

Case Report

Acyclovir Induced Reversible Renal Failure in an Immunocompromised Child with Extensive Cutaneous Herpes Zoster

Eman R Al-Matter, Mona H Bourahma, Kadankandy C Aboobacker
Pediatric Hematology Unit, NBK Children Department, Al-Sabah Hospital, Kuwait

Kuwait Medical Journal 2004, 36 (1): 47-48

ABSTRACT

Acute case of acute renal failure due to acyclovir therapy in a child with extensive cutaneous herpes zoster on maintenance

treatment for acute lymphocytic leukemia is presented, along with a review of similar reports in the literature.

KEYWORDS: acute lymphocytic leukemia, acute renal failure, acyclovir, herpes zoster

INTRODUCTION

Acyclovir is an effective antiviral drug for the treatment of herpes simplex and varicella-zoster virus infections. Adverse effects have been reported in patients receiving both large and low doses of acyclovir by both rapid and slow intravenous infusions as well as with oral use^[1]. Renal dysfunction and acute renal failure caused by this medication are characterized by rapid elevation in blood urea and serum creatinine and gradual return to base line renal function with the discontinuation of the drug^[2]. The efficacy of acyclovir in the treatment of serious herpes simplex and varicella-zoster infections has led to the widespread use of this agent. In spite of acyclovir's good record of safety, acute renal failure is a potential adverse effect of this drug. We report a case of acute renal failure following the use of high dose acyclovir in an immunocompromised child with extensive herpes zoster lesions. To the best of our knowledge this is the first such case report from this country.

CASE REPORT

A 13-year-old Kuwaiti girl was diagnosed in June 1999 as suffering from acute lymphocytic leukemia (ALL)-L1 FAB. She received induction chemotherapy as per UK-MRC-ALL97 protocol in our Unit and went into complete remission in July 1999. Following intensifications, maintenance chemotherapy was started in October 1999 using 6-mercaptopurine orally daily and methotrexate orally weekly along with pulse induction by vincristine every four weeks and prednisolone daily orally for five days every four weeks and I.T. methotrexate every 12 weeks. She was said to have chickenpox at the age of five years.

She was admitted in December 2001 in our unit with extensive herpes zoster lesions over the chest and back of the trunk following contact with chickenpox at school. Her temperature and blood pressure were normal. There was no hepatosplenomegaly. Investigations on admission revealed normal blood parameters, normal urea (3.3 mmol/L), normal creatinine (34 mmol/L), normal electrolytes and normal liver and bone profiles. She was started on I.V. fluids and slow infusion of high dose of acyclovir with 1500 mg/m²/day in three divided doses. Renal profiles were checked daily. On the third day of therapy, the blood urea increased to 7 mmol/L and then to 13.2 mmol/L. The serum creatinine also increased from 34 to 351 mmol/L. The blood pH, serum bicarbonate serum uric acid and urine analysis were unremarkable. The blood pressure remained normal. There were no signs of dehydration. She was not on any antibiotic therapy. A diagnosis of acyclovir induced renal failure was made. Acyclovir was stopped and I.V. fluid was increased to 3 liters/m²/day along with alkalization of urine. She passed a good amount of urine and maintained her BP. Her renal function started to improve and within the next six days her blood urea returned to 2.6 mmol/L and creatinine to 54 mmol/L. She was then discharged from hospital with well-healed herpetic lesions and was able to resume her maintenance therapy four days later.

DISCUSSION

Acyclovir is an important antiviral agent in the therapy of herpes simplex and varicella-zoster infections in immunocompromised host. Optimal use of this drug requires an understanding of its

Address correspondence to:

Dr. K.C. Aboobacker, P.O. Box 43470, Hawally 32049, Kuwait. Tel.: 4835826, Fax 4835826, email: kcaboobacker@hotmail.com

pharmacology and potential adverse effects^[3]. The kidney accounts for 75-80% of the total clearance of acyclovir. Renal clearance of the drug is approximately three times that of creatinine, suggesting rapid elimination by glomerular filtration and tubular secretion, and high concentration in the tubular lumen. Renal excretion of unchanged drug accounts for approximately 60-90% acyclovir elimination^[4]. In addition, acyclovir is relatively insoluble in the urine, particularly in the distal tubular lumen, where urine flow is sluggish. These characteristics explain why intravenous infusion of acyclovir may cause intra-tubular precipitation of crystals in the kidney^[4], thus leading to obstructive nephropathy^[2]. Acyclovir induced acute tubulo-interstitial nephritis has also been described^[3]. Indeed acyclovir induced renal failure had been reported since its inception in the late 1970s. Selby *et al* initially reported transient blood urea nitrogen elevations in two patients treated with intravenous acyclovir^[5]. A reduction in acyclovir dosing and an increase in fluid intake improved renal function^[2]. Risk factors of acyclovir nephrotoxicity include high blood concentration of acyclovir caused by dosage greater than 1500 mg/m² per day, bolus intravenous administration, pre-existing renal disease, dehydration and associated use of other nephrotoxic agents^[1]. Nephrotoxicity usually is a self-limiting condition that resolves with discontinuation of the drug and the intake of a good amount of intravenous fluid (3 liters/m²/day). Severe cases of renal failure may need hemodialysis^[3,6]. The risk of nephrotoxicity can be minimized by ensuring adequate hydration and a high urine flow and by giving acyclovir as a slow infusion rate over one hour^[3]. In patient with pre-existing renal disease, acyclovir dosage should be modified.

Cutaneous herpes zoster infection is a problem frequently encountered in clinical practice^[7]. High dose of acyclovir has been reported to shorten the duration of viral shedding, decrease the formation of

new vesicles and reduce the incidence of post herpetic neuralgia. Our patient received high dose of acyclovir because of extensive herpes zoster lesions while on chemotherapy. However the child developed renal insufficiency with acyclovir even when she was taking adequate fluid intravenously, and by mouth. In spite of stoppage of the medication, she continued to have good healing of the herpetic lesions, probably because of adequate blood level of acyclovir in the presence of impaired renal function.

In conclusion, it is important to monitor renal function in all children receiving acyclovir and treat promptly the renal dysfunction, if and when it occurs, in order to avoid severe renal failure.

ACKNOWLEDGEMENT

We would like to thank Miss Haya Al-Mutiri for her assistance in preparing this manuscript and to all the doctors and nurses in the Pediatric Hematology Unit, Sabah Hospital for their care of the patient.

REFERENCES

1. Vachvanichsanong P, Patamasucon P, Malagon M, Moore ES. Acute renal failure in a child associated with acyclovir. *Pediatr Nephrol* 1995; 9:346-347.
2. Becker BN, Fall P, Hall C, *et al*. Rapidly progressive acute renal failure due to acyclovir: case report and review of the literature. *Am J Kidney* 1993; 22:611-615.
3. Kriebel BF, Rudy DW, Glick MR, Clayman MD. Case report: acyclovir neurotoxicity and nephrotoxicity - the role for hemodialysis. *Am J Med Sci* 1993; 305:36-39.
4. Perazella MA. Crystal-induced acute renal failure. *Am J Med* 1999; 106:459-465.
5. Selby PJ, Powles RL, Janeson B, *et al*. Parenteral acyclovir therapy for herpes virus infections in man. *Lancet* 1979; 2:1267-1270.
6. Khajehdehi P, Jamal JA, Bastani B. Removal of acyclovir during continuous veno-venous hemodialysis and hemodiafiltration with high efficiency membranes. *Clin Nephrol* 2000; 54:351-355.
7. Eck P, Silver SM, Clark EC. Acute renal failure and coma after a high dose of oral acyclovir. *N Engl J Med* 1991; 325:1178-1179.