Pneumococcal Necrotizing Pneumonia and Pleural Fluid Lactate Dehydrogenase Level

To the Editor—I read with interest the recent article by Bender et al. [1] about pneumococcal necrotizing pneumonia (NP) in children. The results of the study confirm the severity of this entity in children (as reported elsewhere [2–4]), and the study enhances the previous findings with more detailed serotype analysis. Similar to the findings of Bender et al. [1], we have recently seen at our institution severe presentations and bad outcomes of pneumococcal NP associated with serotype 3 and other serotypes [5, 6]. Of concern to us, very high initial lactate dehydrogenase (LDH) levels were seen in pleural fluid specimens obtained from children who received an initial diagnosis of pneumococcal empyema and who subsequently developed severe NP and required extensive decortications, segmentectomies, or lobectomies. In retrospect, some of these children eventually would have benefited from earlier surgical interventions.

Although children with complicated pneumococcal pneumonia who require decortication drainage may have higher levels of LDH in pleural fluid [7], it is uncertain whether patients with pneumococcal NP exhibit significantly higher LDH levels in pleural fluid, compared with patients with NP due to *Staphylococcus aureus* or other organisms. In the 2 largest series of NP in children, an in-depth analysis of this issue was not performed [8, 9]. Similarly, studies comparing pleural fluid LDH levels in children with complicated pneumococcal pneumonia caused by non-pneumococcal conjugate vaccine–7 serotypes versus pneumococcal conjugate vaccine–7 serotypes have not been performed.

LDH, a useful parameter in pleural fluid analysis for patients with complicated pneumonia (among others), reflects cellular injury and can be released by cells undergoing either primary or secondary necrosis. Recent research findings in mice have revealed that, during severe pulmonary inflammation (i.e., bacterial pneumonia), apoptotic neutrophils undergoing secondary necrosis are the primary source of LDH in bronchoalveolar lavage fluid [10]. The clinical relevance of these findings is unknown for children with complicated pneumonia; however, it is likely that these changes also occur in the lungs of individuals with NP, which may partially explain the elevated LDH levels seen in these individuals. These high or abnormally high values should alert clinicians about the possibility of ongoing necrosis or liquefaction of the pulmonary parenchyma, and clinicians must give special attention to this issue in the present era, in which NP is more commonly reported.

The study by Bender et al. [1] is admirable, and I understand that the objectives that they intended at the beginning were different from the issues that I discuss here. However, considering that their study involved children with necrotizing pneumonia, mention of other aspects of this entity is important and would benefit their study. No mention was made about pleural fluid LDH levels or about findings of examination of lung biopsy specimens from those who underwent surgical procedures and the respective intraoperative findings. Could the authors provide LDH findings in this cohort (i.e., ranges and mean values)? Were there any serotypes associated with higher levels of LDH?

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Reply to Ulloa-Gutierrez

To the Editor—We thank Dr. Ulloa-Gutierrez [1] for his interest in our recent article about the association of Streptococcus pneumoniae serotypes with necrotizing pneumonia in children in Utah [2]. Ulloa-Gutierrez [1] addressed parameters other than S. pneumoniae serotype that may be predictors of severity. Specifically, an elevated lactate dehydrogenase (LDH) level appears to be associated with severe necrotizing pneumonia caused by serotype 3 in the Hospital Nacional de Niños de Costa Rica (San José) [1]. An elevated LDH level likely represents cellular damage to lung parenchyma, and it is reasonable to hypothesize that the degree of elevation correlates with the extent of necrosis. If S. pneumoniae serotype 3 causes more extensive necrosis, it stands to reason that LDH levels will be more elevated in patients with pneumonia caused by serotype 3.

At the suggestion of Ulloa-Gutierrez [1], we retrospectively evaluated the pleural fluid LDH levels in the 14 patients with serotype 3 pneumonia in our study. Five of the 14 patients had pleural fluid LDH levels measured. The median LDH level was 49,460 U/L (range, 39,700–118,041 U/L). These values represent a 40–120-fold increase over the upper limit of normal for serum LDH level in our laboratory (975 U/L). These findings appear to be consistent with those of Ulloa-Gutierrez [1]. However, care should be taken when comparing pleural fluid indices from retrospective studies because of the variability in time to presentation and other clinical and laboratory factors.

Complicated pneumonia in children is a growing problem worldwide. We agree with Ulloa-Gutierrez [1] that pleural fluid indices might prove to be a useful adjunct in predicting outcomes and directing management. In a separate study, we demonstrated that among children with empyema, those with pleural fluid indices including higher WBC counts, lower glucose values, and the presence of bacteria on Gram stain or culture were more likely to require surgical intervention than were those without these findings [3]. The degree of LDH elevation, however, was not associated with the need for surgical intervention.

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References