VIRTUAL SALON SERIES

Lessons from Bergamo: Discoveries in Treating Critically-ill COVID-19 Patients

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Dr. Jeffrey Laurence discloses that he has received research grants and honoraria, and is on advisory committees, related to:

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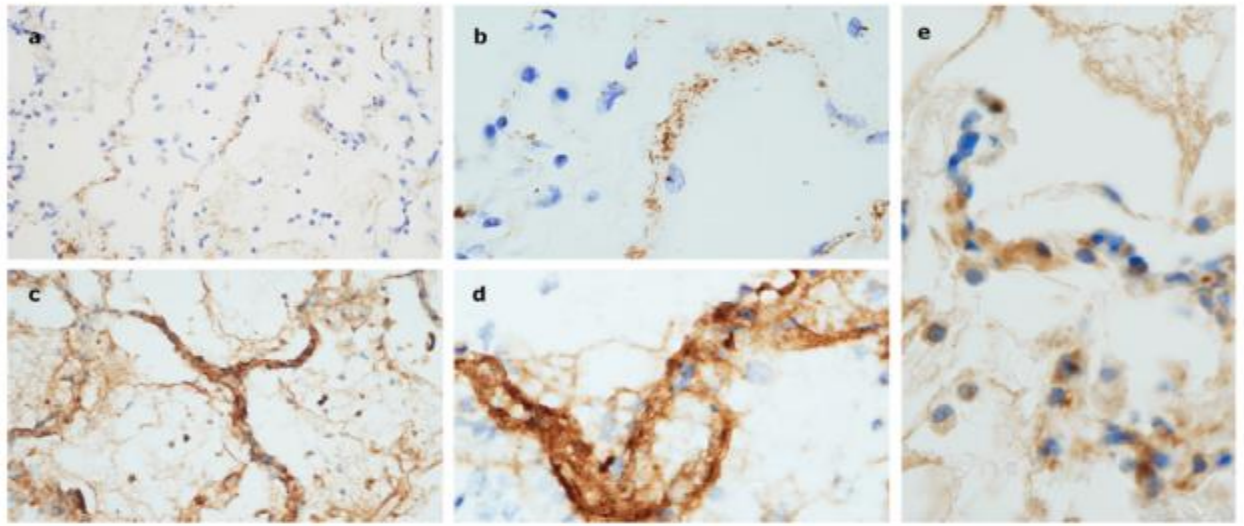

Fig 4. Immunohistochemistry analysis of pulmonary autopsy samples from Case 2. **A,** There was striking deposition of C5b-9 within the microvasculature of the interalveolar septa. (Diaminobenzidene, 200×). **B,** Higher power magnification again shows localization of C5b-9 within the septa, including C5b-9 deposits in areas of normal appearing lung, suggestive of systemic complement activation. (Diaminobenizdene, 1000×). **C,** C4d deposition was largely localized to the interalveolar septa in areas of microvascular injury. (Diaminobenzidene 400×). **D,** A higher power image demonstrates the extensive degree of C4d deposition within the septa. (Diaminobenzidene, 1000×). **E,** MASP2 staining showed granular and punctate deposits localized to the interalveolar septa.

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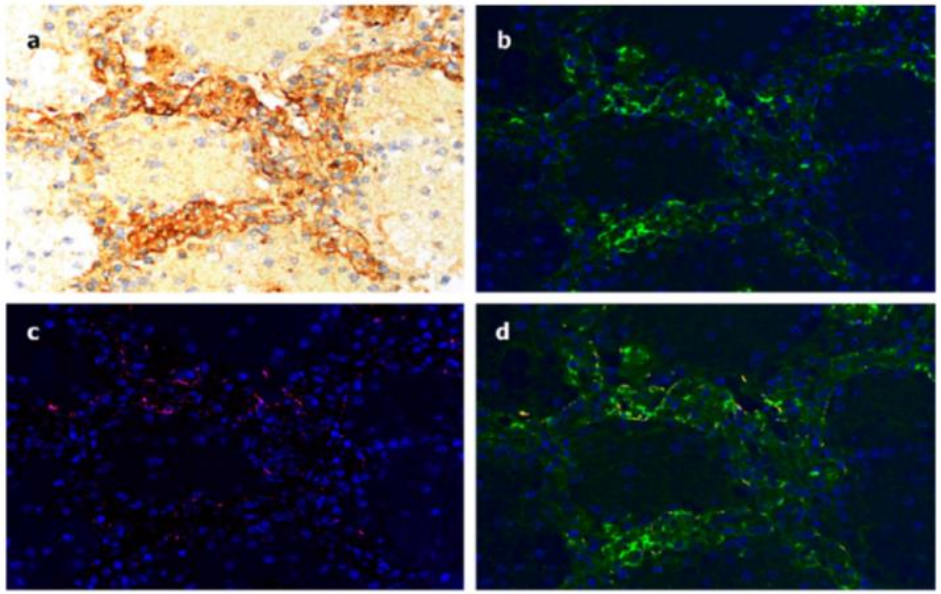

Fig 8. Demonstration of co-localization of complement components with SARS-CoV2 spike glycoprotein in the lung of Case 1. **A,** Striking deposition of C4d within the interalveolar septa of the lung was first demonstrated by DAB staining. Using NUANCE software the C4d image appears green (**B**) while the SARS-CoV2 spike protein appears red (**C**). **D,** A merged image shows a significant degree of C4d and SARS-CoV2 co-localization, as revealed by intense yellow staining. **E–H,** A similar pattern was observed using an anti-C5b-9 reagent whose image appears green, with a significant degree of C5b-9 and SARS-CoV2 co-localization, as revealed by intense yellow staining.

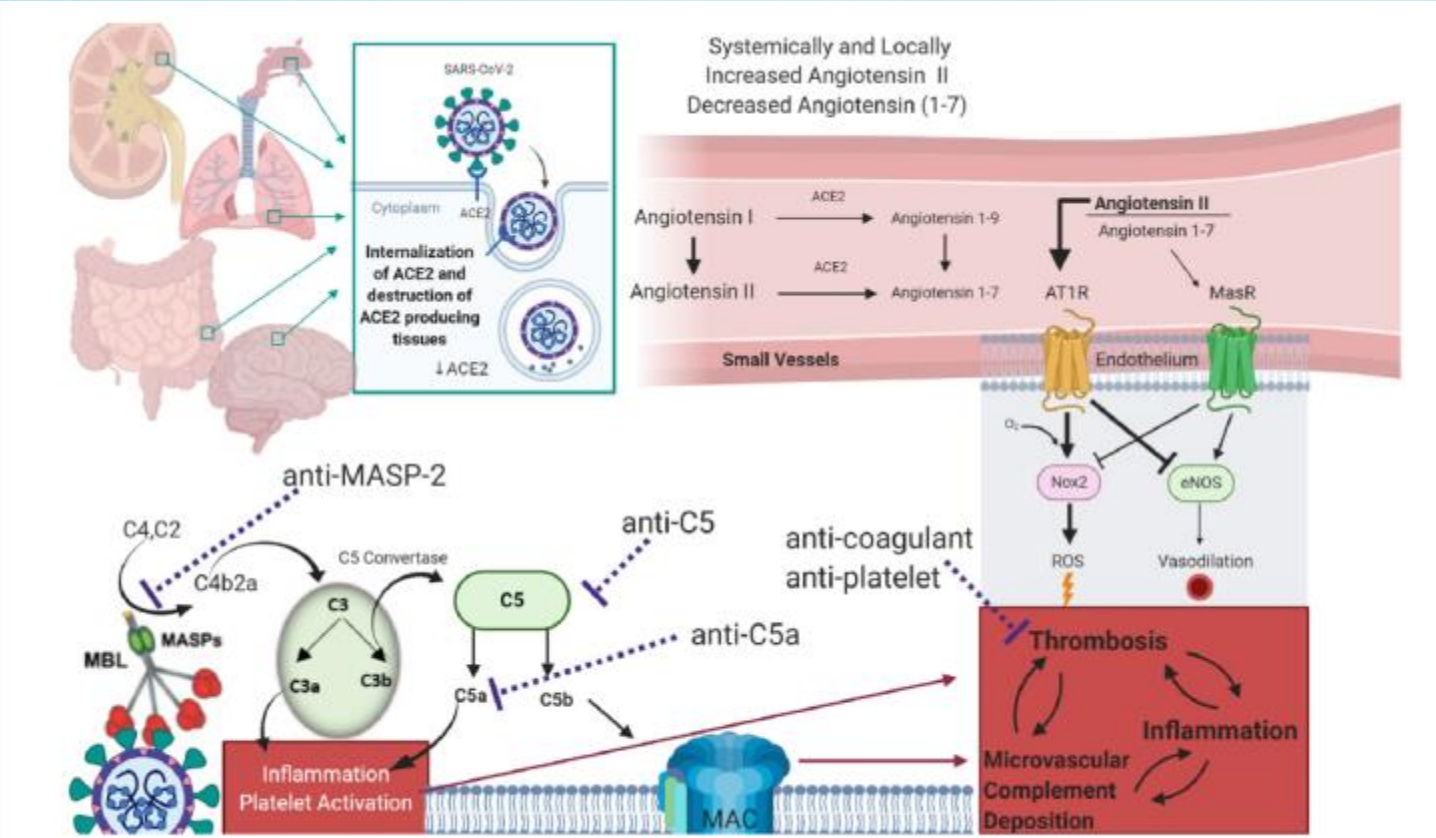

Fig 10. Model for AP and LP complement activation by SARS-CoV2, and its interaction with coagulation cascades.

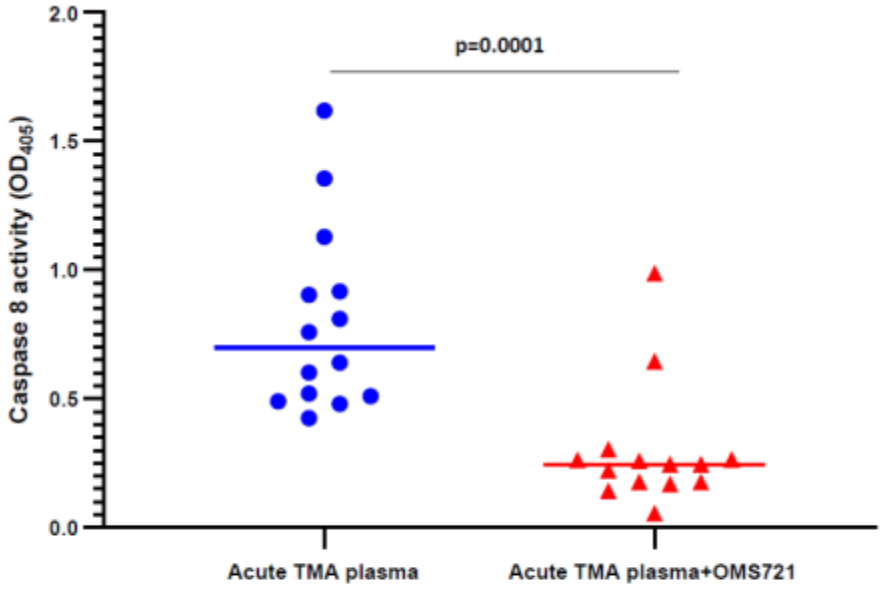

Fig. 3. Acute thrombotic microangiopathy (TMA) plasmas induce caspase 8 activation in human microvascular endothelial cell (MVEC), which is blocked by anti-mannose-binding lectin-associated serine protease 2 (MASP2) monoclonal antibody (mAb) narsoplimab. Cultures of primary human neonatal dermal microvascular endothelial cells were exposed to plasmas from patients with acute thrombotic thrombocytopenic purpura (TTP) or non-TTP types of TMA not associated with transplantation for 24 h in the presence or absence of anti-MASP2 mAb narsoplimab (1-2 μg/ml). Caspase 8 activity was analyzed in cell lysates.