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Selected Topics: Toxicology

ALTERED MENTAL STATUS FROM ACYCLOVIR

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□ **Abstract—Background: Acyclovir is widely used in the treatment of herpes virus infections, particularly herpes simplex virus and varicella-zoster virus. Acyclovir, when given promptly upon the start of a herpes zoster eruption, speeds healing and diminishes acute pain. Objectives: Because acyclovir is a commonly used medication, it is crucial for health providers to be aware of appropriate dosing as well as possible side effects. We present this case to increase awareness of the potential for inappropriate dosing of acyclovir and the presentations of patients with toxic effects. Case Report: We report the case of a 65-year-old man with a past medical history significant for chronic kidney disease who presented to the Emergency Department with progressive confusion and ataxia over 2 days. Thorough questioning in the patient's native language revealed that he had recently started a medication for a "rash." Neither he nor his family knew the name of the new medication; further investigation revealed it to be acyclovir. Although other diagnoses were considered in the differential diagnosis for this patient with altered mental status, he was treated for presumed acyclovir toxicity and given prompt dialysis, upon which his symptoms resolved. Conclusion: It is important for physicians to remember that even common medications such as acyclovir can have serious side effects and complications. In this case, renal dosing was not used in a patient on hemodialysis. Acyclovir must be renally dosed and carefully monitored through drug level measurement in patients with limited kidney function to prevent serious side effects, such as the neurological sequelae demonstrated in this case report. Emergency physicians should be aware of the potential for inappropriate dosing of this medication and the presentations of patients with toxic effects. © 2011 Elsevier Inc.**

□ **Keywords—altered mental status; acyclovir; herpes zoster virus; end-stage renal disease**

INTRODUCTION

Acyclovir is a common medication prescribed for herpes infections, and is generally well tolerated by patients. Although the side-effect profile is low, it can have significant systemic effects. Acyclovir toxicity is dependent on renal function, and also must be adjusted in special populations, such as those at both ends of the age spectrum (pediatric or elderly). The presentation of altered mental status due to acyclovir toxicity can range from mild confusion to states of severely depressed consciousness. This case report of neurological toxicity after acyclovir treatment in an elderly man with systemic organ failure highlights the importance of appropriate dosing of this medication and the detrimental neurological toxic sequelae that it can have on patients with end-stage renal disease.

CASE REPORT

A 65-year-old man with a history of diabetes mellitus type 2 and end-stage renal disease, on hemodialysis for the last 4 years, presented to the Emergency Department (ED) with altered mental status. The patient was brought

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to the hospital by his daughter, who stated that he was normally very alert and functional and had no history of dementia. The altered mental status began gradually about 2 days before his evaluation in the ED. On the first day, the patient's family noticed he was having trouble finding words and understanding commands. On the following day, he became confused, unsteady while walking, and unable to recognize his family members. Before this, he had been in his usual state of health with no recent illnesses, except for a painful rash on the right side of his chest that had developed several days before his confusion began. He saw his primary care provider 5 days before his ED visit, and was prescribed "some medication" for the rash.

The review of systems was negative. Pertinent past medical history included a history of hypertension, hypothyroidism, anemia, bradycardia, and a meningioma that was removed in 2001. He also sustained an intracranial hemorrhage complicated by development of a seizure disorder and mild dysphasia in 2002. His medications were aspirin, glipizide, amlodipine, benazepril, lasix, calcium carbonate, hydralazine, simvastin, thyroxine, and phenytoin. The patient had no known drug allergies. He was currently retired, living with his family, and had a history of "lots of drinking when he was younger" (per his daughter) but denied any current alcohol, tobacco, or other drug use.

On physical examination, temperature was 36°C, with a blood pressure of 195/75 mm Hg, heart rate of 56 beats/min, respiratory rate of 16 breaths/min, and oxygen saturation of 93% on room air. His general appearance was sleepy, but arousable. The oropharynx was clear, tongue was midline, and pupils were equally round and reactive to light. The cardiac examination revealed a regular rate and rhythm, with a 2/6 systolic ejection murmur heard best at the left upper sternal border without any radiation. The jugular venous pressure was 8–9 cm. The lungs were clear to auscultation bilaterally, with no crackles or wheezes. The abdomen was soft, nontender, non-distended, and he had normoactive bowel sounds. The liver was palpable 1 cm below the right costal margin. The distal pulses were 2+, and the legs were warm and non-edematous. He had normal bulk and tone, and strength was 5/5 throughout. The skin had scattered erythematous, crusted papular lesions on the right anterior chest wall with a dermatomal distribution. On neurological examination, the patient was alert and oriented to self, with slurred speech in Spanish, and he was distracted and rambling. The cranial nerves were intact, except for fatigable horizontal nystagmus on lateral gaze. He was ataxic, and was unable to stand without assistance. Laboratory results revealed that he had no abnormalities in white blood cell count, hemoglobin, platelets, or basic electrolytes. The phenytoin level was slightly sub-therapeutic, and his thyroid-stimulating hormone was at his baseline (10.11 mU/L), as he was being treated for hypothyroidism. Computed tomography scan of the head was performed, which was normal, and electrocardiogram and chest X-ray study were unremarkable.

Further investigation into the patient's hospital record of the unknown, recently prescribed medication revealed that he was prescribed acyclovir at the standard dose of 500 mg po of 800-mg pills five times a day without renal adjustment, for presumptive treatment of herpes zoster. Herpes-related illnesses were included in the initial differential diagnosis of altered mental status-herpes encephalitis and acyclovir toxicity. Upon discussion with the renal specialists, it was thought that because he had already been on treatment for 3 days, although herpes encephalitis was possible, the more probable diagnosis was acyclovir toxicity. Although the diagnosis of acyclovir-resistant herpes was entertained, all providers involved decided that acyclovir toxicity was more likely given the rarity of herpes-resistant acyclovir. These possibilities were discussed with the family, and they (because the patient was unable to verbalize understanding of the procedure and implications) did not want to pursue the possibility of a lumbar puncture (for herpes encephalitis or meningitis from other etiologies). As a result, it was decided that dialysis would be performed to dialyze off any potential drug, and that he would be observed for toxicity and evaluated for clinical improvement. If the patient did not improve significantly, then further investigations, including a lumbar puncture, would be reconsidered.

The patient was admitted to the hospital that evening and received dialysis the next morning. Within 3 days his confusion, as well as his ataxia, completely resolved.

DISCUSSION

Altered mental status, with findings of asterixis and nystagmus, can have a plethora of etiologies, including systemic illness, isolated organ system dysfunction, drug intoxication or withdrawal, psychiatric illness, or neurologic disease (1). Although the differential diagnosis of altered mental status is extensive, in this particular patient, with his recent history of a dermatomal rash being treated with acyclovir, and with renal failure and being on hemodialysis, several etiologies had to be considered. These included: uremic encephalopathy, electrolyte abnormalities secondary to renal failure or hemodialysis, phenytoin toxicity, cerebrovascular etiology, herpes encephalitis, or acyclovir toxicity. Most of the etiologies are fairly easy to distinguish with laboratory testing. When assessing for phenytoin toxicity in this patient, an unbound level should be obtained, rather than the serum