Activation of the tryptophan/serotonin pathway is associated with severity and predicts outcomes in pneumonia: results of a long-term cohort study

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As part of the immune defense during infection, an increase in enzyme activity of indoleamine 2,3-dioxygenase (IDO) leads to a breakdown of tryptophan to kynurenine. In previous animal studies, therapeutic antagonism of IDO resulted in reduced sepsis mortality. We investigated the prognostic ability of tryptophan, serotonin, kynurenine and IDO (represented by the ratio of kynurenine/tryptophan) to predict adverse clinical outcomes in patients with community-acquired pneumonia (CAP).; We measured tryptophan, serotonin and kynurenine on admission plasma samples from CAP patients included in a previous multicenter trial by liquid chromatography coupled with tandem mass spectrometry (LC-MS/MS). We studied their association with inflammation (C-reactive protein), infection (procalcitonin) and clinical outcome.; Mortality in the 268 included patients was 45% within 6 years of follow-up. IDO and kynurenine showed a strong positive correlation with markers of infection (procalcitonin) and inflammation (C-reactive protein) as well as sepsis and CAP severity scores. Tryptophan showed similar, but negative correlations. In a multivariate regression analysis adjusted for age and comorbidities, higher IDO activity and lower tryptophan levels were strongly associated with short-term adverse outcome defined as death and/or ICU admission within 30 days with adjusted odds ratios of 9.1 [95% confidence interval (CI) 1.4-59.5, p=0.021] and 0.11 (95% CI 0.02-0.70, p=0.021). Multivariate analysis did not reveal significant associations for kynurenine and serotonin.; In hospitalized CAP patients, higher IDO activity and lower tryptophan levels independently predicted disease severity and short-term adverse outcome. Whether therapeutic modulation of IDO has positive effects on outcome needs further investigation.
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