The management of pain due to cancer is challenging and often requires invasive therapy in addition to medication management. Intrathecal drug delivery is a form of advanced therapy that delivers medication locally in the intrathecal space while reducing systemic side effects associated with high doses of opioids. Although risks associated with intrathecal drug delivery are low, some common complications include dislodgement, kinking, or fracture of the catheter, bleeding, neurological injury, infection, and cerebrospinal leaks.

We present a case of a 38-year-old woman with a medical history significant for stage IV breast cancer, L2 metastatic lesion, opioid tolerance, and chronic neck and low back pain who was admitted to the hospital for intractable pain. She had failed multiple interventional procedures in the past including lumbar medial nerve radiofrequency ablation, epidural steroid injection, and trigger point injections as well as a kyphoplasty at the L2 level. Failing both oral and parenteral opioid treatments, the decision was made to place an intrathecal pump in the patient. After placement of the intrathecal catheter and prior to any bolus of medication being given, the patient became bradycardic with a heart rate in the 20s and experienced a 10 second pause. The patient had intermittent bradycardia over the following days and symptoms resolved only after removal of the intrathecal catheter itself. To our knowledge, this is the first reported case with a complication of recurrent bradycardic and asystolic episodes prior to the administration of intrathecal opioid but shortly after placement of the intrathecal catheter itself.

**Key words:** Intrathecal drug delivery, complications, cancer pain, intrathecal analgesia, bradycardia, opioids

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Management of cancer-related pain with intrathecal drug delivery is an advanced form of therapy that is beneficial for patients who fail to get adequate pain control with medication management despite using increasing doses and switching the class of opioids (1). Intrathecal pumps consist of a small battery-powered programmable pump that is implanted under the subcutaneous tissue of the abdomen. It is connected to a small catheter that delivers small doses of medication directly to the spinal fluid. Intrathecal administration of opioids is beneficial in patients who are unable to tolerate the systemic side effects of these medications (2). Patients who most benefit from this form of treatment are those who have a life expectancy greater than 6 months because it often takes time to optimize the appropriate dose and medication. The only Federal Drug Administration (FDA) approved intrathecal opioid is morphine. However, hydromorphone has been used in place of morphine for many years without any significant difference in side effects or complications (3). The common complications associated with intrathecal pain pumps can be categorized into surgical and mechanical. The most common mechanical complications are associated with the catheter itself and include dislodgement, fracture, or kinking of the catheter.
catheter, intravenous or subarachnoid migration of the catheter, and formation of an intrathecal catheter granuloma. The noteworthy surgical complications include bleeding, neurological injury, infection, and cerebrospinal leaks. Bleeding related to implantable pain pump catheters can be superficial bleeding and deep intraspinal bleeding in the epidural or intrathecal space. Neurologic injury is secondary either to the physical placement of the catheter or from an inflammatory response that occurs at the catheter tip associated with drug delivery. Other noteworthy complications include nausea and vomiting, sedation, respiratory depression, apnea, and pruritus. (2,4). To our knowledge this is the first reported case with a complication of recurrent bradycardic and asystolic episodes prior to the administration of intrathecal opioid but shortly after placement of the intrathecal catheter itself.

**CASE REPORT**

A 38-year-old woman with medical history significant for stage IV breast cancer, L2 metastatic lesion, opioid tolerance, chronic neck pain, and low back pain was admitted to the hospital for intractable pain. She had failed multiple interventional procedures in the past including lumbar medial nerve radiofrequency ablation, epidural steroid injection, and trigger point injections, as well as a kyphoplasty at L2 level. She was having persistent cervical and lumbar spine pain that was radicular in nature. After failing both oral and parenteral opioid treatments, the decision was made to place an intrathecal pump in the patient. We decided to forego a formal intrathecal medication trial, as she was a cancer patient that had intractable pain and had failed all other treatment options.

An intrathecal catheter was inserted at the L4-L5 level and the tip of the catheter was placed at the T11 level with no intraoperative complications. There was free flow of cerebrospinal fluid (CSF) and no difficulty placing the catheter. No bolus of intrathecal medications was given and the intrathecal pump testing was normal. Immediately post-op, the patient became bradycardic with a heart rate in the 20s and experienced a 10 second pause. The patient was immediately admitted to the Intensive Care Unit (ICU) and seen by cardiology. She was given 0.5 mg atropine with a good response with return to normal sinus rhythm. She underwent a bedside echocardiogram, which demonstrated normal ejection fraction with no evidence for structural or valvular heart disease. The patient denied prior occurrence of similar symptoms. Several hours after the procedure, the patient’s heart rate was noted to be persistently bradycardic in the 30s to high 50s although she was asymptomatic. She was also started on isoproterenol overnight.

The following day, after consulting with cardiology, the patient’s implanted intrathecal pump was started to a dose of hydromorphone 3 mg/per day. Overnight the patient was noted to have persistent bradycardia with 6 – 8 second pauses. Consequently, the intrathecal pump was reprogrammed to the lowest possible dose and finally switched off. Despite it being switched off, the patient continued to have bradycardia with pauses. The following day the intrathecal catheter was removed. Overnight the telemetry demonstrated 2 additional asymptomatic shorter pauses from 2 to 4 seconds. Thereafter, the patient’s bradycardia resolved and the patient no longer had any pauses. The pump site eventually became infected and the entire system was removed without complication.

**DISCUSSION**

Intrathecal pain pumps have proven to be effective in the management of pain in patients suffering from metastatic cancer. The complications associated with intrathecal pain pumps have been well documented in the literature as discussed earlier. These complications include infection, bleeding, and neurologic injury, and are viewed as exceedingly rare. This case report demonstrates an unusual complication with the occurrence of recurrent bradycardic and asystolic episodes after placement of an intrathecal pain pump.

The patient had no known history of any cardiac related complications while taking both methadone and hydromorphone for several months prior to placement of the intrathecal pump. A case report from 2011 demonstrated bradycardia with prolonged sinus pauses up to 7.1 seconds in a patient given Patient-controlled analgesia (PCA)hydromorphone. However, our patient was taking oral hydromorphone for several months and had been given Intravenous (IV)hydromorphone in the past with no evidence of any sinus pauses. Additionally, the patient’s symptoms began prior to receiving any dose of hydromorphone intrathecally and continued even after hydromorphone was held. This leads us to believe that the patient’s symptoms cannot be related to the medication itself.

The causes of sinus bradycardia can be separated into intrinsic and extrinsic etiologies. Some of the common intrinsic causes of bradycardia include ischemic
heart disease, cardiomyopathy, and infection. Some of the common extrinsic causes of bradycardia include medication-related bradycardia, autonomically mediated bradycardia, hypothyroidism, hypothermia, hyperkalemia, or hypoxia. The patient had no known history of cardiovascular disease or any of the other intrinsic causes of sinus bradycardia. Additionally, the extrinsic factors were excluded and could not have resulted in sinus bradycardia in our patient.

Considering that the patient’s bradycardia and asystolic episodes resolved after removal of the intrathecal catheter leads us to suspect a mechanical explanation for the symptoms. Two ways this could be accomplished is by suppression of the sympathetic cardiac fibers or stimulation of the parasympathetic cardiac nerves by the catheter tip. The fact that the catheter tip was located at the T11 level and there were no local anesthetics introduced into the intrathecal space makes this difficult to explain. The sympathetic cardiac fibers are at the T1 to T4 level and the parasympathetic nerves involved with the heart branch off in the cervical region which are far enough away from the intrathecal catheter to explain the symptoms. She could have an anatomic anomaly which could explain these findings more clearly.

References
