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Case Report

Intrathecal pump catheter-tip granuloma recurrence with associated myelomalacia – How safe is intrathecal analgesic infusion therapy? A case report

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ABSTRACT

Background: A serious complication of intrathecal (IT) infusion therapy for pain management is catheter-tip-associated granuloma. Catheter-tip granulomas can lead to permanent severe neurological sequelae if not promptly detected.

Case Description: We report a patient with a recurrence of a catheter-tip granuloma causing a high-grade paresis of the lower extremities and we review briefly the literature.

Conclusion: Patients with IT pump therapy presenting new neurological findings need prompt imaging of the spinal axis to rule out a catheter-tip granuloma. In case of catheter-tip granuloma, early surgical decompression is important.

Keywords: Catheter-tip granuloma, Complications, Intrathecal pump therapy

INTRODUCTION

Invasive nonmalignant pain management with intrathecal (IT) analgesic infusion therapy is a common strategy for the treatment of "failed back surgery syndrome" (FBSS). Catheter-tip-associated granulomas are a known but rare complication of IT analgesic infusion therapy with potentially severe neurological consequences occurring in <3% of morphine pump patients.[2] Due to the increasing frequency of IT morphine pump implantation as a management strategy for chronic pain due to FBSS, the fast radiological detection and surgical decompression of such lesions are paramount to neurological preservation.

IT drug therapy is known to be an effective treatment method for patients with FBSS.[2,6,9,12] As the drug is being delivered directly into the central nervous system, it reduces adverse effects such as sedation, nausea, and vegetative and cognitive symptoms seen with drugs delivered peripherally.[9]

An utmost serious and underestimated adverse effect of the central route is the formation of a catheter-tip-associated granuloma.[7,12,13] The lesion can block the catheter-tip hinder drug delivery causing ineffective pain management. More seriously, the lesion can lead to compression of the spinal cord causing permanent neurological deficit. As many cases of catheter-tip-associated granuloma likely remain unreported, the exact prevalence cannot be determined.[6,7] It is of paramount importance that each case of catheter-tip-associated granuloma is reported to accurately balance the benefits and risks of IT therapy in pain

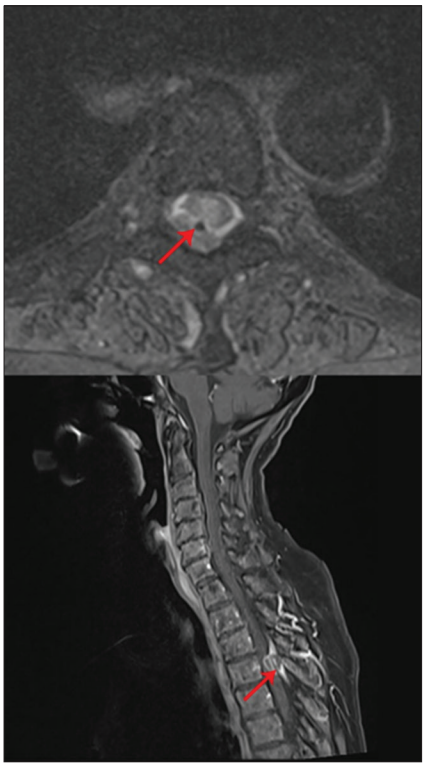

Figure 1: Upper image: T2 axial image of the lesion surrounding the catheter (red arrow). The granuloma appears as an extra-axial lesion isodense to the myelon. Lower image: T1 contrast sagittal image showing a space-occupying, ring-enhancing, inhomogeneous, extra-axial mass (red arrow) in the spinal canal at the level of T4.

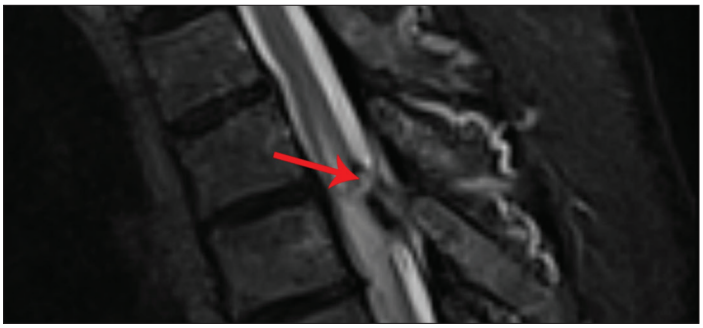

Figure 2: T2 sagittal image of the same lesion with clearly visible extensive T2 signal changes in the spinal cord. The tip of the catheter is seen encased in the granuloma substance (red arrow).

management. We report a patient who suffered a recurrence of a catheter-tip granuloma leading to a high-grade paresis of the lower extremities.

CASE PRESENTATION

A 75-year-old female patient with a history of multiple spine surgeries, chronic pain syndrome (cervicalgia and lumbalgia), and a slightly ataxic gait was treated with IT morphine and clonidine infusion (SynchroMed II Pump Medtronic) since 2012.

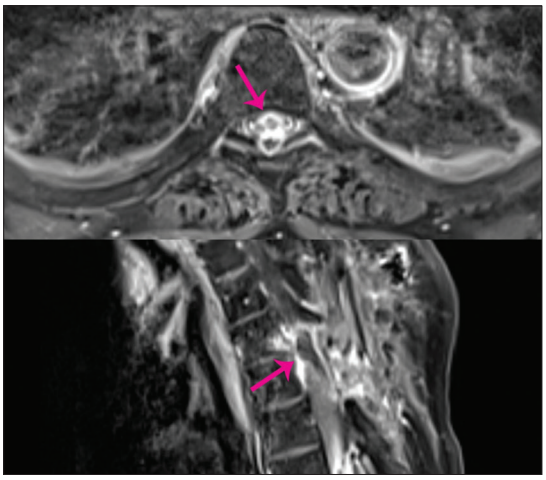

Figure 3: T1 contrast imaging. Upper image: Axial image showing a large recurrence overshadowing and compressing the spinal cord (pink arrow). Lower image: The recurrent granuloma is seen here as a large, ring-enhancing, inhomogeneous, mass-causing high-grade compression of the spinal cord (pink arrow).

In April 2018, she presented with new-onset paresthesia sub-T5. A magnetic resonance imaging (MRI) of the spine showed high-grade compression of the spinal cord (with compression-induced myelomalacia) at T3–T5 corresponding to the location of the catheter tip with suspicion of a catheter-tip-associated granuloma [Figures 1 and 2].

A right-sided hemilaminectomy of T4 as well as a partial hemilaminectomy of T3 and T5 was performed. The exposed dura was thickened and adherent to the surrounding structures. After removal of the adhesions and preparation of the dura, a necrotic-seeming central thickening, continuous with the surrounding normal dura, was identified as the granulomatous mass. This highly adherent mass was carefully resected along a clearly defined plane between the granuloma and the normal dura. A partial resection of the healthy dura surrounding the right T4 nerve root was required. The catheter was then identified inside the spinal canal and removed. Due to adherence to the T4 nerve root, the decision was made to sacrifice the T4 nerve. The granuloma was then carefully resected along with the divided nerve. The underlying spinal cord had signs of metal deposits from the catheter as well as signs of myelomalacia. The spinal cord was completely decompressed, and the primary closure of the dura was possible.

Postsurgery, the patient showed a moderate- to high-grade proximally pronounced paresis of the right lower extremity, which slightly improved in the days following surgery. MRI revealed a satisfactory decompression of the spinal cord and removal of the granuloma. However, the MRI showed a more marked (preexisting) myelomalacia extending now from T2 to T7. Additional oral analgesia oxycodone 5 mg twice daily and trimipramine 100 mg once daily had to be continued unchanged, for the persistence of foremost lumbar pain. After an initial stable clinical course, she

complained of increasing neuropathic pain initially located mostly in the T9–T12 area and subsequently ascending into the thorax approximately 2 months after admission. Pain medication had to be increased by adding pregabalin and cannabis oil (drops) and increasing the morphine and clonidine pump dosage yet without clinical benefit. Clinically, the patient complained of instability and sensory loss in the left leg. A lumbar MRI was performed, which did not explain the new findings. Within 1 week, the patient deteriorated dramatically loosing almost all motor strength in the lower extremities. A cervical and thoracic MRI [Figure 3] showed a mass suspicious for a catheter-tip granuloma causing a compression of the thoracic spine at T7–T11 associated with a secondary myelomalacia now extending proximally to the conus medullaris.

A laminectomy of T6 was performed. The underlying tissue was granulomatous, and the catheter was identified within the granulomatous mass. The lesion was excised leaving a dural defect that could not be repaired with primary closure. Watertight closure with a Gore-Tex patch was achieved. The remaining catheter was removed through a separate incision, and a new catheter was not placed.

The histopathological finding showed typical granuloma tissue formed by histiocytes, granulocytes, necrotic areas, and abundant hemorrhagic residues. The neurological state of the patient improved mildly after device removal, granuloma excision, and intense rehabilitation foremost gaining slight-to-moderate motor strength in the left leg.

DISCUSSION

The literature describes several cases of IT pump catheter-tip-associated granuloma (CG), a phenomenon possibly due to an inflammatory response to the infused drug or a foreign-body reaction to biomaterials.[1,3,13] The first case was described in 1991 by North *et al*.[13] The incidence rate of symptomatic granulomas is approximately 0.4%.[2] Given the slow and silent growth of granulomas, the approximate time period of granuloma formation cannot be established as most become detected only once symptomatic. CG was reported primarily with analgesics, foremost with morphine, but also with ziconotide, hydromorphone, fentanyl, bupivacaine, clonidine, and sufentanil.[4,6,9] Very few cases of CG were reported with baclofen.[8] Contrary to primary granuloma formation, granuloma recurrence is rarely described. The review of Deer *et al*.[6] individuated only two granuloma recurrences.[4,10] In our patient, the recurrence occurred only 5 months after the initial granuloma removal and catheter repositioning and was associated with a marked myelomalacia, possibly consequence of myelocompression and toxic drug-induced tissue alterations.

Granuloma recurrence

Granuloma recurrence is rarely described in the literature. The first report on granuloma recurrence was reported by Hoederath *et al*.[10] in a patient who developed a catheter-tip granuloma at T8–T9 level 20 months after IT morphine treatment. After surgical removal and a new catheter implantation, IT ziconotide was administered for 6 months and replaced subsequently with hydromorphone. Only 1 month later, a second catheter-tip granuloma had formed at T10–T11 level, which was only 9 months after the first catheter-tip granuloma. De Andrès *et al*.[4] reported a 60-year-old patient who complained of progressive motor and sensory deficits after two granuloma recurrences: one that occurred after 5 months and a second recurrence 3 years after the first surgical granuloma removal.

Granuloma formation with analgesics

Deer *et al*.[6] reported that in 6 of 208 patients (3%) with IT pump therapy and CGs, the average time of drug infusion in the patients developing CGs was 27 months. Drugs used were morphine, hydromorphone, fentanyl, bupivacaine, and clonidine. A two-center retrospective study by Kratzsch *et al*.[11] identified CG in 13 out of 159 patients after a mean of 6.9 years of follow-up. The authors found in their study a CG prevalence of 8.2%. The authors noted that CGs were more frequent when the catheter tip was placed in the middle thoracic spine (T5–8). Other risk factors in developing CG were previous spinal surgery, invasive catheter testing by injecting contrast agent, and the use of morphine, especially in higher drug concentrations. The length of IT therapy appeared not to be associated with increased risk. The authors assumed that clinical symptoms of CG are secondary to catheter lumen obstruction causing signs of pump malfunction presenting in the form of pain unresponsive to increasing drug dosage. Phillips *et al*.[14] described in more detail the imaging appearance of IT catheter-tip granulomas in three patients. One patient with chronic lower back pain became unresponsive to increasing doses of morphine, with progressive lower extremity weakness and 2 days of urinary retention. MRI imaging showed a mass at T12–L1 at the level of the tip of the IT catheter causing compression and displacement of the conus medullaris. Surgery relieved the back pain; however, the lower extremity weakness progressed to a severe paraparesis despite rehabilitation. In a second patient with acute onset of paraplegia, decreased rectal tone, and bladder dysfunction, imaging showed a lesion ventral to the spinal cord at T10 level. Despite surgery and rehabilitation, the patient remained paraplegic with neurogenic bladder and bowel dysfunction. A third patient treated with IT hydromorphone presented with bladder and bowel dysfunction. MRI imaging revealed a mass at T12 located approximately 1.5 cm proximal to the catheter tip. Postsurgical course was complicated by pseudomeningocele formation requiring a second surgical intervention. Arnold *et al*.[2] who described four patients with CG hypothesized that several mechanisms might be responsible for the granuloma formation, such as morphine-induced cytokine formation leading to an inflammatory response. Decramer *et al*.[5] who reported a catheter-tip-associated granuloma in a 53-year-old female

patient treated for 18 years with IT infusion therapy (morphine and clonidine) for phantom and stump pain concluded that in patients with suspected granuloma, close clinical and imaging monitoring (MRI) is needed.

CONCLUSION

CGs are rare but serious complications of IT infusion treatment as they can lead to permanent neurological sequelae. As our case demonstrates, diagnosis of granuloma occurrence in this pool of patients risks to be delayed considering the multimorbidity of these patients. New or worsening symptoms might be attributed initially to other conditions. Therefore, patients with IT showing neurologic symptoms should obtain prompt spine imaging to rule out a spinal cord-compressing granuloma. Asymptomatic patients with a history of granuloma should obtain regular spine MRI to rule out a recurrence. From the few reports and from our case, it appears that recurrence occurs within a brief time period of approximately 6 months. CG cases need rigorous reporting to be able to estimate accurately the benefit–risk ratio of IT therapy in pain management.

Take-home points

1. IT pump dysfunction should always be suspected if the patient is unresponsive to increasing drug dosages.
2. Morphine seems to be associated with the highest risk of granuloma formation.
3. All patients with IT pump therapy showing new neurological findings need prompt imaging of the whole spinal axis to rule out a catheter-tip granuloma.
4. Asymptomatic patients with a history of catheter-tip granuloma need regular spine MRI as granuloma recurrences appear to occur within months of the preceding granuloma.
5. Catheter-tip granuloma diagnosis must be followed by prompt surgical decompression.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient has given her consent for her images and other clinical information to be reported in the journal. The patient understands that her name and initials will not be published and due efforts will be made to conceal her identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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