News Release

Title

Elucidation of Changes in Blood Coagulation Profiles in Severe COVID-19: Clarifying the Relationship between the Disappearance of a Hypercoagulable State and Poor Clinical Outcomes

Key Points

•It has been clarified that the profile of blood coagulation in COVID-19 changes significantly with the severity of the disease.

•The disappearance of a hypercoagulable state is associated with poor clinical outcomes in COVID-19 treatment. This disappearance was related to the consumption of the complement alternative pathway.

•Evaluating the blood coagulation profile is expected to enable the assessment of different clinical courses in severe COVID-19, leading to the development of treatments targeting coagulation abnormalities in refractory cases.

Summary

A multicenter clinical study led by Dr. Daisuke Kasugai, Dr. Taku Tanaka, and Dr. Naonori Yamamoto, and Dr. Takako Suzuki, and Dr. Yukari Goto, Director of the Emergency Medical Center of Nagoya Ekisaikai Hospital (former Lecturer in the Department of Emergency Medicine at Nagoya University Hospital), has revealed that in severe cases of COVID-19, the disappearance of the hypercoagulable state—responsible for facilitating the formation of blood clots in various sites—is associated with poor treatment outcomes in critical COVID-19 illness.

Previous studies have shown that COVID-19 patients exhibit a hypercoagulable state. While therapeutic anticoagulation has proven effective in moderately ill COVID-19 patients requiring hospitalization, its efficacy in severely ill patients needing intensive care unit (ICU) care has not been confirmed in several large randomized controlled trials. The study, conducted in collaboration with several centers across Japan, is a prospective, multicenter, observational study that utilized the ROTEM Sigma ™ to assess changes in the coagulation profile during the course of severe COVID-19 disease. The findings indicated that the platelet component contributes to the hypercoagulable state and that the degree of hypercoagulability increases in severe cases. However, the prognosis is poor for patients in with the normocoagulable state disappears. This disappearance is

linked to the consumption of C3, which plays a role in the complement pathway, particularly the alternative pathway. This condition was found to be associated with platelet loss, decreased hematocrit, and other changes akin to thrombotic microangiopathy (TMA). The study demonstrates that coagulation abnormalities distinct from hypercoagulability are related to refractoriness in severe COVID-19. It is expected to aid in elucidating the pathogenesis and developing effective therapies for refractory cases.

Research Background

COVID-19 will not be eradicated even after the widespread distribution of vaccines, and periodic outbreaks continue to occur, resulting in numerous deaths worldwide. Since the early stages of the pandemic, there has been a reported tendency for increased blood clot formation in COVID-19, and many clinical trials have been conducted to control this condition. As a result, therapeutic anticoagulation has been found effective for moderate COVID-19 cases, but its efficacy has not been demonstrated for severe COVID-19. The clear reason why therapeutic anticoagulation is not effective for severe COVID-19 cases has not been elucidated until now. Furthermore, how the coagulation profile of COVID-19 changes during the progression to severe disease has also not been clarified.

Research Results

This study conducted a prospective observational study of 166 COVID-19 patients admitted to 14 hospitals in Japan from March 2021 to March 2022. During the progression to severe disease, the most hypercoagulable state was observed in patients requiring non-invasive respiratory support (such as nasal high-flow or NPPV), which is a precursor to the severity necessitating mechanical ventilation. In severe COVID-19 cases requiring mechanical ventilation, being in a hypercoagulable state was actually associated with a better prognosis. In the group of severe COVID-19 patients not in a hypercoagulable state requiring mechanical ventilation, a marked decrease in complement C3 consumption was observed. The decreasing trend of C3 was associated with a decrease in platelets, a decrease in hematocrit, an increase in fibrinolysis markers (FDP, D-dimer), an increase in endothelial injury markers (soluble thrombomodulin), and an increase in alveolar epithelial cell injury markers (KL-6). These results indicate that in severe COVID-19, the coagulation profile changes due to a different mechanism of coagulation disorder centered on the activation of the complement alternative pathway, leading to poor clinical outcomes.

Research Summary and Future Perspective

This study suggests that by evaluating the coagulation profile, it is possible to determine the different clinical courses of severe COVID-19. Consequently, the development of treatment strategies targeting, for example, the complement alternative pathway, is expected for COVID-19 cases presenting with distinct coagulation profiles.

Publication

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Association between Loss of Hypercoagulable Phenotype, Clinical Features and Complement Pathway Consumption in COVID-19.

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