treated with immunoglobulin infusion for two days and oral steroids for three days. Subsequently, he was anticoagulated with the new oral anticoagulant edoxaban after platelet numbers recovery. In a few days, platelets normalized, and D-dimer levels decreased, while anti- PF4-dependent enzyme-immunoassay test results showed a slow decline. He was discharged taking oral edoxaban without any sequeal.

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CONTRIBUTION OF NEUTROPHIL EXTRACELLULAR TRAPS (NETS) AND PLATELET ACTIVATION TO COVID-19 CLINICAL COURSE AND INHIBITORY EFFECT OF ANTICOAGULANTS AND PLATELETS ON NETS RELEASE

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Introduction: Thrombotic events are common in the course of COVID-19 and are related to the release of Neutrophil Extracellular Traps (NETs). Identifying the moment during the time course of the disease when the stimulus for NETs and platelet activation occurs and finding potential drugs that inhibit these mechanisms is mandatory. **Aim:** To evaluate changes in the levels of inflammatory, platelet activation and NETs markers during COVID-19 hospitalization and their association with adverse outcomes. We also analyzed whether antiplatelets and anticoagulants were capable of inhibiting NETs release "in vitro". **Methods:** First we quantified circulating levels of IL-8, IL-6, TNF-α, RANTES and citrullinated histone H3 (cit-H3) on four occasions during COVID-19 hospitalization (admission, day 4, day 8 and end of hospitalization) between May and July 2020 and we assessed their association with clinical outcomes. Second, we stimulated healthy neutrophils with Phorbol Myristate Acetate (PMA) or serum from severe COVID-19 patients (n=15) in the presence of heparin (25 ug/mL, 50 ug/mL and 100 ug/mL), enoxaparin (25 ug/mL, 50 ug/mL and 100 ug/mL), aspirin (1 mM, 2.5 mM and 5 mM) or ticagrelor (1 uM, 2.5 uM and 5 uM) and in the absence of these drugs. Images of the cells incubation were obtained after 1.5 hour using Incucyte, the number of cells that suffered netosis and did not suffer was obtained. Finally, the percentage of netosis was calculated. **Results:** IL-6 levels were higher in non-survivors than in survivors from day 4 to the end of hospitalization and remained unchanged from admission until the end of hospitalization in non-survivors while decreased in survivors. IL-8 levels were higher in non-survivors than in survivors during the entire hospitalization period. TNF-α levels remained higher in non-survivor than in survivors during the entire hospitalization. CitH3 levels were similar between non-survivors and survivors until day 8, but were 2-fold higher in non-survivors at the end of hospitalization. CitH3 levels were 2-fold higher on day 4 of hospitalization in patients who had thrombosis than in those without this complication. RANTES levels were similar between survivors and non-survivors and were not associated with thrombosis. The percentage of COVID-19-induced NETs were higher in non-treated neutrophils than in pretreated neutrophils with heparin and enoxaparin at all 3 concentrations. Aspirin was capable of modulating COVID-19 induced netosis at the two highest concentrations, but not at 1 mM. Heparin and enoxaparin also decreased netosis at the 3 concentrations after PMA stimulus, while aspirin reduced netosis induced by PMA only at 2.5 mM and 5 mM. Ticagrelor showed no effect on either COVID-19 or PMA induced NETs release. **Conclusion:** IL-6, IL-8, TNF-α and cit-H3 levels were related to poor clinical outcomes in COVID-19 patients. Since the beginning of the hospitalization, an increased inflammatory response was observed, while markers of NETs arose later. Heparin, enoxaparin and aspirin were capable of "in vitro" reducing netosis induced by COVID-19 and PMA. Such findings suggest that thromboinflammatory stimulus occurs later during COVID-19 clinical course and provide evidence on possible effects of heparin and aspirin on modulating NETs formation.

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AVALIAÇÃO DOS NÍVEIS SOLÚVEIS DE PODOPLANINA E CLEC-2 EM PACIENTES COM COVID-19

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A imunotrombose é definida pela ativação da hemostasia resultante de uma resposta inflamatória e/ou infecciosa. Recentemente, a via PDPN/CLEC-2 tem se destacado em processos que medeiam a ativação plaquetária e a formação trombótica. Além disso, alguns estudos em modelos animais sugerem que a via pode desempenhar um papel importante no processo de proteção pulmonar na Lesão Pulmonar Aguda (LPA). Embora o papel da via PDPN/CLEC-2 não seja totalmente compreendido, evidências sugerem que ela pode se encaixar como uma nova via no conceito de imunotrombose. O objetivo do estudo foi avaliar os níveis circulantes de PDPN e CLEC-2 em pacientes com COVID-19 e explorar sua relação com a gravidade da doença e a ativação da hemostasia. Foram incluídos 30 pacientes diagnosticados com COVID-19, além de 30 controles saudáveis, com aprovação ética (CAAE 36528420.3.0000.5404 e 30227920.9.0000.5404). As medidas de PDPN foram realizadas com kits de ELISA nos momentos D0 e D4 (4° dia após a admissão); A dosagem de CLEC-2 também foi realizada por ELISA apenas no tempo D0. Os dados clínicos e laboratoriais foram obtidos de prontuários eletrônicos. Para avaliar a expressão de PDPN em células pulmonares foi realizada uma análise "in silico" de scRNAseq. O tempo médio de permanência hospitalar (LOS) foi de 12,9±9,8 dias, doze pacientes (40%) necessitaram de UTI com tempo médio de UTI de 6,1±9,7 dias. O D-dímero médio foi de 3,609±