Clinical History
The patient was a 52 year old male with Grave disease, myasthenia gravis (treated with azathioprine), and asymptomatic COVID-19 infection detected 7 weeks before his final hospitalization. He presented on admission with a 1 day history of headaches, fevers, and abnormal gate. COVID-19 RNA-SARS test was negative at the time. His hospital course was complicated by a diffuse pustular rash (pictures A, B).

Surgical Pathology
A shave biopsy of the skin was performed which revealed fibrin accumulation within vessels and marked associated acute inflammation (C) with the following comment:

The presence of vascular occlusion by fibrinous material and overlying ischemic epidermal changes were concerning for a coagulopathic process. There was also significant inflammation to a degree not always seen in association with coagulopathies (such as disseminated intravascular coagulation, DIC). This raised the possibility of an infectious process occurring either in conjunction with coagulopathy or possibly promoting a coagulopathic process.

Special stains and immunohistochemical studies showed:
- Periodic acid-Schiff (PAS) – negative for fungal organisms
- Silver (GMS) – negative for fungal organisms
- AFB – negative for mycobacterial organisms
- Gram – negative for bacterial organisms
- HSV1, HSV2 and CMV – no labeling of any cells.

He was transferred to the medical ICU for worsening respiratory failure requiring intubation and DIC (D-dimer >66,000 FEU, platelets 18x10^9/L, INR 14.9). He died one week after admission and an autopsy was requested to exclude infection or malignancy. The autopsy was performed 8 weeks after the initial positive COVID-19 test.

Autopsy Findings
Evidence of coagulopathy was seen in multiple other organs (i.e. mesentery in D). Microscopically, similar appearing inflammatory foci consisting of neutrophils, possibly with a left shift, and histiocytes were found associated with the coagulopathy in the microvasculature (E, F). The possibility that clotting had caused ischemia resulting in attraction of inflammation was a consideration. Although the inflammatory foci included immature myelocytes, no myeloblasts, such as in myeloid sarcoma were identified. The patient additionally had laboratory evidence of a myocardial infarction (high sensitivity troponin 10219 ng/L; reference ≤19.8 in males) in the setting of DIC. Despite further immunohistochemical studies on autopsy, no infectious organisms or malignancy were identified to account for the coagulopathy.

Discussion
The possibility that the findings represented tissue manifestations of COVID-19 was a consideration. According to the literature, the virus attacks the endothelial cells which line the blood vessels, initiating the clotting cascade. This is particularly noticeable in the microvasculature. It may be why the virus has such widespread systemic effects, even causing neurological strokes. Although examination of the brain in this case did not reveal infarctions, there was severe cerebral edema and widespread metabolic gliosis that could be seen in a wide variety of metabolic perturbations including systemic infection, acidosis, renal or hepatic failure, among other conditions. In summary, though the patient had a positive COVID-19 test two months before his death, which is considered a remote infection by the CDC, immunosuppression for myasthenia gravis may have delayed his immune reaction, allowing coagulopathy to manifest in other organs even after the virus was no longer detectable by nasal swabbing.

Reference