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Evaluation of the Ability of COVID-19 Infected Sera to Induce Netosis Using an Ex-Vivo NETosis Monitoring Tool

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Abstract : Introduction: NETosis has emerged as a crucial yet paradoxical factor in severe COVID-19 cases. While neutrophil extracellular traps (NETs) help contain and eliminate viral particles, excessive NET formation can lead to hyperinflammation, exacerbating tissue damage and acute respiratory distress syndrome (ARDS). Aims: This study evaluates the relationship between COVID-19-infected sera and NETosis using an ex-vivo model. Methods: Sera from 8 post-admission COVID-19 patients, after receiving corticoid therapy, were used to induce NETosis in neutrophils from a healthy donor. NET formation was tracked using fluorescent markers for DNA and neutrophil elastase (NE) every 2 minutes for 8 hours. The results were expressed as a percentage of DNA/NE released over time. Key metrics, including T50 (time to 50% release) and AUC (area under the curve), representing total NETosis potential), were calculated. A 27-cytokine screening kit was used to assess the cytokine composition of the sera. Results: COVID-19 sera induced NETosis based on their cytokine profile. The AUC of NE and DNA release decreased with time following corticoid therapy, showing a significant reduction in 6 of the 8 patients ($p<0.05$). T50 also decreased in parallel with AUC for both markers. Cytokines concentration decrease with time after therapy administration. There is correlation between 14 cytokines concentration and NE release. Conclusion: This ex-vivo model successfully demonstrated the induction of NETosis by COVID-19 sera using two markers. A clear decrease in NETosis potential was observed over time with glucocorticoid therapy. This model can be a valuable tool for monitoring NETosis and investigating potential NETosis inducers and inhibitors.

Keywords : NETosis, COVID-19, cytokine storm, biomarkers
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