Reviewer's report

Title: Clinical and Microbiological Characteristics of Purulent and Non-purulent Cellulitis in Taiwanese Adults in the Era of CA-MRSA

Version: 3
Date: 14 April 2015

Reviewer: Michael David

Reviewer's report:

Thank you for the opportunity to review the manuscript “Clinical and Microbiological Characteristics of Purulent and Non-purulent Cellulitis in Taiwanese Adults in the Era of CA-MRSA” by C.-Y. Lee, et al. The authors performed a retrospective review of purulent and non-purulent skin infections in 2013 at a single medical center in Taiwan, comparing these 2 groups by clinical comorbidities, demographic characteristics, etiologic bacterial agents, antimicrobial susceptibilities, and classification as CA- or non-CA-MRSA in the cases of cultured MRSA infections. The authors state that the goal of their study is to support guidelines for treatment of skin and soft tissue infections in Taiwan. This is an important study, although limited by its retrospective design, because few similar studies have been published. The authors found that S. aureus was the most commonly identified pathogen among patients with purulent infections and that #*-hemolytic streptococci were the most common among non-purulent infections. They determined that nonpurulent infection patients were more likely to be older, to have tinea pedis, to have lower extremity infections, to have stasis dermatitis, and to have a recurrence within 6 months. In contrast, the purulent infection patients were more likely to have a “wound”, and they required a longer duration of stay and a longer duration of antibacterial therapy than those with non-purulent lesions.

I have several comments and questions for the authors:

Major Compulsory Revisions

1. line 58. It is not clear here what is meant by the term “wound”. Can the authors rephrase this to indicate whether they mean a pre-existing ulcer or other lesion? Also, see below on this issue.

2. lines 63-64. “staphylococci” -- Are the authors here including other species of Staphylococcus (i.e., CONS) or does the denominator for this percentage (50%) reflect all S. aureus only?

3. lines 87-88. It may be important to note here that these data are derived from 3 cited studies in the U.S. If there are similar data available from Taiwan, can the authors cite them? If not, this is another reason that the present study is very important.

4. lines 128-130. I am concerned about a bias that may be introduced into the
study with limited number of ICD-9 codes included. Patients with more severe, deeper skin and soft tissue infections, such as necrotizing fasciitis, likely had worse outcomes than those with an uncomplicated cellulitis or skin abscess. The patients with such severe infections may not have been given a separate ICD-9 diagnosis code among those listed as inclusion criteria although their severe infection may have originally developed from a purulent or non-purulent cellulitis or an abscess of the skin. The omission of patients with ICD-9 codes indicating more severe skin and soft tissue infections thus may bias the reported outcome data on recurrence, death, length of stay and duration of antibiotic therapy. This should be noted as a limitation of the study or perhaps the authors could examine the medical records of patients with ICD-9 coded diagnoses for more severe soft tissue infections at this center during 2013 to determine 1) what type of infection of the skin they derived from and 2) what the reported outcomes were for the infections in these patients.

5. lines 155-156. How was it decided which patients were tested for initial ASOT? How was it decided which patients were tested for convalescent ASOT? Were all patients tested in this way if they had no positive wound or blood culture? If not, this is likely a major limitation of the study that should be noted in the discussion.

6. lines 181-182. The criterion of previous MRSA infection is no longer used in CDC surveillance criteria to exclude a person from the category of “CA-MRSA.” The authors should note that there is this difference in their criteria from the current CDC criteria. They might also consider a secondary analysis determining the percentage of patients in each study group who had CA- and HA-MRSA infections excluding this “previous MRSA infection” criterion.

7. line 210, Table 1. “wound” -- it is not defined in the manuscript what is meant by this term. Please define the term in the Methods. Does this refer to a pre-existing skin lesion at the time of skin infection onset? Does it include surgical site infections? Does it include trauma? There is a brief and inadequate list of examples of “wounds” in the Discussion (lines 279-280), but this is not adequate.

8. lines 231 and 234. “rate” would be better denoted “prevalence” in both lines.

9. lines 283-288. This paragraph includes interesting data from the literature. Can you engage it by comparing and contrasting your results with those cited here?

10. Lines 302-304. These are results and would be best included in the results section of the manuscript. It would be very relevant to assess whether the use of an appropriate medication (i.e., covering the pathogen that was cultured if one was cultured) or a non-appropriate medication for each of the infections was used and if there was a correlation between using an active antimicrobial agent and the risk of recurrence, for example.

11. How was a recurrence of infection defined in this manuscript? Was the recurrent lesion at necessarily at a different anatomic site? Was it required that there be evidence of a cure prior to the diagnosis of a “recurrence”?
12. Lines 323-324. “most commonly” This seems like an overstatement. Is this statement a reflection of data in just the one cited manuscript? There are no data that I have seen to demonstrate what the most commonly used combination therapy is in the U.S.

13. lines 338-342. Was logistic regression performed all on patients in the study, including those who had no pathogen identified? If so, the result here may be biased. Among the many patients with an unknown pathogen in the non-purulent group, is it not possible that they had an infection caused by S. aureus (including MRSA)? Because of this problem, which is always present in studies of non-purulent cellulitis, the choice of empiric therapy is difficult. The implication that I derive from the logistic regression analysis is that S. aureus (and MRSA) is relatively rare as a cause of non-purulent cellulitis, but I am not sure that the dataset demonstrates this (see also note on Table 4).

14. Table 2. For recurrence within 6 months, does this denominator include those who died within 3 months?

15. Table 2. Please indicate “days” as the unit for the “length of stay” and “Duration of antimicrobial therapy”.

16. Table 3. It is not clear to me what is meant by “diagnostic tool”.

17. Table 3. “rate” is not appropriate in any of the 4 times it is used in this table – this would be better “prevalence” or simply to provide the n and percent.

18 Table 3. What is meant by “one set” compared with “paired”? Is “one set” the same as one single-time testing point?


20. Table 4. Footnote. For “CA-MRSA”, you might want to add that you are defining this by epidemiologic criteria, and not by genotypic criteria.

21. Table 4. Consider a footnote to define the meaning of “GNB”.

22. Table 4. The authors are not consistent in using “(%)” for each row of data. It may be easier to simply indicate this notation at the top of the relevant columns.

23. Table 4. It may be more relevant to use as a denominator in this table (after the first row of data) the n of isolates in each group that did have a final bacteriologic diagnosis made (rather than the total n in each group). As it is, comparing (and assigning a p-value to) the percentage of purulent and non-purulent lesions, for example, with MRSA or GNB, is difficult to interpret. This is because those lesions with no final bacterial diagnosis were presumably caused by some unknown bacterial pathogen, and we usually presume that the majority were caused by staphylococci or streptococci. As this table now stands, I believe, the comparisons do not reflect the data actually in hand; the analyses shown are skewed by the large number of “unknown” lesions in the non-purulent
group. The unknown lesions add noise to the analysis. Can the authors either show the results of an analysis using a denominator omitting the unknowns or discuss the issue in the text of the manuscript to justify the current presentation of the data?

24. Table 5. I believe that there is a typo in this Table. In the row for “Levofloxacin” in the column under “Non CA-MRSA”, should it state “5 (50)”?

25. Table 5. Please define what is meant by the abbreviation “TMP-SMX”.

26. Table 5. Footnote. Does the susceptibility result for clindamycin reflect results of the D-test for inducible resistance? If so, can the authors note this in the footnote?

Discretionary revisions

1. lines 309-311. Why did the authors choose to cite the Sanford Guide? While it is a clinically useful guide, it is not a peer-reviewed document. The authors may thus want to consider omitting this citing this guidebook in their paper.

Once again, I thank you for the opportunity to review this manuscript.

Level of interest: An article of importance in its field

Quality of written English: Acceptable

Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests:

I declare that I have no competing interests.