

Systemic inflammation in chronic pulmonary diseases – are we here now?

Sistemske okužbe pri kronični pljučni bolezni – ali smo že tu?

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It was strongly confirmed that patients with lung cancer compared to healthy people have significantly higher levels of inflammatory markers such as C-reactive protein (CRP).¹⁻³ What is the relationship between elevated CRP levels and cancer? One possibility is that elevated CRP levels are a result of inflammatory stimulus by cancer, whereas other researchers believe that chronic inflammation and elevated CRP might have a causal role in carcinogenesis. Some studies in fact suggested that CRP is not merely a marker of current, but is also associated with incident cancer.⁴

Prognostic importance of CRP for survival of patients with lung cancer⁵ was recently confirmed by Ovčariček et al.⁶ The authors found that duration of progression free survival time in patients with advanced non-small cell lung carcinoma treated by chemotherapy critically depends on the level of CRP and hemoglobin concentration, but only borderline on comorbidities.

Many other pulmonary diseases have very well known systemic consequences. Obvious examples are sepsis in pneumonia or metastatic spread of lung cancer. On the other hand, there is accumulating evidence that very complex and probably even bidirectional relationship exists between chronic pulmonary diseases and systemic response.⁷⁻⁹ An interesting example of such systemic disease is chronic obstructive pulmonary disease (COPD), which affects

not only the lungs but also skeletal muscles and the brain.¹⁰⁻¹¹ Comorbidities associated with COPD are hypertension, diabetes, ischemic heart disease, heart failure, pulmonary infections, pulmonary vascular disease and – last but not least – lung cancer. COPD and heart diseases even share a complex interrelationship between neuro-hormonal activation and chronic inflammation.¹¹ Many patients with COPD die of non-respiratory disorders such as cardiovascular diseases or lung cancer.¹² Patients with chronic obstructive pulmonary disease (COPD) present with increased serum levels of CRP. This may be related directly to COPD and its associated systemic inflammation or occurs secondary to concomitant ischemic heart disease or smoking status.

Diagnosis of acute or chronic pulmonary embolism is far from easy and there is still lively debate as to which test or score is the most appropriate.¹³ It was recently found that CRP levels were increased in chronic thromboembolic or primary pulmonary artery hypertension compared with those in control subjects, these levels being even a predictor of outcome and response to therapy, thus revealing that systemic inflammation is also involved in these two pulmonary vascular diseases.¹⁴

Systemic inflammation of non-metastatic lung cancer was studied extensively while systemic inflammatory manifes-

tations of metastatic lung cancer were much less studied. Studies as performed by Ovčariček⁶ are obviously more than welcome, especially since mechanisms by which inflammation influences survival are virtually unknown. Elevated CRP may be a marker of a higher total tumor mass. Another possible explanation is that higher release of CRP has catabolic effects on the host metabolism with significant effects on the survival.^{11,15}

However, some results of this not-so-small study with excellently performed statistical analysis should be regarded carefully as COPD or heart failures were not reported individually for studied patients. Comorbidities were estimated only by general comorbidity index, which is a mixture of very divergent pathologies. Patients with COPD or heart failure without clinical signs of infection have usually small yet sometimes quite high levels of CRP and most of them are not polycythemic but rather anemic. So, those diseases with different basic inflammatory processes could significantly influenced CRP or hemoglobin concentrations and probably even prognosis of studied patients.

Patients diagnosed with lung cancer wait too long before seeking appropriate medical assistance.¹⁶ Perhaps routine measurements of CRP could help to identify patients who need accelerated diagnostics.

Still, this study⁶ can be viewed as very interesting and should encourage further similar but preferably prospective and better designed studies, not only in cancer but also in patients with COPD or heart failure. By improving our knowledge of the role of chronic inflammation in many pulmonary diseases – not only in cancer – new approaches, involving – besides rather nonspecific CRP changes – also other markers of systemic inflammation, which could be more specific for individual pulmonary diseases,¹⁷ or with better understanding of the established treatments, may direct future therapeutic approaches.

Certainly we are “not here” – yet.

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