Granulomatous Conduit for Intrathecal Infusion of Morphine and Bupivacaine

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Objective: Intrathecal drug delivery systems (IT-DDSs) have gained more widespread use in patients with non–cancer-related pain, notably failed back surgery syndrome and spinal arachnoiditis. Secondary to the longer life spans of these patients, more complications have been discovered with IT-DDSs. With an estimated incidence of 1% to 3%, an uncommon but serious complication is that of granuloma formation.

Case Report: We describe a case of a 38-year-old woman with a malfunctioning IT-DDS containing morphine and bupivacaine. The device had stopped providing relief for several months because of presumed leakage from the connection site between the pump and the proximal catheter. The IT-DDS spontaneously resumed functioning. The IT-DDS was explanted for low battery life, upon which we discovered that the leakage site had been encapsulated by drug concretion and granuloma formation, thus providing a sealed conduit that reestablished drug flow between the pump and the catheter.

Conclusions: This case report reinforces the view that the infusate is the causal agent of this lesion.

CASE REPORT

Intrathecal drug delivery systems (IT-DDSs) have gained more widespread use in patients with non–cancer-related pain, notably failed back surgery syndrome and spinal arachnoiditis. Secondary to the longer life spans of patients using IT-DDSs, more device-related complications are now being discovered. With an estimated incidence of 1% to 3%, an uncommon but serious complication is granuloma formation.1–3 Of the reported cases, all typically occurred in the subarachnoid space at the catheter tip and were associated with either loss of therapeutic effect or compression of nerve roots and/or spinal cord. Several etiologies, including infection, reaction to catheter material, implantation trauma, or the infusate itself, have been suggested.4–7 Morphine has been well documented as a possible causal agent in granuloma formation. For example, the regression of a granuloma with discontinuation of morphine has been reported.8 There have also been rare reports of fentanyl or baclofen pumps causing granulomatous formation.9 Furthermore, strong associations of the dose-dependent effects of morphine on granuloma formation are well known; the majority of these intrathecal granulomas are near or surrounding the catheter tip, thus suggesting that the accumulation of high, local infusate concentrations in this region can promote the formation of a granuloma.10 We present a case report of a granuloma formation at the leakage site between a morphine pump and its proximal catheter in the abdominal pocket, reinforcing the view that the infusate may be the causal agent of this lesion. In our case, the granuloma encapsulation appeared to have provided a sealed conduit for resumption of drug flow in an IT-DDS.

CASE REPORT

History

A 38-year-old woman on chronic intrathecally administered morphine and bupivacaine therapy for chronic gastrointestinal pain related to Crohn disease and diabetic gastroparesis presented to our clinic requesting replacement of her IT-DDS because of low battery life. Initially, the patient had maintained infusion of 10.5 mg/d of morphine sulfate and 5.3 mg/d of bupivacaine. With the loss of drug effect, the infusion was increased to a final maximum of 15.0 mg/d of morphine sulfate and 9.0 mg/d of bupivacaine.

The patient reported that after her IT-DDS had provided adequate analgesia for 4 years, she experienced a rapid decline in drug benefit approximately 1 year before her presentation to our center. The patient did not have any reported systemic withdrawal symptoms but stated she began to have a recurrence of previously suppressed symptoms, and her pain rapidly increased to its prepump baseline. An evaluation of the system with x-ray revealed evidence of a hub fracture. The patient was managed with oral medication, although she had only minimal benefit. Months later, the patient experienced a rapid return of pain relief to the level experienced when her IT-DDS was functioning well in the absence of any adjustments to her oral drug regimen. She was able to wean from and discontinue her oral drug. At that time, the patient declined any further management of the hub fracture until months later when the low-battery alarm sounded. The patient approved reporting of this case.

Surgery

Upon opening the abdominal pocket for the IT-DDS, a granulomatous structure was noted surrounding the region of the pump nozzle and the hub connector in situ (Fig. 1). With manipulation of the soft tissues to better expose the region, this conduit broke into several pieces because of its adherence to the surrounding soft tissue. After explantation of the pump, it was clear that this material had sealed the region of the fracture (Fig. 2). With removal of the material from the pump, the hub fracture was confirmed. A new hub connector was attached to the free end of the spinal catheter and then connected to the...
nozzle of a new pump. The new IT-DDS was programmed to deliver 90% of the original dose.

Postoperative Course
The patient described ongoing benefit identical to her response before surgery. She continues to have good relief of pain more than 1 year after surgery. No new symptoms were reported, and no further therapy was recommended.

DISCUSSION
Although intrathecal morphine catheter-associated granulomas were first described in the early 1990s, the incidence of the problem initially was not widely known. It is now recognized that distal catheter tip lesions may occur in up to 3% of cases, with the majority remaining asymptomatic. Similar device-related lesions outside the spinal canal have been cited, but their incidence is unknown, having been excluded from previous reports.

These lesions typically arise from the distal tip, consistent with the argument that granuloma formation is a result of a concentration-dependent inflammatory reaction to the medication itself, rather than subclinical trauma, chronic infection, or silicone hypersensitivity. Some authors have invoked an immunologic mechanism mediated by lymphocyte μ-opioid receptors to promote increased lymphocyte activity and changes in mast cell activity, although there are significant gaps in the understanding of this process.

Although there are no identifiable risk factors for the formation of granulomas in conjunction with morphine IT-DDSs, some authors have suggested that granulomas may be associated with morphine doses greater than 10 mg/d. Indeed, interrogation of the pump at first presentation to our clinic revealed a dose of approximately 15 mg/d. Furthermore, the infusate in our patient was a combination of morphine and bupivacaine. Interestingly, there have been reports of granuloma formation at lower morphine doses when used in combination with bupivacaine.

Although the mechanism to granuloma formation remains unknown, this case report would further suggest an association with the infusate, rather than trauma, infection, or reaction to the catheter material.

CONCLUSIONS
Our finding of granuloma formation at the leakage site between a pump and its proximal catheter is consistent with the view that the infusate, in this case morphine and bupivacaine, is the causal agent of this lesion. To our knowledge, this is the first report of a granuloma encapsulation providing a sealed conduit for drug flow in an IT-DDS.

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