Pentraxin-3 to better delineate necrotizing soft tissue infection: not really!

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See related research by Hansen et al., http://ccforum.biomedcentral.com/articles/10.1186/s13054-016-1210-z

Necrotizing soft tissue infection (NSTI) is a devastating condition with high morbidity and a dismal prognosis. Timely and adequate surgery and early aggressive treatment of associated sepsis are imperative to improve survival [1–3]. Pentraxin-3 (PTX3) is a glycoprotein released by endothelial and inflammatory cells upon stimulation by cytokines and endotoxins. In contrast with C-reactive protein (CRP) which is produced in the liver in response to systemic inflammation, PTX3 is thought to better reflect local vascular inflammation and bacterial load [2]. PTX3 assessment might thus be a more appropriate marker of severity and prognosis of NSTI. This was corroborated by Hansen et al. [1], who reported a significant association between high baseline PTX3 levels and occurrence of septic shock, amputation, dialysis need, and risk of death in a large cohort of patients with NSTI. PTX3 also performed better than the "classical" inflammatory markers CRP and procalcitonin (PCT).

These findings are interesting but mandate careful reflection. First, they are not unexpected. Measurement of PTX3 has been shown to improve patient risk assessment and persistently elevated levels during evolving sepsis may contribute to tissue damage and predict poor patient outcome [2]. Second, when looking closely at the study results, PTX3 levels appeared to be fairly in line with PCT concentrations for assessing NSTI-associated morbidity and mortality. PCT also outperforms CRP in predicting severity of infection and organ dysfunction in sepsis [4] but is more readily available than PTX3. Finally, many patients with NSTI develop acute kidney injury, necessitating renal replacement therapy (RRT) (25 % of the patients studied by Hansen et al.!). PTX3 has a molecular weight of approximately 35 kDa [2] and thus in theory can be removed by RRT. Recently, Schilder et al. [5] demonstrated some adsorption but no elimination of PTX3 by convection across the system of continuous veno-venous hemofiltration (CVVH), resulting in unaltered plasma levels. Whether this is also relevant when CVVH is performed at higher convection flux or with different types of dialysis membranes (especially highly adsorptive) remains to be determined.

Authors’ response

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The authors would like to thank Dr Honore and Dr Spapen for their interest in our article. In their letter, Honore and Spapen propose three important points for consideration. First, they address the observation that PTX3 has been shown to improve risk assessment in septic patients. We agree that previous, but few, studies have investigated PTX3 in patients with sepsis. However, PTX3 has not been investigated in patients with NSTI. This is important to address because the immunological processes are probably different during infections that cause massive necrosis, as in the case of NSTI. Since NSTI is an uncommon disease, treatment and surveillance procedures in the ICU rely, primarily, on knowledge obtained from studies on septic patients. Thus, it is important to establish solid evidence for the treatment strategies in patients with NSTI as well, which also includes investigating the different aspects of the immunological response. In addition, suspicion of NSTI is currently based on the patient’s clinical presentation,
making it interesting to investigate the predicting abilities of new biomarkers, such as PTX3.

Second, they underline that both PTX3 and PCT are good predictors of morbidity and mortality. We agree with this and the fact that both biomarkers outperform CRP. Our results suggest that PTX3 can be considered a reliable marker of infections on equal terms to PCT in patients with NSTI. However, the PTX3 level was significantly higher in patients needing amputation. This was not the case for CRP or PCT. PTX3 might therefore be useful to identify different subgroups of patients from PCT.

Third, Honore and Spapen speculate whether PTX3 can be removed by RRT, thus altering the levels in the study cohort. Despite PTX3 having a molecular weight of 45 kDa as a monomer, it forms an octamer in plasma composed of two covalently linked tetramers with a weight above 400 kDa [6–8]. It is therefore unlikely that PTX3 will be removed by RRT. Moreover, the baseline samples were taken upon admission and before initiation of RRT in the vast majority of patients.

**Abbreviations**

CRP: C-reactive protein; CVVH: continuous veno-venous hemofiltration; NSTI: necrotizing soft tissue infection; PCT: procalcitonin; PTX3: pentraxin-3; RRT: renal replacement therapy.

**Authors’ contributions**

PMH and HDS designed the article and participated in drafting the manuscript. PMH and HDS read and approved the final version. MBH designed and drafted the manuscript. PG, OH, MBM, DB, PG and LSR revised the manuscript critically.

**Competing interests**

MBM is subinvestigator on a randomized controlled trial that is partly funded by CSL Behring. The remaining authors declare they have no conflicts of interest.

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