Reply to Zhang et al

TO THE EDITOR—In a recent letter, Zhang et al expressed concerns on our recent report on hypervirulent *Klebsiella pneumoniae* (hvKP) in China [1, 2]. We would like to address their points of concerns.

First, Zhang et al stated that “the genetic relatedness of clinical isolates should be further identified by molecular analysis” [2]. It is generally agreed in publications and clinical practice that, in patients with a positive *K. pneumoniae* bacterial culture obtained from >1 site, metastatic infectious disease could be diagnosed. Molecular analysis has its merits on differentiating strains. However, metastatic infections of hvKP were commonly seen in chronically infected patients under antibiotic therapy. The distribution of antibiotics and microenvironment of various organs also differ. These may lead to mutations in a small fraction of the target bacteria in different infection sites. This is not an uncommon phenomenon in bacterial infection. Therefore, even if molecular analysis revealed differences on isolates from different infection sites, one could not conclude that they are not metastatic infection, unless the difference is significant.

Second, Zhang et al mentioned that specific genomic markers were more reliable than hyperviscosity, and should have been used in our study [2]. However, currently there is no such marker available to differentiate hvKP. Virulent gene *rmpA1* and capsular antigen K1 were reported to be associated with hvKP [3]. Kfu, a mediator of ferric iron uptake, was more prevalent in hvKP [4, 5]. Several other genes were also found to be important for the virulence and survival of hvKP [3]. But none of them is specific enough to identify hvKP. Further studies are required to find an appropriate marker, or a combination of genomic markers to define hvKP.

Finally, Zhang et al believed that the sample size of this study was limited and may not represent the epidemiology of China [2]. We agree that there is room for improvement in this study. But this is by far the only study targeting hvKP in China, and the sample size is one of the largest among all related studies in the world. Currently, there is no other reported annual proportion analysis of hvKP. We believe that our results provided important preliminary information on hvKP. Further studies with a larger sample size would provide more definitive information.

In conclusion, there are a large number of knowledge gaps on hvKP. Our report provided key preliminary information on this new virulent strain, but a large multicenter study should be conducted to confirm our findings.

Notes

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