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### **Title**

Cytomegalovirus-induced Coagulopathy

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### **Authors**

Roosta, Tina

Lorber, Jeremy

Dowling, Erin

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**CLINICAL VIGNETTE**

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**Cytomegalovirus-induced Coagulopathy**

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Tina Roosta, Jeremy Lorber, M.D. and Erin Dowling, M.D.

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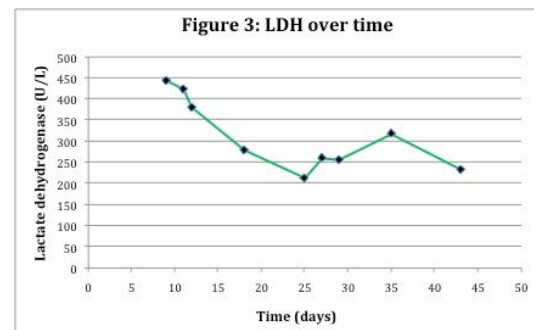
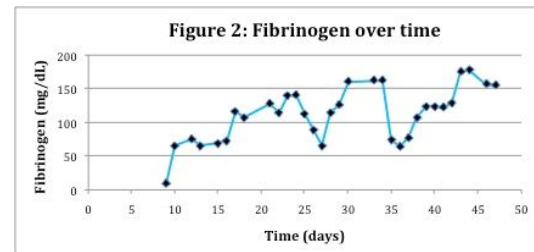
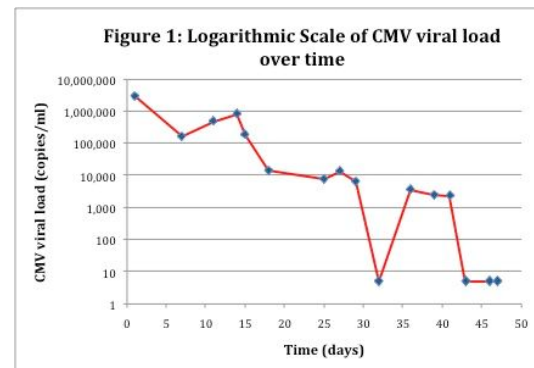
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**Case Report**

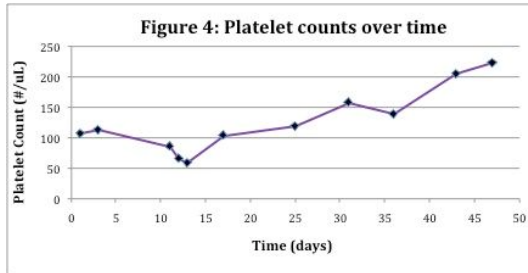
A 52-year-old African American male with history of renal transplantation for end stage renal disease secondary to focal segmental glomerulosclerosis presented to the hospital with three days of fevers to 39.5 degrees Celsius. In addition he reported chills, diarrhea, hematochezia and productive cough. His past medical history was significant for renal transplantation 18 months prior, in which the donor was CMV positive. His transplantation was complicated by acute rejection, treated with immunosuppressants and plasmapheresis, with ultimately preserved graft function. In addition, he had a history of hemophilia B and hepatitis C. The patient was admitted for further evaluation of his fevers. His initial labs were remarkable for creatinine of 2.5 (baseline 1.7) as well as CMV viremia with viral load 3 million copies/ml. Ganciclovir was initiated for presumed CMV viremia, nephropathy, and colitis. Additionally, intravenous immunoglobulin (IVIG) was started as adjunctive therapy for CMV nephropathy.

Seven days after admission, his INR unexpectedly increased from 1.3 to 5.5, and his PTT increased from 38.0 to 55.5 seconds with associated bleeding from line sites. Because of the patient's history of hemophilia B, factor IX levels had been followed and were stable (38-43%) with factor IX concentrate replacement. The fibrinogen level was found to be decreased at <25 mg/dl and D-dimer >10,000 ug/L. Lactate dehydrogenase (LDH) was elevated at 444 U/L and haptoglobin depressed at <8 mg/dl. His hemoglobin was stable at 11.9-12.4 and his platelet count, which was initially 106,000-139,000 decreased to approximately 60,000 over the next week. A peripheral smear showed moderate schistocytosis. His acute kidney injury progressed and his creatinine worsened to 6.4. Of note, the CMV viral load increased from 166,400 to 481,800 copies/ml two days prior to

the onset of coagulopathy, having previously declined from admission with ganciclovir treatment (See Figures 1-4).



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While disseminated intravascular coagulation (DIC) was felt to be the most likely diagnosis, given the degree of schistocytosis and persistent kidney injury, thrombotic thrombocytopenic purpura and hemolytic uremic syndrome were considered, and plasma exchange was started empirically. A renal biopsy was performed, which showed an antibody-mediated rejection consistent with known ABO-incompatibility, but negative for thrombotic microangiopathy. ADAMTS13 activity was also normal. Plasma exchange was then discontinued after only two sessions. For presumed DIC, supportive transfusions of cryoprecipitate were given with normalization of fibrinogen, INR, and aPTT along with resolution of bleeding. Cryoprecipitate was required for four weeks for persistent hypofibrinogenemia; however, on hospital day 44, fibrinogen levels increased spontaneously to 178 mg/dl and remained stable, coinciding with complete resolution of CMV viremia by PCR. Our patient's fluctuating renal function led to variable dosing of the ganciclovir. The patient's secondary hematological abnormalities resolved only after sufficient treatment of the DMV viremia.

### Background

DIC is a rare but important complication of CMV viremia. There have been three case reports of disseminated CMV infection precipitating DIC in immunosuppressed patients<sup>1,2</sup>. Rat models of CMV infection reported abnormal coagulation studies similar to DIC involving endothelial infection, thrombosis, and organ hemorrhage<sup>3</sup>. *In vitro* experiments show that endothelial cells infected with CMV induce a procoagulant phenotype with local generation of thrombin<sup>4</sup>.

### Conclusion

Treatment of CMV-associated coagulopathy should consist of supportive transfusions and treatment of underlying CMV infection. However, one case report demonstrated possible benefit from plasma exchange in patients without thrombotic thrombocytopenic purpura, possibly due to clearance of pro-inflammatory cytokines, activated coagulation factors, and removal of viral particles from the bloodstream<sup>5</sup>.

Physicians should be aware of the association between DIC and severe CMV viremia in immunocompromised patients. Every attempt should be made to treat the underlying CMV infection. However, plasma exchange or plasmapheresis should be considered if the patient's condition is worsening.

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