A Case of Oral Valacyclovir–Induced Acute Kidney Injury

Geethika Thota, MD[1] ▪ Mehak Bassi, MD[2] ▪ Niraj Ballam Nagaraj, MD[3]

Abstract

Acute kidney injury (AKI) is defined as a rapid reduction in kidney function (within 48 hours) as measured by an increase in serum creatinine level, decrease in urine output, or need for renal replacement therapy, or all of the above. Herein, we present a rare case of AKI induced by oral valacyclovir. Nephrotoxicity due to valacyclovir is caused by intratubular precipitation of acyclovir crystals. A 39-year-old woman presents with acute onset of nonspecific reports of low back pain, nausea, and vomiting. After determining there was an AKI, the patient was treated with intravenous fluids and was monitored for improvement. The cause was deduced to be oral valacyclovir, which was being used to treat herpes labialis, and ultimately caused crystal-induced nephrotoxicity. Due to the rapid speed of renal excretion, acyclovir can surpass the solubility, and hence crystals can accumulate in the distal and collecting ducts. This can cause the symptomatology such as in this patient. In this case presentation and discussion, we review the presenting symptoms, diagnostic testing, differentials, and pathophysiology regarding crystal-induced AKI, specifically from valacyclovir.

Key words: AKI, valacyclovir, acute kidney injury, crystal nephrotoxicity.

A 39-year-old woman with no significant medical history presented to the emergency department (ED) reporting low back pain, nausea, and vomiting for 1 day. She was in perfect health prior to this episode.

Her medication history was significant for intake of 4 tablets of valacyclovir, 2 g every 12 hours for herpes labialis on the day before and the day of presentation to ED. She also reported use of an herbal supplement for weight loss for 1 week prior to the presentation. She did not report associated fever, chills, dysuria, urinary urgency, increased frequency, or hematuria. On reviewing her outpatient laboratory studies, her previous complete blood cell count, liver enzymes, and renal function test results were within normal limits.

Physical examination

Upon presentation, the patient was febrile with a temperature of 37.2 °C, had a heart rate of 82 beats/min, had a respiratory rate of 20 breaths/min, and had a blood pressure of 144/96 mm Hg. Results of a physical examination showed that the patient was healthy and well-nourished. Results of cardiac, respiratory, and abdominal examinations were unremarkable. Bilateral costovertebral angle tenderness was negative.

Diagnostic testing

Laboratory testing showed a normal complete blood cell count and liver enzyme level. Results that were concerning included an elevated serum creatinine level of 1.96 mg/dL (reference, 0.52-1.04 mg/dL) and blood urea nitrogen level of 22 mg/dL (reference, 6-20 mg/dL). Her electrolyte level was within the normal range. Urinalysis revealed +2 proteinuria with a specific gravity of 1.004, and no leukocyte esterase or nitrites. A small blood sample was negative for eosinophils. Urine was bland and negative for casts, crystals, and cells. Immunological tests for antinuclear, antineutrophilic cytoplasmic, and anti-dsDNA antibodies were negative, and the complement factors C3 and C4 levels were within the normal range. Tests for HIV, hepatitis B, and hepatitis C infections were negative. A urine toxicology screening returned negative results. A renal ultrasonography revealed mildly echogenic bilateral renal cortical echo texture and mild bilateral perinephric fluid. Noncontrast abdominal computed tomography revealed moderate to extensive bilateral

AFFILIATIONS:
[1]Internal Medicine Resident, Saint Peters University Hospital, Rutgers Robert Wood Johnson Medical School, New Brunswick, NJ
[2]Chief Resident, Internal Medicine, Saint Peters University Hospital, New Brunswick, NJ
[3]Internal Medicine Department, Saint Peters University Hospital, Rutgers Robert Wood Johnson Medical School, New Brunswick, NJ

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CORRESPONDENCE:
Geethika Thota, MD, Saint Peter's University Hospital, 254 Easton Ave, New Brunswick, NJ 08901 (prathima.thota95@gmail.com)

perinephric infiltration and edema. The kidneys appeared amorphous or enlarged.

Discussion

Our case highlights the rare adverse effect of oral valacyclovir–induced nephrotoxicity. Our patient rapidly developed an acute kidney injury (AKI) after receiving a total of 8 g of oral valacyclovir. Despite the patient's history suggesting a high probability for the cause of AKI, it was imperative to keep a broad differential for the cause of AKI. There were no postrenal symptoms and no evidence of a prerenal cause of the rise in creatinine levels. Considering the patient's history of using herbal supplements for 1 week prior to the episode, herbal medication–induced nephropathy was a differential in this case. Thorough research into the ingredients of the herbal supplement was done; however, they were not found to be nephrotoxic.

The patient developed nonspecific symptoms and imaging findings of pyelonephritis, without any changes to her urine studies, but an elevated creatinine level was concerning. Given that there was recent intake of the medication, and the highest creatinine value was approximately within the window of valacyclovir excretion, it was determined that valacyclovir had caused the AKI.

Oral valacyclovir–induced nephrotoxicity is rare, compared with more commonly encountered cases of nephrotoxicity caused by intravenous infusion of acyclovir.[1-4] In our case, as in other similar cases, AKI developed within 24 to 48 hours of valacyclovir administration, as indicated by the rapid rise in the patient's serum creatinine level.[1-4] After oral administration, valacyclovir is converted to acyclovir, and with the intratubular precipitation of acyclovir crystals, there is increased resistance to renal blood flow with subsequent elevation of serum creatinine.[1,4,5] Because of the rapid speed of renal excretion, acyclovir can surpass the solubility, hence crystals can accumulate in the distal and collecting ducts.[6] The patient's history of valacyclovir intake just prior to the episode, along with laboratory correlation, made the diagnosis of crystal-induced nephropathy more likely.[1,3,4]

Our case of an unexpected association between AKI and oral valacyclovir should serve as a wakeup call to physicians, particularly in the primary care setting, that care should be taken while prescribing valacyclovir to patients with underlying chronic renal insufficiency. Timely intervention with adequate hydration would contribute to a favorable prognosis.[1,4] Expert opinion from nephrology service can be helpful if there is no improvement in creatinine level with fluids.

Patient outcome

The patient's creatinine levels gradually increased from 1.96 to 2.23 to 2.50 mg/dL on day 2 of admission. The patient was initiated on intravenous fluids, and her renal function began to improve, with her creatinine level at 1.21 mg/dL on day 4. She was discharged with outpatient follow-up and laboratory testing to be completed in 1 week. The patient remained symptom-free with complete recovery.

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