

Case Report

Intrathecal catheter-associated inflammatory mass in a neurofibromatosis type-1 patient receiving fentanyl and bupivacaine

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Abstract

Background: Catheter-associated inflammatory masses (CIMs) are a rare but serious complication of intrathecal drug delivery devices. CIM formation is influenced by local medication concentration, which is determined in part by flow dynamics at the catheter tip. Underlying spinal pathologies, such as neoplasms, may alter flow at the catheter tip, thereby contributing to CIM formation. Moreover, they may also complicate the clinical and radiologic diagnosis of a CIM.

Case Description: A 36-year-old man with neurofibromatosis type 1 presented to our emergency department with complaints of increased back pain and leg weakness. To treat pain secondary to his multiple spinal masses, he had previously undergone placement of an implantable drug delivery system, which infused a compounded drug of fentanyl and bupivacaine. Imaging studies depicted numerous masses consistent with neurofibromatosis, including a compressive mass located circumferentially at the porous catheter terminus and proximal to the catheter tip. Surgical removal of this mass was performed; pathologic findings were consistent with a catheter tip granuloma.

Conclusions: In the described case, CIM formation likely resulted from a combination of, 1) an unusually high fentanyl concentration, and, 2) altered infusate flow due to spinal neurofibromas. Consideration of underlying spinal pathologies, particularly mass lesions, is critical to the management of intrathecal drug delivery devices.

Key Words: Catheter-associated inflammatory mass, chronic pain, fentanyl pump, granuloma, intraspinal drug therapy, intrathecal catheter

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INTRODUCTION

Catheter-associated inflammatory masses (CIMs), traditionally referred to as “catheter granulomas,” are a rare but potentially serious complication of intrathecal drug delivery devices. These masses, which typically occur near the tip of implanted drug catheters, and comprise a range of pathologically defined abnormalities, including intrathecal and intraparenchymal granulomas, epidural fibrosis, drug precipitates, and infectious collections.^[11,16,18,19] Clinically, CIM formation often manifests as a decrease in the therapeutic effect of the system, whereby the patient requires higher infusion levels to control his or her pain.^[4] In severe cases, CIM formation causes spinal cord or nerve root compression, leading to progressive or sudden neurologic findings such as weakness, spasticity, urinary incontinence, radicular pain,^[3] and, in rare cases, permanent spinal cord injury. Previous case reports have described CIMs mimicking other spinal pathologies, such as neoplasms and hematomas, but there have been no reported cases in which a previously identified neoplasm complicated the management of an intrathecal drug delivery device.^[11,13,19]

Here we describe a neurofibromatosis type-1 patient, who presented with a symptomatic spinal mass in the setting of an intrathecal fentanyl and bupivacaine pump. The mass, initially thought by referring physicians to be a nerve sheath tumor, was resected and found to be a catheter granuloma. In this case, the tip of the catheter was compressed by a neurofibroma, which caused the catheter to take on a concave shape, likely altering the dispersion of the intrathecal infusate. We believe this, along with excessively high medication dosages, resulted in the formation of the CIM. The patient received immediate surgical intervention to prevent permanent spinal cord injury and made good neurologic recovery.

CASE DESCRIPTION

History and presentation

In August of 2015, a 36-year-old man with neurofibromatosis type 1, multiple peripheral nerve sheath tumors and chronic pain presented to our emergency department with complaints of worsening back pain and progressive right leg weakness. In 2010, he had undergone placement of an intrathecal catheter and drug infusion pump at an outside hospital. At the time of presentation, the pump was administering 8.9 mg/day of fentanyl and 22.2 mg/day of bupivacaine (fentanyl concentration, 14 mg/mL; bupivacaine concentration, 35 mg/mL). Ten days prior to presentation, the patient had undergone lumbar epidural steroid injection at an outside hospital for complaints of cramping in his bilateral quadriceps. Five days prior to presentation, he

noted onset of paresthesias in his right foot, then, 3 days prior to presentation, he began to experience progressive right leg weakness resulting in an inability to ambulate. He denied any history of recent trauma.

Examination and initial treatment

Motor examination revealed full strength in the bilateral arms and left leg. The right leg was flaccid, with 2/5 right hip flexor strength, and 1/5 strength in all other muscle groups. Bilateral numbness was noted below the T8 level, and was more pronounced in the left leg. Reflex examination revealed diminished patellar reflexes; myoclonus was absent.

Spinal imaging was performed [Figure 1]. This depicted numerous peripheral nerve sheath tumors throughout the bilateral spine, consistent with the patient’s history of neurofibromatosis. The intrathecal catheter was noted to enter the spinal canal at the L2-L3 level, and terminate in the dorsal intrathecal space at the superior T9 level. At the level of the T9-T10 interspace, magnetic resonance imaging (MRI) demonstrated a strongly enhancing, compressive intrathecal mass, with associated T2 cord hyperintensity spanning from the T4 level to the level of the conus.

Given the patient’s rapid neurologic decline, and radiologic evidence of thoracic spinal cord compression, the patient was admitted for surgical treatment. The intrathecal pump was set to the minimum infusion rate. The patient was given dexamethasone (4 mg every 6 h) for spinal cord inflammation, and he received systemic pain medications, including intravenous fentanyl and ketamine (200 µg/h and 2 µg/kg/min, respectively), transdermal clonidine (200 µg/day), and intravenous methadone (10 mg every 8 h). His outpatient oral



Figure 1: Gadolinium-enhanced T1-weighted sagittal (a) and axial (b) magnetic resonance images depicting the catheter-associated intrathecal granuloma. T2-weighted sagittal image (c) depicts extensive hyperintensity from the T4 level to the conus. T2-weighted axial image (d) depicts spinal cord compression from the dorsal intrathecal granuloma

medications were continued (baclofen 10 mg every 8 h and oxycodone 30–60 mg every 4 h as needed). A fiducial screw was percutaneously placed using computed tomography guidance at the right T9 lamina.

Operation and pathology findings

On the day after admission, the patient was taken to the operating room for thoracic spinal decompression. A T9-T10 laminectomy was performed to expose the thecal sac at the level of the lesion. At the T9-T10 neuroforamen, a 1.1 cm × 0.4 cm × 0.2 cm mass was adhered to the exiting nerve root; this lesion was resected and later identified by pathological examination to be a neurofibroma. The exposed dura was incised, revealing an adherent, 1.2 cm × 0.6 cm × 0.5 cm, soft tissue mass just proximal to the terminus of the intrathecal catheter [Figure 2]. The mass was completely dissected from the dura and the catheter. After resection of the mass, the dorsal spinal cord remained slightly deformed due to prior mass effect. The dural incision was sutured, the overlying paraspinal tissues were reapproximated, and the skin was closed using sutures and staples.

The spinal segment of the catheter was then removed through a small incision over the lumbar region. The implanted drug pump and the abdominal portion of the catheter were left in place for potential future pain management. A needle was used to access the pump reservoir; the fentanyl-bupivacaine admixture was removed, and replaced with sterile saline. The pump was then confirmed to be in minimum rate to avoid damage to the internal pump mechanism and allow for future reactivation.

On histologic examination, the catheter-associated mass was found to contain dense fibrous tissue with necrotic

debris and chronic inflammation, consistent with granuloma [Figure 3].

Postoperative course

Following surgery, the patient's right leg strength began to improve, and his lower body sensation returned. Five days after surgery, at the time of discharge, he exhibited full strength throughout his left lower extremity, and 4/5 strength throughout his right lower extremity. The patient did not experience withdrawals from cessation of intrathecal therapy; his pain was managed with fentanyl infusion, methadone, transdermal clonidine, and a low-dose ketamine infusion. Sensation was intact in his left leg, and it had improved in his right leg. The patient was able to ambulate with a walker, and reported pain equal to his baseline, presurgical level.

The patient's discharge pain medication regimen consisted of transdermal fentanyl (200 µg/h), transdermal clonidine (200 µg/day), oral methadone (10 mg every 8 h), oral baclofen (10 mg every 8 h), and oral oxycodone (30–60 mg every 4 h, as needed).

DISCUSSION

The patient described here presented with complaints typical of CIM, namely, increasing medication infusion requirements and a severe, new neurological deficit. However, this case is unique in that: 1) Preoperative identification of the CIM was complicated by his spinal neurofibromatosis, 2) The catheter tip abutted a spinal tumor, caused a deflection in the catheter which likely impaired the flow of cerebrospinal fluid and intrathecal medication, and 3) The patient received a compound formulation of fentanyl and bupivacaine that contained a rather high concentration of fentanyl (14 mg/mL).

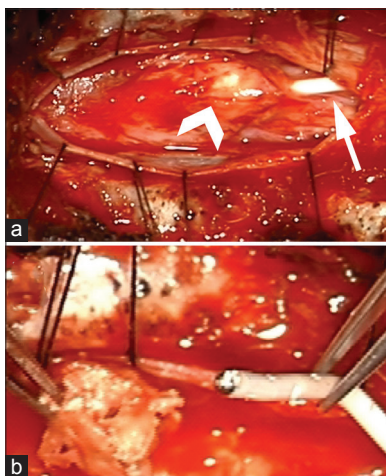


Figure 2: Microscope images obtained during resection of the intrathecal catheter-associated granuloma. (a) Prior to resection, the granuloma (chevron) surrounded the distal end catheter (arrowhead). (b) The granuloma (at left) was separated from the distal end of the catheter (right) and spinal cord. Image orientation, cephalad at left

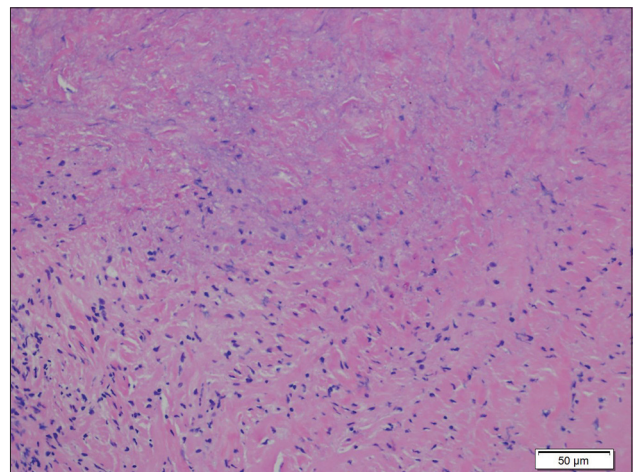


Figure 3: Histologic examination of the catheter mass demonstrated dense fibrous tissue with necrotic debris and chronic inflammation composed of histiocytes and small mature lymphocytes, consistent with granuloma (hematoxylin and eosin preparation; ×20 magnification)

The formation of an intrathecal CIM typically manifests as a slow reduction in pain control, which may then be followed by new, progressive neurologic deficit.^[10] Similarly, in this case, the patient required dose escalation of his intrathecal infusion leading up to surgery. Three days prior to presentation, he experienced severe right leg weakness. This patient's constellation of findings likely reflected a progressive process that ultimately led to spinal cord compression. Given his history of spinal tumors, these findings could have been attributable to a neoplasm. However, his surgical history of intrathecal catheter placement, as well as his increasing medication infusion requirements, suggested formation of CIM. Prompt radiographic evaluation was undertaken to discern between these processes.

Other case reports have described catheter tip masses that mimicked other pathologic entities, such as epidural hematoma or spinal cord neoplasm.^[11,13,19] In this case of a patient with neurofibromatosis, there was potential for the CIM to be confused for a neoplasm. Radiologically, CIMs are best visualized on gadolinium-enhanced, T1-weighted MRI sequences, through which they appear as distinct, spherical lesions.^[10] These radiologic features are somewhat similar to those of spinal schwannomas, which also appear as distinct, globular, and contrast-enhancing masses on MRI.^[17] This patient exhibited multiple spinal schwannomas on radiologic examination, and thus, the mass near the catheter tip could have been mistaken preoperatively for a spinal schwannoma. However, its close apposition near the tip of the intrathecal catheter was suggestive of other pathology, namely, CIM. Regardless of the preoperative diagnosis (i.e., schwannoma or CIM), the presence of spinal cord compression, combined with a rapid neurologic deficit necessitated urgent laminectomy and mass resection.^[6] In cases of less severe compression and mild resultant neurologic findings, laminectomy and duraplasty, repositioning of the catheter tip, and cessation of the infusion may be an appropriate treatment strategy.^[6]

CIM formation has been described in cases involving opioids such as morphine, hydromorphone, diamorphine, sufentanil, and tramadol, as well as non-opioids such as baclofen.^[2,8,9,14,15] Altogether, the majority of CIM cases appear to involve morphine.^[7] It must be noted; however, that patients typically receive multiple medications through intrathecal delivery systems, making it difficult to attribute CIM formation to a specific medication.^[3,20] In this case, the patient was receiving intrathecal fentanyl and bupivacaine at the time of presentation. Other case reports have described CIMs in the setting of multiagent infusions that included bupivacaine, and it is thus possible that this was the responsible agent.

To our knowledge, this is only the second description of a CIM in a patient receiving intrathecal fentanyl.^[2,11,12,21]

Animal studies have suggested that fentanyl-associated CIMs are likely to be rare; in a canine model, CIM formation occurred after infusion of numerous single opioids, such as morphine, dilaudid, and methadone, but not fentanyl.^[1] This case; however, suggests CIM formation can occur with infusion of bupivacaine and high-dose fentanyl (14 mg/mL). Notably, the recent Polyanalgesic Consensus Conference guidelines suggest that no granulomas have been reported in patients receiving IT admixtures with fentanyl as the IT opioid.^[5] The current case; however, may suggest caution for the use of compound admixtures containing fentanyl and bupivacaine, particularly when fentanyl is used at a very high concentration.

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Conflicts of interest

There are no conflicts of interest.

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