Case Report

Navigating Herpes Zoster and Acyclovir-Induced Acute Kidney Injury in Pregnancy: A Case Report

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ABSTRACT

Acyclovir, despite its favourable safety profile, has been observed to cause nephrotoxicity associated with its administration. We report a case involving a 31-year-old woman who was pregnant at six weeks gestation, presented with a 5-day duration of painful, non-pruritic rashes on the abdomen, back, and upper thigh. Examination revealed multiple painful vesicles with an erythematous base distributed along the right T9, L2, and L3 dermatomes. Initial blood investigations, including renal profile, were unremarkable. A diagnosis of multi-dermatomal herpes zoster was made, and intravenous acyclovir was initiated. Subsequently, the patient developed acute kidney injury, characterized by elevated serum creatinine levels, suspected to be due to crystal-induced nephropathy, a known adverse effect of acyclovir. Aggressive intravenous hydration was initiated, and acyclovir was discontinued, leading to gradual improvement in renal function and recovery. This report highlights the importance of early recognition and prompt intervention in managing acyclovir-induced nephrotoxicity during pregnancy.

Keywords: Herpes zoster, acyclovir, acute kidney injury

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1.0 Introduction

Herpes zoster (HZ) is rare in pregnancy, affecting approximately 1 in 20,000 pregnancies and generally poses minimal risk to the fetus, although its incidence has risen among adults due to various factors (1,2). Risk factors for complications include advancing age, immunocompromised states (e.g., HIV, cancer, organ transplant recipients), and pregnancy-induced immune changes. Additional risk factors include female gender, Caucasian ethnicity, psychological stress, mechanical trauma, and lack of prior varicella exposure (3). Early antiviral treatment is essential, with acyclovir as the preferred therapy. Reports of HZ in pregnancy, treated with acyclovir, including this case, highlight its efficacy and safety (4). Acyclovir's adverse reactions can range from mild symptoms like nausea and diarrhoea to severe conditions such as neutropenia, hepatitis, and Stevens-Johnson syndrome. A significant complication is acute kidney injury (AKI), characterized by a rapid decline in renal function within 12-48 hours post-administration (5), primarily due to acyclovir crystal formation affecting 5-10% of patients receiving intravenous administration (6,7).

2.0 Case Presentation

A 31-year-old woman, who was pregnant at six weeks gestation with iron deficiency anaemia, was admitted to the gynaecology ward due to a threatened miscarriage. During assessment, multiple vesicles were observed on her back, prompting a dermatology consultation. She reported a 5-day history of painful, non-pruritic rashes on her abdomen, back, and upper thigh. Examination revealed multiple painful vesicles with an erythematous base distributed along the right T9, L2, and L3 dermatomes. A diagnosis of multi-dermatomal HZ infection was made. Intravenous acyclovir at a dosage of 5 mg/kg 8 hourly at 250 mg per dose with a total of daily dose 750 mg was commenced, along with topical chloramphenicol over the crusted lesions. Full blood count (FBC) and renal profile during admission were unremarkable.

Two days after starting acyclovir, the kidney function declined, with serum creatinine rising to 437 µmol/L and urea to 9.5 mmol/L, leading to a nephrology consultation. Blood gas analysis showed a pH of 7.39 and bicarbonate of 19 mEq/ L.

Further laboratory investigations revealed a white blood cell count (WBC) of 6.4×10^9/L, an absolute eosinophil count of 0.04×10^9/L, and a platelet count of 244×10^9/L. Haemoglobin was 7 g/dL with a low mean corpuscular volume of 75 fL and also low mean corpuscular haemoglobin of 22.7 pg. A peripheral blood film analysis showed microcytic hypochromic anaemia. WBC and platelet counts were adequate and unremarkable. Iron studies confirmed iron deficiency anaemia (iron at 3.8 µmol/L, ferritin 7.7 µg/, transferrin saturation 6%), which remained unchanged at follow-up.

Electrolytes, coagulation profile, and liver function tests were within normal ranges. Urinalysis showed the presence of 1+ red blood cells with no white blood cells, granular casts, or crystals. Specific gravity was 1.003, and pH was 5.5. The urine protein-to-creatinine ratio was 53 mg/mmol. Renal ultrasound findings were normal. Viral screening, including tests for HIV, hepatitis B, and C, was negative.

There was no history of risk factors for acyclovir-related AKI, such as underlying renal insufficiency, dehydration, regular medication use, or positive family history related to kidney disease or connective tissue disease. No other conditions were identified that could lead to the rapid elevation of creatinine, such as rhabdomyolysis. Urine output remained normal, and the patient was clinically well and hydrated, with

unremarkable examinations of the lungs, cardiovascular, and abdominal systems. Suspecting crystal-induced nephropathy based on renal changes, aggressive intravenous fluid hydration was initiated, and acyclovir was discontinued. The patient received intravenous acyclovir at a dose of 250 mg over 30 minutes per infusion, totaling 1500 mg prior to onset of AKI. Figure 1 illustrates the creatinine trend, showing improvement with hydration and acyclovir cessation. The patient's renal function improved with hydration and sustained a high urine output rate. She was discharged upon recovery, and a follow-up two weeks later confirmed full resolution from AKI.

3.0 Discussion

HZ typically presents with a viral prodrome, including fatigue, mild fever, and localized pain 3-5 days before the rash. Reactivation and replication of the virus cause sensory ganglia necrosis and inflammation, leading to a dermatomal rash of grouped vesicles (8). These vesicles crust within 7-12 days, with the entire course lasting 2-3 weeks in healthy individuals. HZ can affect any dermatome, most commonly the thoracic region (50-56% of cases), followed by the head (20%).

Maternal zoster typically does not harm newborns as they acquire protective maternal antibodies; however, rare cases of congenital malformations associated with maternal HZ are linked to viremia rather than localized infection (3). It is crucial to cover lesions to reduce transmission risk, especially in non-immune pregnant women.

Early antiviral treatment is essential for managing HZ, with acyclovir as the first-line option (800 mg orally five times daily for 7-10 days) or intravenous acyclovir 5mg/kg 8 hourly (9).

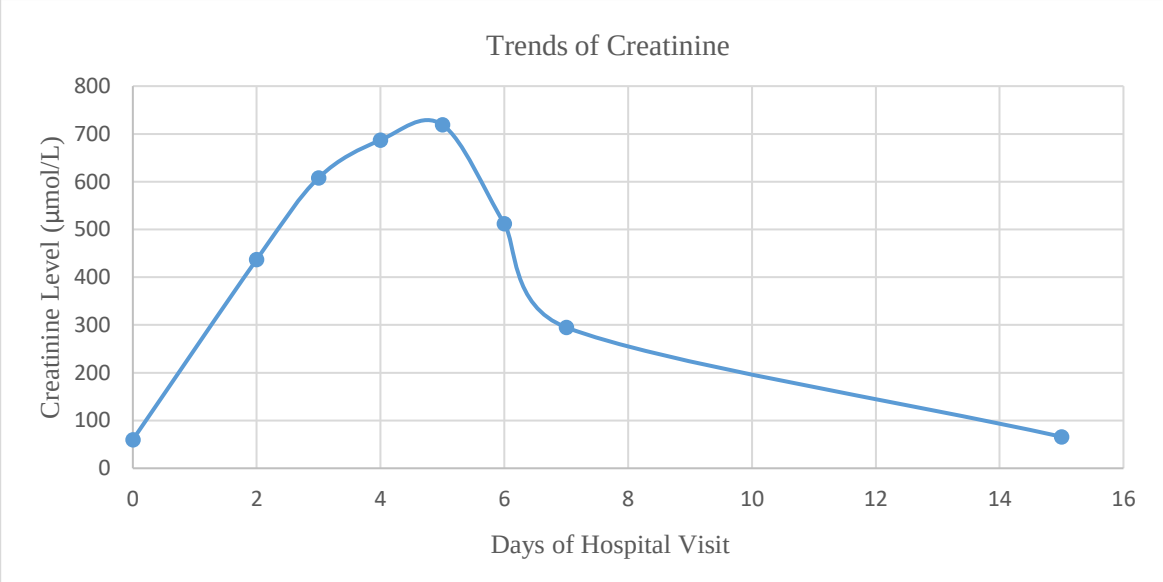

Figure 1: Trend of serum creatinine level (µmol/L) during hospitalization and follow-up.

Acyclovir is considered safe during pregnancy (FDA category B). Other options include prodrugs like valacyclovir and famciclovir. Antiviral therapy should ideally begin within 48-72 hours of symptom onset (2,3).

HZ can lead to significant complications, with post-herpetic neuralgia (PHN) being the most common. Other complications include ocular issues (zoster ophthalmicus), disseminated HZ (primarily in immunocompromised individuals), and secondary bacterial infections. Pain management in pregnant patients is complex and requires careful selection of analgesics due to potential risks associated with certain medications (3).

The varicella zoster vaccines are not recommended for pregnant women or those who may become pregnant within 30 days of vaccination. Non-immune pregnant women exposed to varicella or HZ should have anti-VZV immunoglobulin (Ig) G antibodies measured and may receive VZ Ig within 72-96 hours to prevent severe maternal chickenpox. Neonates should receive VZ Ig if maternal disease onset occurs between five days before and two days after delivery (3).

In this case, a pregnant woman developed AKI due to crystal nephropathy following intravenous acyclovir for HZ. While alternative mechanisms of injury, such as acute interstitial nephritis and acute tubular necrosis, are plausible, obstructive nephropathy is the most frequently reported mechanism (4,10). Acyclovir-induced AKI is a recognized complication, with studies reporting an incidence ranging from 12% to 48% of cases (5). This variability is influenced by dosage, administration route, hydration status, and renal function. Diagnosis of crystal-induced nephropathy relies on clinical history and its temporal link to acyclovir use.

Pregnancy-related physiological changes, including increased plasma volume, glomerular hyperfiltration, and altered clearance, can elevate the risk of acyclovir-induced AKI. Faster drug elimination may paradoxically concentrate acyclovir in renal tubules, leading to crystal formation and obstruction (5). Uterine compression and fluid shifts further contribute to urinary stasis and dehydration. These factors emphasize the need for careful dosing, hydration, and renal monitoring when using acyclovir in pregnancy.

Acyclovir's low solubility in urine leads to high concentrations and the risk of crystal formation, especially in patients with reduced urine flow rates (5). Bolus intravenous therapy, particularly in volume-depleted patients, increases the likelihood of crystal deposition within the renal tubules, resulting in intratubular obstruction and interstitial inflammation (6,7). Renal excretion accounts for 60-90% of acyclovir elimination, and intratubular crystal deposition can obstruct nephrons, increasing resistance to renal blood flow and raising serum creatinine levels (4, 10).

Typically, renal function starts to decline within 24 to 48 hours of initiating acyclovir therapy, with patients possibly experiencing nausea and flank pain due to urinary tract obstruction (5-7). Although the reduction in kidney function is often mild, severe instances can occur, marked by significant elevations in plasma creatinine concentrations. Fortunately, full recovery is common, usually occurring within four to nine days after discontinuation of acyclovir.

Diagnosis may involve observing needle-shaped acyclovir crystals in urine, particularly under polarized light. A definitive diagnosis is established through histological examination from a kidney biopsy. However, a biopsy is generally not recommended in AKI associated with a known crystal-inducing medication unless atypical features arise.

In this patient, no crystals were observed, likely due to alternative mechanisms. While crystal nephropathy is the most common cause, acyclovir-induced AKI can also result from direct tubular toxicity or interstitial nephritis, even in the absence of crystals (4). Renal biopsies, in some cases, have shown tubular damage and interstitial inflammation without crystal deposition, suggesting that the absence of urinary crystals does not exclude acyclovir as the cause. Sufficient hydration and high urine output may have helped prevent crystal formation in this case.

Management of acyclovir nephrotoxicity primarily involves supportive measures, including discontinuing or reducing the drug and maintaining a high urinary flow rate through intravenous fluids and frusemide administration (4). In cases of severe renal failure or inadequate response to treatment, hemodialysis may be necessary to eliminate the causative drug and provide supportive measures for renal function (4, 5).

4.0 Conclusion

HZ during pregnancy is generally benign with minimal fetal risk, though it can cause significant maternal concern, warranting appropriate treatment. Early antiviral therapy is safe and can prevent severe morbidity. Acyclovir, while commonly prescribed during pregnancy, requires careful monitoring due to potential nephrotoxicity. Timely recognition and intervention, including discontinuation of the drug, aggressive hydration, and close monitoring of renal function, are crucial for optimal patient care and preventing adverse outcomes. Awareness of these risks is essential for ensuring the best outcomes for patients receiving acyclovir, especially pregnant patients.

Authorship contribution statement

NAA: Conceptualization, Resources, Visualization, Writing – original draft, review & editing; **SAW**: Conceptualization, Visualization, Resources, Supervision, Writing – review & editing

Conflict of Interest

The authors declare no conflict of interest in the current work.

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