant when the level of test of significance were inferior or equal to 5%.

2. Results

Three hundred and four cases of ADH and 82 of cellulitis were diagnosed between July 1, 2005 and December 31, 2011.

2.1. Epidemiology of acute dermohypodermitis and cellulitis

The epidemiological, clinical and therapeutic differences between the two groups are listed in Table 1. The patients presenting with ADH were older ($P = 0.007$), presented more frequently with venous insufficiency ($P = 0.015$) and less frequently with cancers, compared to patients with cellulitis ($P = 0.007$).

The clinical presentation was also different; ADH was more often localized on inferior limbs than cellulitis, 83% versus 56%, $P < 0.001$. The others localizations were the upper limbs (13% versus 23%), the face (4% versus 12%) and the thorax (< 1% versus 11%).

The bacteriological data concerned essentially superficial sampling (Table 2). Hemoculture was made for 359 patients (93%), 29 of these were effectively bacteremic (7.5%), without any significant difference between ADH and cellulitis. Forty-eight strains of *Streptococci* (group A, B, C, or G) were isolated, including 34 in ADH (12%) and 14 in cellulitis (15%).

The antibiotic therapy protocols were significantly different between these two groups. The protocol observance was better in ADH patients ($P < 0.001$, Table 1). The analysis of 162 antibiotic therapy prescriptions not complying with the protocol (42%) showed they were justified 75 times, but less frequently in ADH: 11.5% versus 49%, $P < 0.001$. The bacteriological data was the main source of deviation from protocol, observed in 36/75 cases (48%, Table 1).

The duration of hospitalization was significantly shorter in case of ADH, close to 48 hours, compared to cellulitis ($P = 0.005$, Table 1).

The poor outcomes were less frequent for ADH compared to cellulitis: 16 (5%), versus 10 (12%), $P = 0.026$.

2.2. Diagnostic and therapeutic impact of the antibiotic therapy protocol

Observance of the therapeutic protocol was better for patients with ADH compared to those with cellulitis, during all the study period: 68% versus 21%, $P < 0.001$.

The protocol was made in April 2009. We compared the treatment for 223 patients with cutaneous infections included between July 2005 and March 2009, including 167 cases of ADH

Table 1
Epidemiological and therapeutic features of the 386 patients presenting with acute dermohypodermitis (ADH) or cellulitis.
Caractéristiques épidémiologiques et thérapeutiques des 386 patients présentant une dermo-hypodermites aiguës (DHA) ou une cellulite.

	ADH, $n = 304$ (%)	Cellulitis, $n = 82$ (%)	P
Age (years ± standard deviation)	62 ± 19	55 ± 20	0.007
Sex-ratio (H/F)	1.76	2.15	0.451
Comorbidities			
Liver failure/alcohol abuse	51 (17)	10 (12)	0.312
Diabetes mellitus	36 (12)	9 (11)	0.828
Venous insufficiency	40 (13)	3 (4)	0.015
Progressive cancer	20 (6)	13 (15)	0.007
Obliterative arterial disease of the lower limbs	23 (7)	7 (6)	0.770
IV addiction (prior or active)	19 (7)	7 (9)	0.463
Allergy to penicillins	5 (2)	1 (2)	0.782
Site of the infection			< 0.001
Lower limb	251 (83)	44 (54)	
Upper limb	41 (13)	19 (23)	
Head	11 (4)	10 (12)	
Others	1 (< 1)	9 (11)	
Antibiotics prescribed			< 0.001
Amoxicillin	162 (53)	4 (5)	
Amoxicillin + clindamycin	10 (3)	2 (2)	
Clindamycin	3 (1)	5 (6)	
Pristinamycin	18 (6)	0	
Amoxicillin + clavulanic acid	23 (8)	13 (16)	
Other first lines therapies	35 (13)	40 (43)	
≥ 2 consecutive courses of antibiotic therapy	55 (18)	23 (28)	
Complying with protocol (n = 224)	207 (68)	17 (24)	< 0.001
Not complying with protocol but justified (n = 75/162)	35 (11.5)	40 (49)	< 0.001
Reason for prescribing outside of protocol			0.393
Microbiological data	16 (5)	20 (24)	
Associated comorbidities	11 (4)	9 (11)	
Associated diagnosis	5 (2)	10 (12)	
Clinical failure	3 (1)	1 (2)	
Duration of hospitalization	7.6 ± 5.1	9.7 ± 6.8	0.005
Adverse outcome[a]	16 (5)	10 (12)	0.026

[a] Adverse outcome: need for surgery, hospitalization in the ICU, or death.

(75%) and those of 163 patients included between April 2009 and December 2011, including 137 cases of ADH (84%). This data suggests a relative increase of ADH since the incidence of cutaneous infections did not significantly change between these two periods (5/months). Indeed, the ADH/cellulitis ratio was lower in the first period, compared to the second: 2.98 versus 5.26 ($P = 0.029$).

The antibiotic prescriptions were less often compliant with the therapeutic protocol before April 2009, compared to the following period: 53% versus 64%, $P = 0.033$ (Table 3).

The comparison of the two periods, before and after protocol initiation, revealed a difference in length of hospital stay (average 8.3 days versus 7.5 days, $P = 0.037$). There was no difference for the clinical outcome; it was poor 15 times in the first period (7%), and 11 times in the second period (7%). Nevertheless, on the overall study period, the protocol observance was associated to a shorter duration of hospitalization (6.9 ± 4,7 versus 9.5 ± 6.2 days, $P < 0.001$) and to a better prognosis, with 16 poor outcomes for 162 non-consensual antibiotic therapy prescriptions (9.8%) versus 10 for 224 consensual antibiotic therapy prescriptions (4.4%), $P = 0.037$.

3. Discussion

3.1. Should the concept of "cellulitis" be (re-) introduced consensually?

The dermatologic infectious diseases account for 9.5% of patients hospitalized in our infectious diseases unit all etiologies included [4], or 820 patients in 6.5 years of recording in our DB. Among these patients, 42% present with erysipelas and ADH. Likewise, a French survey performed in 98 dermatology units revealed the great number of patients hospitalized for these infections, around 3,500 cases of erysipelas were managed every year [7].

Our study, made 10 years after the last French consensus conference on ADH, shows that more than 20% of cutaneous bacterial infections are labeled "cellulitis". In our study, age,

Table 2
Bacteriological results for the two diagnosis group, acute dermohypodermitis (ADH) and cellulitis. Two hundred and eighteen patients had not undergone microbiological sampling (56%); the 112 skin samples are detailed after exclusion of bacteremic patients.
Résultats bactériologiques selon les deux groupes diagnostiques, dermo-hypodermites aiguës (DHA) et cellulite. Un total de 218 patients n'avait pas de prélèvement microbiologique local (56%). Les 112 prélèvements locaux sont décrits après exclusion des patients bactériémiques.

	ADH, $n = 304$ (%)	Cellulitis, $n = 82$ (%)	P
Hemocultures performed	285 (94)	74 (90)	0.269
Positive hemocultures	24 (7.8)	5 (6.0)	0.639
Bacteria isolated from hemocultures			0.319
Groupable *Streptococci* (A, B, C, or G)	18 (5.9)	2 (2.4)	
Polymicrobial hemocultures	2 (0.6)	1 (1.2)	
Non-groupable *Streptococci*	2 (0.6)	0	
Staphylococcus aureus	1 (0.3)	1 (1.2)	
Gram-negative bacilli	1 (0.3)	1 (1.2)	
Other samples			< 0.001
Groupable *Streptococci* (A, B, C, or G)	19 (6.2)	11 (13.4)	
Staphylococcus aureus	17 (5.5)	10 (12.1)	
Polymicrobial	11 (3.6)	13 (15.8)	
Enterobacteria	11 (3.1)	4 (4.8)	
Other bacteria	9 (2.9)	5 (6.0)	
Non-groupable *Streptococci*	1	1	

venous insufficiency, and localization of the cutaneous infection on lower limbs were associated to a diagnosis of ADH, rather than that of cellulitis made by senior clinicians in our unit. This diagnosis of cellulitis was more made when progressive cancer was documented in a patient and/or in case of infectious localization other than the lower limbs. The authors of a previous study had already reported that some clinical presentations suggested cellulitis to clinicians ($n = 52$) more than ADH ($n = 771$), especially for a localization other than the lower limbs [2]. Lazzarini et al. also reported a different distribution of cutaneous lesions between erysipelas and cellulitis. Cellulitis (53% of cases) was effectively more frequently located on the upper limbs [8]. Nevertheless, the retrospective aspect of our study, as well of reported studies in this article, prevents studying other anamnestic or clinical elements, which may have contributed to the semantic choice between ADH and cellulitis.

These epidemiological and clinical differences led to prescribing significantly different antibiotic therapy between the two groups (Table 1), and *in fine* cellulitis appeared to be more severe than ADH, the duration of hospitalization and the rate of poor outcome being more important than that of ADH.

An increase of bacterial infections considered as ADH was observed after protocol initiation (ratio ADH/cellulitis: 2.98 before protocol initiation and 5.26 after, $P = 0.029$). Our study results thus suggest that the epidemiological, clinical, and therapeutic discussion having led to the implementation of the therapeutic protocol influenced *a posteriori* the definitive diagnosis.

Thus, there are definitely diagnostic difficulties between ADH and cellulitis, logically leading to differences of antibiotic therapy.

These cases of cellulitis account for 20% of cutaneous infection cases included in the infectious diseases unit, and the analysis of medical files shows that non-consensual antibiotic therapy was justified in close to half of cases (Table 1). Given these different elements, it seems legitimate to take into account the semantic difference, which calls for a better definition of cellulitis, and presumably to therapeutic adaptation.

3.2. Should antibiotic therapy be adapted to the diagnosis (acute dermohypodermitis versus cellulitis)?

Our study revealed a great diversity in antibiotic therapy, especially in case of cellulitis. The authors of several studies focusing on the prescription of antibiotic therapy for cutaneous infections reported a great therapeutic variability [7–10]. The authors of a 7-year Italian study on the management of 200 cases of cutaneous infections, reported that amoxicillin + clavulanic acid was the first line antibiotic therapy for 90 patients (45%), and that two consecutive lines were prescribed to 62 patients (31%) [8]. The authors of a Canadian study conducted in five emergency units, including 416 adult patients, reported that the most frequently prescribed antibiotic therapy, cefazolin, accounted for only 47% of all prescribed therapeutic lines; the second line was cephalexin for only 8% des prescriptions [9]. The authors of a previously mentioned study reported that 50% of cellulitis cases were treated by an antibiotic combination [7].

All this data confirms the need to homogenize antibiotic therapy for bacterial cutaneous infections, based on the most specific definitions possible for ADH and cellulitis.

Thus, we implemented an internal antibiotic therapy protocol in 2009 based on the therapeutic suggestions of the 2000 French consensus conference. The internal protocols are drafted by senior infectious diseases specialists, and grouped in files available in every ward. They are updated regularly with digital data from the DB. The analysis of the protocol impact revealed that consensual antibiotic therapy had increased, because of increased amoxicillin prescription by 13% ($P = 0.013$) and a lesser use of pristinamycin by −6% ($P = 0.006$). Bernard et al. studied the impact of a therapeutic consensus in 2005; they included 235 patients with erysipelas, in 41 French units [11]. The comparison, before and after consensus, revealed a

Table 3
Clinical features and antibiotic therapy for 386 skin infections before and after implementing our therapeutic protocol.
Présentation clinique et modalités thérapeutiques de 386 infections cutanées avant et après institution du protocole thérapeutique.

	< April 2009 $n = 223$ (%)	> April 2009 $n = 163$ (%)	*P*
Age (years ± standard deviation)	60 ± 18	62 ± 20	0.157
Sex-ratio (H/F)	1.68	2.07	0.917
Comorbidities			
Liver failure/alcohol abuse	33 (15)	28 (17)	0.526
Diabetes mellitus	22 (10)	23 (15)	0.199
Venous insufficiency	22 (10)	21 (13)	0.351
Cancers	21 (9)	12 (7)	0.475
Addiction	15 (7)	11 (7)	0.821
Obliterative arterial disease of the lower limbs	10 (4)	20 (12)	0.004
Allergy to penicillins	4	28 (17)	0.656
Site of the infection			0.768
Lower limb	172 (77)	123 (75)	
Upper limb	32 (14)	28 (17)	
Head	12 (5)	9 (6)	
Others	7 (3)	3 (2)	
Antibiotic therapy prescribed			
Amoxicillin	84 (38)	82 (50)	0.013
Amoxicillin + clindamycin	11 (5)	1 (1)	0.007
Clindamycin	5 (2)	3 (2)	0.726
Pristinamycin	16 (7)	2 (1)	0.006
Amoxicillin + clavulanic acid	19 (8)	19 (12)	0.307
Other first lines therapies	44 (20)	31 (19)	0.030
≥ 2 consecutive courses of antibiotic therapy	44 (20)	34 (21)	0.785
Complying with protocol (n = 224)	119 (53)	105 (64)	0.033
Not complying with protocol but justified (n = 75/162, 46%)	52 (23)	23 (14)	0.863
Reason for prescribing outside of protocol			0.768
Microbiological data	26 (12)	10 (6)	
Associated comorbidities	13 (6)	7 (4)	
Associated diagnosis	11 (5)	4 (2)	
Clinical failure	2 (< 1)	2 (< 1)	
Duration of hospitalization	8.3 ± 5.5	7.5 ± 5.5	0.037
Adverse outcome[a]	15 (7)	11 (7)	0.993

[a] Adverse outcome: need for surgery, hospitalization in the ICU, or death.

significant decrease of venous echo-Doppler examinations, and blood cultures. But, the therapeutic trends were unchanged, with only 8% of amoxicillin prescribed in first intention and 16% of non-consensual prescriptions (> 40% according to 2000 French recommendations).

The weak observance of the antibiotic therapy protocol seems to be related to three essential causes:

- the prescribers' lack of participation in the protocol drafting;
- the absence of feedback (or measure of the impact);
- the non-belief in improvement of service to patients by using protocols.

Indeed, in this study the inclusion of patients included until December 2011 and previous studies precedents shows that our DB avoids these three pitfalls [4,5].

Finally, it should be noted that during the 6.5 years of patient inclusion in the DB, there was a significant association between compliance to the protocol and duration of hospitalization, and patient outcome. This correlates with the results of an American study in which therapeutic failure was defined by the prescription of more than one line of antibiotic therapy [10]. The authors of this study including 10,782 patients presenting with a cutaneous infection reported therapeutic failure in 22% of cases, associated to a 2.91 fold increased risk for adverse outcome. But our initial goal was not to determine the risk factors for adverse outcome, and our result cannot be considered as definitive. Nevertheless, this data encourages compliance to implemented protocols.

In fine, our study and published data [12,13] stress the need to reappraise the clinical and therapeutic approach of cutaneous infections.

4. Conclusion

The term "cellulitis" is still widely used for bacterial cutaneous infection. Its validity, and its differentiation with ADH, could justify updating the therapeutic recommendations.

Disclosure of interest

The authors have not supplied their declaration of conflict of interest.

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