



PALLIATIVE CARE CASE OF THE MONTH

“Ziconotide (Prialt): A Blessing and a Curse”

by

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Case: Mr. RF is a 63-year-old man with a past medical history of metastatic thyroid cancer with bony metastases to his sacrum s/p sacrectomy who has been followed in the outpatient palliative care clinic for pain management. He has a history of severe lower extremity neuropathy as a complication of his surgery for which he was tried on multiple systemic analgesics including opioids and neuropathic agents without relief of his symptoms. In the past year he had a ziconotide (Prialt) intrathecal pump placed which was effective in controlling his pain. In the weeks prior to his admission to the hospital, he began exhibiting odd behaviors including obtaining a new credit card to buy expensive gifts for others and for himself. He became increasingly agitated and confused and this prompted his wife to bring him to the hospital where his agitation manifested as physical violence and verbal threats towards staff. He was transferred to the ICU and required placement in an enclosed Posey bed due to the potential risk of harm to staff.

During his hospital admission, he was treated with neuroleptics, analgesics, and benzodiazepines with no improvement in his symptoms. An extensive workup including a head CT, brain MRI and EEG revealed no acute abnormalities. There was no evidence of infectious or metabolic etiology on laboratory evaluation. A paraneoplastic panel was also negative. Multiple consulting services were involved including palliative care, psychiatry, neurology, and the chronic pain service. Palliative care was consulted for symptom management.

Discussion: Delirium is a common presentation in palliative care. Quick recognition of the symptoms and appropriate identification of the etiology can help improve the patient’s condition. Delirium is defined as a transient, usually reversible cause of cerebral dysfunction that can present with a wide range of neuropsychiatric abnormalities, most prominently a disorder in attention.¹ Potential causes of delirium include infection, substance intoxication or withdrawal, trauma, CNS pathology, metabolic abnormalities, hypoxia, nutritional deficiencies, endocrine abnormalities, toxins or drugs, heavy metals, and acute vascular events.² A thorough history with attention to medication changes, evidence of infection, as well as substance intoxication or withdrawal is imperative. A detailed physical examination including neurologic exam and assessment of mental status is also helpful in guiding the diagnostic workup. Basic laboratory studies can include a complete blood count, basic metabolic panel, liver function, thyroid function, and arterial blood gases. Additional studies including a urine toxicology screen, EEG, and CNS imaging may be helpful.

In our patient’s case, his delirium was ultimately attributed to his intrathecal ziconotide. Ziconotide is a synthetic equivalent of a naturally occurring conopeptide found in the venom of the marine snail *Conus magnus*.³

It was approved in 2004 by the FDA for the management of severe chronic pain in patients who are intolerant of or refractory to other treatments. Ziconotide is an N-type calcium channel blocker that targets pre-synaptic calcium channels on nerves that transmit pain signals. This medication acts by inhibiting glutamate release thus decreasing the amount of stimulation at the dorsal horn neuron.⁴

Although this drug is effective in the treatment of pain, it has many adverse side effects. The safety profile for ziconotide warns “that severe psychiatric symptoms and neurological impairment may occur during treatment with this drug,” and “patients with pretreatment psychiatric disorders may be at increased risk”.⁵ In clinical trials with ziconotide involving 1,254 patients, delirium was reported in 2% of patients, and psychosis was reported in 1% of patients.⁶ In published case reports this has been shown to occur anywhere from immediately after treatment initiation up to several months afterwards. Ziconotide has also been shown to worsen depression with a risk of suicide in susceptible patients. Patients receiving this treatment should be monitored frequently for depressive symptoms and suicidal ideation, and the drug should be discontinued if these develop. Ziconotide can be discontinued abruptly without evidence of withdrawal effects. Typically the CNS-related effects are reversible within two weeks.

Resolution of Case:

After discontinuing ziconotide, Mr. RF’s mental status improved. His scheduled thorazine was tapered down. He was transferred to inpatient rehabilitation due to deconditioning and was then discharged. At a recent ambulatory appointment, his delirium had resolved and his functional status has improved significantly. Unfortunately, his lower extremity neuropathic pain has also recurred.

References:

1. Diagnostic and Statistical Manual of Mental Disorders. 4th ed. Washington, DC, American Psychiatric Association, 2000;143.
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3. Thompson J, Dunbar E, Laye R. Treatment challenges and complications with Ziconotide monotherapy in established pump patients. *Pain Physician*. 2006;9: 147-152.
4. Mathur VS et al. Ziconotide: a new pharmacological class of drugs for the management of pain. *Seminars in Anesthesia* 2000; 19:67-75.
5. Ziconotide [prescribing information]. San Diego, CA: Elan Pharmaceuticals, Inc. 2004.
6. Penn RD, Paice JA. Adverse effects associated with the intrathecal administration of Ziconotide. *Pain* 2000; 85:291-296.

Personal details in the case published have been altered to protect patient privacy.

For palliative care consultations please contact the Palliative Care Program at PUH/MUH, 647-7243, beeper 8511, Shadyside Dept. of Medical Ethics and Palliative Care, beeper 412-647-7243 pager # 8513, Perioperative/ Trauma Pain 647-7243, beeper 7246, UPCI Cancer Pain Service, beeper 644 –1724, Interventional Pain 784-4000, Magee Women’s Hospital, beeper 412-647-7243 pager #: 8510, VA Palliative Care Program, 688-6178, beeper 296. Hillman Outpatient: 412-692-4724. For ethics consultations at UPMC Presbyterian-Montefiore and Children’s page 958-3844. With comments about “Case of the Month” call Dr. Robert Arnold at (412) 692-4834.