Author's response to reviews

Title: European S T80 Community-Associated Methicillin-Resistant Staphylococcus Aureus Orbital Cellulitis in a Neonate.

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Author's response to reviews: see over
Dear Dr. Crow,

We are herewith submitting a revised version of the manuscript entitled “European ST80 Community-Associated Methicillin-Resistant Staphylococcus aureus Orbital Cellulitis in a Neonate”.

We thank very much the reviewers for their constructive evaluation. We address their comments:

Reviewer I:

Major Compulsory Revisions:

1) What this case adds to the existing body of literature - Teaching points:
   • A European ST80 MRSA strain causing a severe orbital cellulitis (abscess) in an extreme age (neonate) without any predisposing condition. The virulence of the European ST80 clone as a pathogen of orbital cellulitis among neonates has not been described in detail previously. The published information is on other clones, mainly on the USA 300 clone.
   • The mother had no clinical staphylococcal disease. The source of this child’s MRSA remained unclear.

Minor revisions:

1) Page 5, paragraph 4, lines 5 - 7: units have been changed to mmol/L.
2) Page 6, paragraph 1, line 1 - 2: The prevalence of MRSA is quite high in our area. Information has been incorporated into the revised text. Our recent publication on the pediatric MRSA infections and the circulating clones has
been included in the references. The empirical use of daptomycin and rifampin is related to the local epidemiology.

3) It is difficult to draw a definite conclusion on whether the clinical course of the described case seemed to be any worse than if caused by an MSSA isolate. Apparently, you mean a PVL-positive MSSA.

   We speculate that the combination of virulence and resistance tends to pose an increased risk for a difficult management and complications.

   It depends on the extent of drainage. As you know well, it is not always feasible to achieve extensive drainage. Sometimes, it requires difficult techniques or multiple procedures. Then, it is the antimicrobial treatment. Use of less active, possibly bacteriostatic or slow bactericidal agents, may leave the virulent PVL-positive MRSA isolate to damage valuable tissues or spread to the central nervous system or other distant foci.

   The reported case was a quite severe orbital abscess. To our opinion, the appropriately selected aggressive and promptly initiated empirical therapy as well as the drainage, as much as feasible, contributed to avoiding complications and permanent sequelae.

4) Teaching points are: a difficult-to-treat as well as to adequately drain purulent infection (orbital abscess) due to an ST80 MRSA strain in an extreme age. The MRSA source was not obvious. As stated in comment #1.

Reviewer II:

1) Page 6, paragraph 1, lines 4 - 7: The molecular methods used for the isolate were PCR for detecting the genes encoding the PVL production and MLST, as previously reported in Reference #2. The relative information has been included in the revised manuscript.
2) We did not characterize the type of SCC\textit{mec} for the specific isolate. However, molecular analysis of Greek MRSA isolates, including several isolates from our area, with the same phenotype, pulsed-field gel electrophoresis type and sequence type ST80 has been previously published by Aires de Sousa et al. J Clin Microbiol 2003; 41: 2027–2032. These isolates were characterized as SCC\textit{mec} type IV variant.

3) In our area, we have high incidence of methicillin- and clindamycin-resistant \textit{S. aureus} isolates. Vancomycin, linezolid or daptomycin are our choices for empirical therapy of severe pediatric infections. This has been included in the text. In the 2010 Clinical Practice Guidelines by the Infectious Diseases Society of America for the treatment of methicillin-resistant \textit{S. aureus} infections, daptomycin has been included in the alternatives for pediatric infections, such as MRSA bacteremia, septic arthritis, and osteomyelitis (Liu et al. \textit{Clin Infect Dis} 2011; 52:e18–e55). Our colleagues at the Department of Paediatrics, based on their experience during the last 5 years, consider that high dose of daptomycin provides good bactericidal activity in deep seated, difficult-to-extensively-drain infections. As the response was good, we considered that we should continue the initial regimen.

4) When the culture results were available, we continued ceftriaxone for the possibility of a mixed infection. It is quite possible that the orbital abscess was secondary to the adjacent ethmoiditis. The cultures of pus were obtained during the fifth day of antibiotic treatment and yielded a limited number of \textit{S. aureus} colonies. The possibility of a not grown fastidious gram-negative co-pathogen could not be excluded in this severe, deep-seated abscess.