



## Case report

## CMV-associated adrenal insufficiency in a renal transplant recipient

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## ABSTRACT

Adrenal insufficiency is a rare manifestation of tissue-invasive cytomegalovirus (CMV) disease. CMV is one of the leading opportunistic pathogens affecting renal transplant recipients. Its prevalence in the adrenal glands of autopsied AIDS cases has been well documented. We report a rare case of CMV-associated adrenal insufficiency in a renal transplant recipient.

## Introduction

Cytomegalovirus is a common pathogen affecting solid organ transplant recipients. More than half of the adult population harbor latent CMV, and nearly three-fourths of solid organ transplant recipients develop CMV infection within one year of transplant [1]. CMV invasion of the adrenal glands has been frequently described in patients with AIDS [2–4]. However, it is a rare cause of adrenal insufficiency in other populations, with one prior case reported in a renal transplant recipient [5]. Here, we describe a second case of CMV-associated adrenal insufficiency in the setting of renal transplantation.

## Case report

A 63-year old man presented with fever and malaise for one week. He had undergone a cadaver unrelated kidney transplant eight months before, with anti-CMV IgG antibody positive in the donor and negative in the recipient. Immunosuppression consisted of mycophenolate mofetil, tacrolimus, and prednisone. He completed CMV prophylaxis with valganciclovir at six months post-transplantation. Examination revealed a temperature of 102.2 °F, blood pressure of 145/68, pulse rate of 89 beats per minute, respiratory rate of 16 breaths per minute, and oxygen saturation of 100% while breathing ambient air. Oral thrush was noted, with the remainder of the systemic examination unremarkable. Laboratory data was significant for acute thrombocytopenia with platelet count of 80,000 cells/mm<sup>3</sup>, creatinine of 1.6 mg/dL from 1.4 mg/dL one month ago, aspartate aminotransferase of 143 Units/L, alanine aminotransferase of 150 Units/L, and C-reactive protein of 48.06 mg/L.

Intravenous ganciclovir was empirically started. CMV quantitative PCR in plasma subsequently resulted as greater than 1,000,000 IU/mL. His viremia improved to 11,340 IU/mL after three weeks. However, he

developed postural hypotension, with a fasting blood glucose of 65 mg/dL, sodium of 133 mEq/L, and potassium of 5.0 mEq/L. An early morning serum cortisol level was noted to be 2.4 µg/dL, and a diagnosis of adrenal insufficiency was made. Hydrocortisone 25 mg/day was started and subsequently tapered over three weeks, with resolution of his hypotension and electrolyte abnormalities.

## Discussion

Cytomegalovirus is among the most pervasive opportunistic pathogens in renal transplant recipients. As in our patient, CMV seronegative recipients who have CMV seropositive donors are at the greatest risk of developing CMV disease [6]. Tissue-invasive CMV disease can affect any organ system, with manifestations including gastrointestinal disease, pneumonitis, hepatitis, CNS disease, retinitis, and nephritis [7]. In addition, CMV adrenalitis has been extensively reported in patients with AIDS. One of the first studies to describe this association examined 15 autopsied AIDS cases, with 14 cases revealing pulmonary or adrenal involvement of CMV [8]. A later study of 37 autopsied cases with AIDS and CMV infection found that the adrenal gland was the most commonly affected organ by CMV, with an incidence of 84% [3]. The pathogenesis of this predilection for the adrenal gland, however, remains unknown [2,9].

Apart from the clinical setting of AIDS, CMV-induced adrenal insufficiency has been reported in one case of congenital CMV infection and two cases of perinatal infection [9,10]. All three infants presented with hypotension, hypoglycemia, hyponatremia, and hyperkalemia, with CMV viral loads of 179,003, 207,360, and 1,220,000 IU/mL [9,10]. They were all successfully treated with ganciclovir and steroid therapy [9,10]. An additional case of CMV adrenalitis was discovered on postmortem examination of a patient with diffuse large B-cell

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lymphoma on chemotherapy with dexamethasone, cytarabine, and cisplatin [11]. He presented with fever and hypotension, and developed hypopituitarism before his death [11]. Autopsy revealed CMV infection of the lungs, pancreatic islets, pituitary gland, and adrenal glands [11].

Among renal transplant recipients, only one prior case of CMV-associated adrenal insufficiency has been documented [5]. The patient was a 24-year old woman, with anti-CMV IgG antibody positive in both donor and recipient [5]. Similar to our case, a considerable interval of at least several weeks was observed between the diagnosis of CMV infection and the development of adrenal insufficiency [5]. One possible explanation for this delay is the use of low-dose glucocorticoids for immunosuppression in both patients, which may have initially masked the signs and symptoms of adrenal insufficiency [5].

In summary, CMV-associated adrenal insufficiency is observed not only in the context of AIDS, but also in drug-induced cellular immunodeficiency, such as in the setting of chemotherapy or post-transplant immunosuppression. Recognition that CMV adrenal involvement can occur beyond the setting of AIDS is critical to caring for immunocompromised patients with this infection.

#### Conflicts of interest

The authors report no conflicts of interest.

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