Artesunate is Ineffective in Controlling Valganciclovir-Resistant Cytomegalovirus Infection

To the Editor—Cytomegalovirus (CMV) disease is a common pathogen and represents a difficult clinical problem in transplant recipients. CMV-naïve patients receiving a CMV-positive allograft may experience complications, such as retinitis, gastritis, colitis, and pneumonia, which may force clinicians to reduce immunosuppressive agents, thereby risking rejection. However oral agents, such as valganciclovir, are effective in controlling such disease.

Unfortunately, CMV resistance to oral valganciclovir is an emerging problem and poses particular management difficulties in renal transplant recipients, because alternative agents, such as foscarin and cidofovir, are renal toxic [1]. Recently, the antimalarial agent artemesunate was reported as an effective agent against both wild-type and ganciclovir-resistant CMV [2]. Unlike ganciclovir, cidofovir, and foscarnet, artemesunate is not nephrotoxic and is believed to inhibit viral replication via an alternate mechanism of action to DNA polymerase.

We recently trialled artemesunate in a renal transplant recipient with documented valganciclovir resistance mutations in CMV (susceptible to cidofovir and foscarnet). Our CMV-naïve, 47-year-old female patient received a CMV-positive renal allograft 12 years previously and presented with a relapse of CMV colitis, with a high CMV load. She experienced 1 previous episode of CMV colitis documented with positive histopathology 2 years prior. Her medications at admission included oral valganciclovir (450 mg twice daily), diltiazem CD (240 mg twice daily), mycophenolate (1 g twice daily), prednisolone (10 mg daily), fenofibrate (48 mg daily), trandolapril (8 mg twice daily), pravastatin (80 mg daily), sertraline (50 mg twice daily), and esomeprazole (40 mg daily). Initial CMV quantitative polymerase chain reaction at admission was \(>1.1 \times 10^5\) copies/mL, exceeding the laboratory CMV disease threshold of 5000 copies/mL. Her estimated glomerular filtration rate (modification of diet in renal disease formula) was 27 mL/min, thus limiting use of standard CMV antiviral agents.

Initial therapy with CMV immunoglobulin and intravenous ganciclovir therapy failed to improve viral load. Immunosuppression was modulated by substituting mycophenolate with everolimus (.75 mg twice daily), and prednisolone therapy (10 mg daily) was continued. Intravenous artemesunate (180 mg daily) was commenced, and the dosage was increased to 240 mg daily on day 7. A total of 20 days of intravenous artemesunate therapy failed to significantly reduce CMV load on serial quantitative polymerase chain reaction assay. Subsequent therapy with foscarnet rapidly suppressed CMV load to undetectable levels.

We found that artemesunate was ineffective against this valganciclovir-resistant CMV strain. Alternate nonrenal toxic agents are needed for the treatment of these cases.

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