TTPA), função renal, DHL e troponina sem alterações. Além destes, o hemograma mostrou uma baixa contagem de leucócitos (400/mm^3), indicativa de agranulocitose e leucopenia grave. Houve também uma significativa redução nos neutrófilos (11/mm^3), com desvio à esquerda até bastão (2/mm^3). Por outro lado, houve um aumento expressivo nas contagens de linfócitos (83 mm^3). Adicionalmente, a contagem de plaquetas estava reduzida, apresentando-se com 34.000/mm^3 plaquetas e evidente anisocitose plaquetária. Para o tratamento, a paciente recebeu antibióticos de amplo espectro e Filgrastim (G-CSF), uma medicação específica utilizada para estimular a produção de células brancas do sangue na medula óssea. Essas intervenções resultaram em uma melhora notável nos valores das células sanguíneas: leucócitos (5000/mm^3), neutrófilos (30/mm^3), bastões (11/mm^3), linfócitos (49/mm^3) e plaquetas (110.000/mm^3). No entanto, apesar dessa melhora, infelizmente a paciente não respondeu ao tratamento e veio a óbito devido a complicações relacionadas à doença. Este caso clínico enfatiza a importância da monitorização regular do hemograma e da contagem de plaquetas em pacientes com COVID-19, especialmente aqueles com risco de desenvolver agranulocitose. A detecção precoce de alterações nesses parâmetros pode auxiliar os profissionais de saúde a iniciarem tratamentos eficazes de forma ágil, melhorando o prognóstico e prevenindo complicações graves. A associação de agranulocitose (granulócitos < 500/mm^3) e COVID-19 já foi reportada em poucos pacientes sem doença prévia. A maioria dos pacientes estavam em terapia antineoplásica, sendo que destes pacientes todos necessitaram de terapia intensiva e evoluíram a óbito. Em conclusão, relatamos um caso raro de agranulocitose em um paciente previamente hígido infectado por Sars-CoV-2, condição esta, que necessita de medidas terapêuticas imediatas devido ao alto risco de complicações infecciosas graves e óbito.

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ASSOCIATION OF SOME HOST GENETIC POLYMORPHISMS WITH PLASMA HYPERCYTOKINEMA IN COVID-19

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Introduction: COVID-19 is a severe acute respiratory syndrome caused by SARS-CoV-2 infection marked by intercontinental variations in its clinical severity and outcomes. However, it is poorly understood if certain host genetic variations are important in determining the severity of the cytokine storm and thus the outcome of COVID-19. **Objective:** To determine if TMPRSS2 SNPs (rs2070788 and rs12329760) and CCR5Δ32 genotypes are associated with plasma hypercytokinemia in unvaccinated COVID-19 patients. **Methods:** 154 PCR-confirmed COVID-19 unvaccinated patients at the Hospital de Clínicas da Unicamp, Campinas-SP/Brazil, were enrolled for this study and genomic DNA extracted from peripheral blood samples. Two TMPRSS2 SNPs [rs2070788 (G>A) and rs12329760 (C>T)] and CCR5Δ32 genotypes were assayed using Taqman genotyping kit and fragment analysis by capillary electrophoresis, respectively, and the 13 plasma cytokines levels were quantified by LUMINEX immunoassay according to manufacturers' protocols. **Results:** 154 COVID-19 patients were grouped as severe group (134 patients with moderate, severe, or critical COVID-19) and mild group (20 patients with mild or asymptomatic COVID-19) with median ages 62 (20-97) *vs* 49 (24-84) years respectively $p = 0.007$. 115 (74.7%) patients were homozygous CC (wild) and 39 were variants of the TMPRSS2 rs12329760 [32 heterozygous (CT) and 7 homozygous (TT)]. The wild group (CC) had a lower plasma levels of IL-37 ($p = 0.0015$), TNF-α ($p = 0.0255$), IL-17A ($p = 0.0044$), IL-1β ($p < 0.0001$) and higher TGF-β ($p < 0.0001$) than those with the variant (CT and TT) group. 32 (20.8%) patients were homozygous GG (wild) and 122 were variants of the TMPRSS2 rs2070788 [72 heterozygous (GA) and 50 homozygous (AA)]. The patients with the GG genotype had a higher CCL2/MCP-1 than those with the variant genotypes (GA and AA), $p = 0.0218$. Only 9 (5.8%) patients had the CCR5Δ32 mutation [1 homozygous and 8 heterozygous] and 145 (94.2%) were without CCR5Δ32 mutation. The COVID-19 patients with CCR5Δ32 mutation had a significantly lower median plasma TNF-α ($p = 0.0024$) and IL-8/CXCL8 ($p = 0.0106$) than the patients without the mutation. **Conclusion:** This study shows that presence of T allele of the rs12329760 was associated to hypercytokinemia in COVID-19 while the wild genotype GG of the rs2070788 was associated to higher levels of CCL2/MCP-1, both SNPs are in the *TMPRSS2* gene. This may have led to worsening cytokine storm and outcome of COVID-19. Contrarily, the presence of the CCR5Δ32 mutation appears to be protective against the plasma hypercytokinemia in COVID-19. These findings further emphasize the role of host genetic variations play in the pathogenesis of SARS-CoV-2 infection. **Funding:** CNPq (#190374/2017-9), CAPES, FAPESP and FAEPEX (#338619).

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