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Case Report Highlighting the Importance of Prevention, Early Detection of Acyclovir Induced AKI

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Abstract

Acyclovir, an antiviral medication widely used for the treatment of herpes simplex and varicella-zoster infections, has been associated with adverse renal effects, including acute kidney injury (AKI). Acyclovir-induced AKI often occurs due to the drug's poor solubility, leading to intratubular precipitation and renal tubular obstruction. Though generally well tolerated, acyclovir can cause acute kidney injury (AKI) due to crystal nephropathy, particularly when administered intravenously or at high doses.

This case report presents a 52 year old patient who developed AKI following acyclovir treatment, illustrating the importance of monitoring renal function during therapy. This case reports evaluates the importance of vigilance regarding potential renal complications associated with Acyclovir therapy.

Introduction

Acyclovir is a widely used antiviral medication primarily for the treatment of herpes simplex virus (HSV) and varicella-zoster virus (VZV) infections. It is a synthetic nucleoside analog that inhibits viral DNA polymerase, effectively treating HSV and VZV infections. Despite its widespread use, nephrotoxicity remains a significant concern, particularly in hospitalized patients receiving intravenous (IV) acyclovir. The reported incidence of acyclovir-induced AKI ranges from 12% to 48%, with a higher prevalence in those with predisposing risk factors such as dehydration, pre-existing renal impairment, and rapid IV administration (1,2).

It is employed in treating widespread herpes virus infections in new-borns and as a preventative measure against recurrent genital herpes infections[5]. It frequently causes crystal nephropathy, which is a common mechanism for the adverse effect. By functioning as an analogue of deoxyguanosine triphosphate, acyclovir inhibits viral DNA polymerase in a competitive manner.

Case Description

A 45-year-old previously healthy male presented to the emergency department with a three-day history of fever, headache, confusion, and photophobia. His family noted increasing irritability, difficulty concentrating, and intermittent episodes of disorientation. Family occasionally found the patient acutely confused, not responsive and mumbling. He had no known chronic illnesses, medication use, or recent history of dehydration. There was no history of recent travel or exposure to sick contacts.

Physical Exam

On clinical examination, the patient was febrile (38.6°C), tachycardic (HR 105 bpm), and normotensive (BP 126/78 mmHg).

Glasgow Coma Scale (GCS): 12/15 (confused, disoriented in time and place).

Cranial nerves examination reveal no focal deficits.No visual disturbances identified on examination.

Neck stiffness and positive Kernig's and Brudzinski's signs was noted, raising suspicion of meningitis or encephalitis.

No focal motor or sensory deficits were present. Extremities were examined for erythema and rashes which were not present.

Hospital Course

The patient was admitted under the medical team and was started on IV acyclovir. Bloods were reviewed on admission. Bloods reviewed on admission S-Cr 0.8, Peak S-Cr 5.3 with BUN 29 (Normal Ranges for S-Cr and BUN are 0.6–1.2 mg/dL and 7–18 mg/dL). Following a rise in S-Cr, urinalysis collected was negative for RBCs, WBCs, granular casts, and eosinophils, no signs of infection or proteinuria. Renal ultrasound did not reveal any hydronephrosis or obstruction.

Initial Investigations:

Laboratory Tests (Baseline)

Test	Result	Reference Range
White Blood Cells	14,200/mm³ (elevated)	4,000-11,000/mm³
Hemoglobin	13.2 g/dL	12.0-16.0 g/dL
Platelet Count	275,000/mm³	150,000-450,000/mm³
Blood Urea Nitrogen (BUN)	29 mg/dL	6-20 mg/dL
Serum Creatinine (Baseline)	0.8 mg/dL	0.6-1.3 mg/dL
Serum Electrolytes	Normal	

Cerebrospinal Fluid (CSF) Analysis:

White Blood Cells: 145 cells/µL (lymphocytic predominance)

Protein: 75 mg/dL (elevated)

Glucose: 48 mg/dL (serum glucose: 90 mg/dL)

HSV-1 Polymerase Chain Reaction (PCR): Positive

Brain MRI reveal hyperintensities in the bilateral temporal lobes, consistent with HSV encephalitis.

Based on clinical presentation, CSF findings, and MRI results, the patient was diagnosed with HSV encephalitis and was immediately started on IV acyclovir.

On day 1, a normal urine output was measured and serum creatinine 1.3 mg/dL (baseline). On day 3 a reduced urine output with mild nausea, and fatigue was noted.

Repeat Laboratory Tests on Day 3:

Test	Result	Change from Baseline
Serum Creatinine	3.4 mg/dL	↑ from 0.9 mg/dL
BUN	42 mg/dL	↑ from 16 mg/dL
Serum Potassium	4.8 mmol/L	Mildly increased
Urinalysis	Microscopic hematuria (10-15 RBCs/hpf), proteinuria (1+), birefringent crystals	Suggestive of acyclovir nephropathy
Fractional Excretion of Sodium (FENa)	<1%	Suggests prerenal or obstructive pathology

Renal Ultrasound Findings:

Normal kidney size and echogenicity

No hydronephrosis (ruling out obstructive uropathy)

Serum acyclovir levels were elevated on further investigation confirming drug accumulation likely contributing to nephrotoxicity. Crystal-induced nephropathy was suspected and the patient was started on aggressive IV fluids. A further decline in renal function with serum creatinine rising to 4.5 mg/dL was noticed on day 5 accompanied by oliguria (urine output< 400 mL/day). Acyclovir was discontinued at this point, and the patient was started on intravenous hydration and supportive care. Based on clinical presentation, rapid deterioration in renal function after the administration of acyclovir, and supportive investigations, a diagnosis of acyclovir-induced AKI secondary to crystal nephropathy was made.

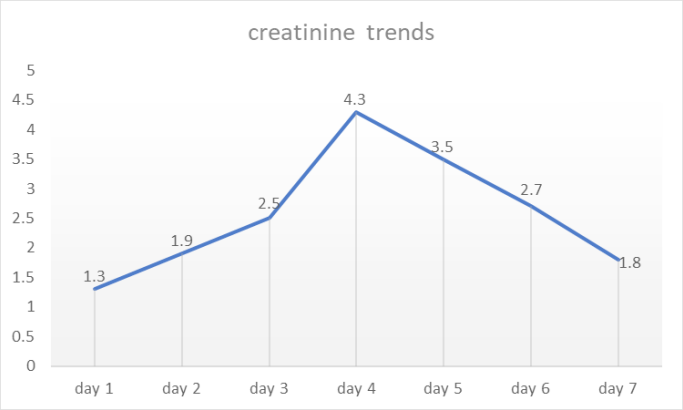
Management

The drug was stopped immediately, and the patient was transitioned to oral valacyclovir after stabilization.

Acyclovir was discontinued, and aggressive intravenous hydration was initiated to promote diuresis and flush out the crystals. Close monitoring of fluid balance, electrolytes, and renal function was ensured.

Aggressive intravenous hydration was initiated. The patient received normal saline at 150 mL/hour, with a target urine output >100 mL/hour.

Sodium bicarbonate infusion was considered for alkalinization of urine but not initiated due to adequate response to IV fluids. Regular monitoring of potassium, sodium, and acid-base balance was performed. Over the course of one week, the patient's renal function gradually improved with serum creatinine stabilizing at 1.8 mg/dL. By day seven, renal function and urine output normalized, and the patient's symptoms resolved.



Discussion

Acyclovir-induced AKI is a rare but serious complication. Acyclovir, when administered at high doses, can precipitate in the renal tubules due to its low solubility. This can result in crystal-induced tubular obstruction and direct tubular toxicity, leading to AKI, particularly in patients receiving high doses or with inadequate hydration (5,6). It can be exacerbated by acidic urine and rapid infusion rates (7). Other mechanisms include acute tubular necrosis (ATN) and acute interstitial nephritis (AIN) (8,9). Risk factors include pre-existing renal impairment, hypovolemia, and concurrent nephrotoxic agents (10,11).

Renal impairment is often reversible with early detection and supportive care (12,13).

Prevention strategies include dose adjustment in patients with renal impairment, particularly in patients with pre-existing CKD (14,15). It is important to ensure adequate hydration and patients should receive intravenous fluids to maintain urine output above 100 mL/hr (16,17).

Slowing infusion rate while administering acyclovir over at least one hour minimizes renal toxicity (18,19).

Discontinuation of the drug and prompt initiation of supportive care led to recovery of renal function. Acyclovir, which is relatively insoluble in urine, is rapidly filtered by the glomeri and secreted by the renal tubules, which can produce high urine concentrations, especially in patients with decreased urine flow rates. (20).

Immediate measures were taken on noticing patient's kidney injury to increase urinary flow before urinalysis could be collected. There has been some evidence in animal models that acute kidney injury can occur secondary to acyclovir administration without crystal obstruction, but from effects on renal microcirculation, although the exact mechanism is unknown (20). Acyclovir has low solubility in urine, especially at higher concentrations and in acidic environments. Crystals precipitate in the renal tubules, leading to tubular obstruction and interstitial inflammation, resulting in acute kidney injury. This often presents within 24-48 hours after starting therapy.

Empiric IV fluids can be used to minimize the risk of acyclovir induced AKI, establishing euvolemia before administration of drug, and avoiding rapid intravenous infusion of drug (infuse slowly over 1-2hours) and adjusting the dose for renal function if necessary (20). Other nephrotoxic drugs such as aminoglycosides and cyclosporine also place the patient at a higher risk of developing kidney injury with acyclovir therapy. Treatment of acyclovir nephrotoxicity is supportive with discontinuation or reduction of the drug in addition to maintaining a high urinary flow rate (>150 cc/hr) with IV fluids and furosemide. [20]

Several studies have documented the nephrotoxic potential of acyclovir, particularly with high-dose intravenous therapy. A retrospective study found a 12% incidence of AKI among patients receiving IV acyclovir, with higher rates in those with underlying renal disease (21). In another study, crystalluria was detected in 38% of cases with AKI, supporting the role of acyclovir precipitation (22).

Table 1. [20]

Risks, diagnosis, prevention, and treatment of acyclovir crystal nephropathy.

Risk factors	Laboratory and clinical findings	Prevention	Treatment
Hypovolemia	Increased Cr, rapid and usually within 12–48 hours	Establish euvolemia before medication administration	If possible, discontinue or reduce dose
Rapid IV infusion	Pyuria	Infuse drug slowly (over 1-2 hours)	Establish high urinary flow with IV fluids and furosemide (>150 cc/hr)
Concurrent acute kidney injury before medication administration	Hematuria	Dose to be adjusted depending on renal function	Hemodialysis if necessary
Excess medication dosage in relation to renal function	Birefringent Needle-shaped crystals	Avoid other nephrotoxic agents	May replace acyclovir with famciclovir in certain instances while increasing urinary flow rate
Concurrent use of other nephrotoxic agents	Pt. may complain of associated flank pain. Patient may be oliguric		

Conclusion

Acyclovir-induced acute kidney injury (AKI) is a clinically significant but preventable complication, particularly with high-dose intravenous therapy. This case underscores the importance of early recognition, prompt intervention, and proactive prevention strategies to mitigate the risk of nephrotoxicity. The patient developed AKI due to crystal nephropathy, a well-documented mechanism of renal injury, which was successfully reversed with timely discontinuation of acyclovir, aggressive intravenous hydration, and supportive management.

This case reinforces the necessity of adequate hydration, renal dose adjustments, and careful renal function monitoring in patients receiving IV acyclovir, particularly those with predisposing risk factors such as dehydration or pre-existing renal dysfunction. Clinicians must remain vigilant in identifying early signs of AKI and adopt appropriate preventive measures to ensure safe and effective antiviral therapy.

Further research is needed to explore optimal dosing strategies, alternative antiviral agents, and pharmacological approaches to reduce the incidence of acyclovir-induced nephrotoxicity while preserving its potent antiviral efficacy. Early recognition and discontinuation of the drug, along with supportive care, are essential for preventing permanent renal damage.

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