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Infectious pleural effusions can be identified by sTREM-1 levels

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Summary
Background and objective: Conventional methods to establish pleural infection are time-consuming and sometimes inadequate. Biomarkers may aid in making rapid diagnosis of infection. In an observational study we evaluated and compared the diagnostic value of pleural fluid levels of soluble triggering receptor expressed on myeloid cells-1 (sTREM-1), C-reactive protein and procalcitonin in intensive care patients with pleural effusions.
Methods: Thirty-six patients with de novo pleural effusions were included and 20 patients with pleural effusions after cardiothoracic surgery and 20 patients with pleural effusions after esophagus surgery acted as controls. Levels of sTREM-1, C-reactive protein and procalcitonin were measured in pleural effusions.

Abbreviations: sTREM-1, soluble triggering receptor expressed on myeloid cells-1; CRP, C-reactive protein; PCT, procalcitonin.

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Results: Levels of sTREM-1 were highest in empyemas, followed by infectious exudates. Levels of sTREM-1 were low in transudates and non-infectious exudates. C-reactive protein levels were highest in exudates and empyemas, while procalcitonin levels were highest in exudates. Pleural fluid with positive culture results contained higher sTREM-1 and C-reactive protein levels as compared to samples with negative culture results. A cut-off level of 50 pg/ml sTREM-1 yielded a sensitivity of 93% and a specificity of 86%, while these were 87% and 67% respectively for a cut-off value of 7.5 μg/ml C-reactive protein, and 60% and 64% respectively for a cut-off value of 0.15 ng/ml procalcitonin.
Conclusion: sTREM-1 is superior to C-reactive protein and procalcitonin in detecting infection.

Introduction

Pleural effusions are an important complication of several diseases and may cause additional morbidity, also in patients admitted to the intensive care.[1] The clinical presentation of a patient is important in establishing the cause of an effusion.[1] However, if the cause of pleural effusion is uncertain or unknown, further diagnostical procedures are warranted. Diagnosing infection is important as delayed antibiotic therapy may result in additional morbidity.[2] Current guidelines recommend routine microbiological studies to aid in the decision of antimicrobial treatment and the need for drainage.[1] However, Gram stains are not always conclusive and awaiting culture results may result in delayed diagnosis and therapy resulting in complicated parapneumonic effusions or pleural empyema.[2] By contrast, treating all patients with antimicrobial agents before culture results are available will lead to overuse of antimicrobial agents with the associated risk of antibiotic resistance and higher costs.[3]

Accurate markers to establish the presence of infection are needed. Several proteins that are elevated in sera of patients with systemic infection have been suggested as markers of infection in pleural effusions.[4–10] Recently, soluble triggering receptor expressed on myeloid cells-1 (sTREM-1) has been proposed by us and others as a specific marker of infection in patients with sepsis, pneumonia or bacterial meningitis.[11–14] Experimental studies have shown that TREM-1 is up-regulated on myeloid cells if these cells make contact with bacterial components.[15] Simultaneously, a soluble form of TREM-1 is released.[15] Studies in patients with pneumonia and bacterial meningitis have shown that if this protein is measured locally, i.e. on the site of infection, its occurrence is strongly correlated with active infection.[12–14] Indeed, two recent studies have shown that levels of sTREM-1 are elevated in infectious pleural effusions.[4,5] In parallel, other locally detectable markers of inflammation were suggested to be useful in the diagnosis of pleural infection. C-reactive protein (CRP) levels were shown to be higher in patients with infectious pleural effusions as compared to effusions in the context of tuberculosis or malignancy.[7] The differentiating capacity of CRP for infection was demonstrated to be superior to that of the inflammatory cytokines interleukin-6 and tumor necrosis factor-α.[7] Furthermore, pleural effusion levels of procalcitonin (PCT) were shown to be higher in patients with tuberculosis as compared to patients with effusions associated to malignancy.[6]

As previous studies have shown that locally measured sTREM-1 levels are highly correlated with the presence of infection, we evaluated the diagnostic value of pleural fluid levels of sTREM-1 as a biological marker of infection in intensive care patients with pleural effusions. Moreover, the diagnostic value of pleural fluid levels of sTREM-1, CRP and PCT has been studied separately only. Therefore, in the present study we evaluated and compared the diagnostic capacity of each of these markers.

Methods

Patients

Critically ill patients with a de novo presentation of a pleural effusion during the course of their stay on the intensive care were eligible for the study. Only patients in whom pleural effusions were drained were included in the study. Indications for drainage were diagnostical purposes in case an exudate was suspected (e.g., in case of suspected infection) or for respiratory failure considered to be the consequence of the pleural effusion. Patients with a pleural effusion within 24 h after cardiothoracic or esophagus surgery served as control patients. In view of the observational nature of the study the institutional ethical committee of the Academic Medical Center mandated neither retrospective patient consent nor formal assent from relatives to be required.

Study protocol

Drainage was performed either by insertion of a sterile Pneumo-cath (Intra special catheters GmbH, Rehlingen-Siersburg, Germany) or a sterile thorax drain (Tyco Healthcare, Tullamore, Ireland). In control patients who had a thorax drain after cardiothoracic or esophagus surgery, pleural fluid was collected from the indwelling thorax drain by aspiration with a sterile needle. Immediately after fluid had been obtained, samples were sent to the bacteriological department and the clinical hospital laboratory for routine analyses. These consisted of culture and measurement of levels of lactate dehydrogenase, total protein and cholesterol, and leukocyte count with differentiation. For study purposes fluid was centrifuged at