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Editorial: Time to explore the missing links: from activated platelets and platelet extracellular vesicles in SARS-CoV-2 infection, through heterogeneity in the host physiological, immuno-inflammatory and haemostatic responses to mRNA-based vaccine or infection induced polyclonal neutralizing antibodies and passive immunity

Editorial commentary

Time to explore the missing links: From activated platelets and platelet extracellular vesicles in SARS-CoV-2 infection, to immuno-inflammatory and hemostatic responses to mRNA -based vaccine or infection to introduce polyclonal neutralizing antibodies and passive immunity.

In this issue of What’s Happening, following up past contributions by Professors Thierry Burnouf and Laura Gutiérrez on “platelet lyases” and “platelets in sepsis”, I have taken a new initiative by inviting Professor Hadi Goubran from Canada, to lead a systematic synthesis of the latest opinions on the current laboratory and clinical aspects of activated platelets and platelet extracellular vesicles induced by SARS-CoV-2 infection. Professor Goubran is a well-recognized international expert in the field of onco-hematology, with extensive knowledge in the laboratory and clinical aspects of platelets in health and disease. It is my pleasure to have shared with Professor Goubran many theme articles focusing on common interests, as he is an appreciated contributor in my section of TRASCI in particular.

SARS-CoV-2 infection results in a systemic inflammatory response, where many players are involved. As it is known, the coagulation system and platelets, beyond participating in hemostasis, work in parallel with immune cells to mount an immunoinflammatory response against infection. However, an exacerbated response may cause multi-organ failure in severe patients. Above all, the heterogeneity of responses is host-dependent. An increase of platelet-derived extracellular vesicles, but also extracellular vesicles derived from other circulating cells, may serve as markers of infection severity and poor outcomes or even serve as therapeutic targets. It is therefore important to note that, despite initially not considered, anti-platelet therapy is currently receiving strong consideration as a prophylactic treatment of COVID-19 patients, even outweighing corticosteroids, which were so popular at the beginning of the pandemic, as previously highlighted in this section of Trasci.

In short, the key message conveyed by this joint publication is that the platelet number and function are altered in COVID-19 patients, in a similar way as in sepsis as recently reported by Professor Laura Gutiérrez (Trasci 2022), and also confirmed by others.

To prevent bleeding, in the case of severe thrombocytopenia of inflammation, platelet transfusions are given, although the threshold platelet count still remains a matter of debate in view of the higher risk of organ damage associated with platelet transfusions in these patients. As it has been hypothesized, “immunoinflammatory conditioned platelets”, are the result of the inflammatory milieu that primes circulating platelets in addition to the inflammatory milieu fine-tuning platelet production. “Immunoinflammatory conditioned platelets” have specific characteristics and may be functionally different during inflammation to counterbalance an exacerbated immune response that would be otherwise deleterious. Platelet activation or priming, as suggested here, produces extracellular vesicles, which increase in number in severe COVID-19 patients. Their significance and role is still not completely understood. Clearly, clinical and translational research will certainly be required to advance and improve the management of patients with COVID-19 infection and other ICU hospitalized patients requiring platelet transfusions.

But, we cannot forget that convalescent plasma, a historical tool to treat infections, has been proposed as a solution in COVID-19 patients. However, the interpretation of the results of many studies from meta-analyses has led to recommend against its use, and currently, in COVID-19 patients convalescent plasma is limited to patients with immunosuppressive disease or those receiving immunosuppressive treatment. Whether convalescent plasma in COVID-19 will be to induce passive immunity in patients might be directly dependent on the host haemostatic and inflammatory status, and we should not forget that convalescent plasma is not a homogenous product (individual differences) and does contain the poorly understood extracellular vesicle fraction (which is pathologically increased in COVID-19 patients). To circumvent this problem, one additional proposal is to use plasma or plasma pools from vaccinated individuals containing a high titer of neutralizing antibodies. Of note, as it has been recently acknowledged, there might be a problem with the timing and the conclusions derived from all the studies with convalescent plasma explain the apparent lack of success. Convalescent plasma might be effective in patients during early infection and not in critical or severe patients. Considering that passive immunity is a valid strategy as treatment, especially in countries where vaccination is not reaching the desired numbers to acquire herd immunity, more studies should be encouraged, where antibody titers, plasma sources (vaccination or infection) and time of host infection and dosage (i.e. boosters with plasma from the same or different pools as to assess provision with varied antibody-antigen repertoire) should be considered.

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I hope the readers enjoy the section, and take this last paragraph of the editorial as an opportunity to thank Professor Gail Rock for agreeing with this approach, and my current colleagues and all others who have helped me to run this section of TAS because I could not do it without their enormous input and timely support.

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