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Does a Narrow Spinal Canal Facilitate Intrathecal Granuloma Formation? A Case Report

Může souviset úzký páteřní kanál s tvorbou granulomu na konci katétru uloženém v intratékálním prostoru? Kazuistika

Abstract

Background/Objective: We report a case of early formation of a catheter tip granuloma in a patient with multilevel degenerative spinal stenosis who developed a granuloma in spite of the fact that morphine dosage was at lower rate and administered for a short period of time only. *Methods:* A 58-year-old woman with a history of chronic low back pain due to the failed back surgery syndrome was treated effectively with 5mg/day morphine via an intrathecal drug delivery system (IDDS). Eight months after IDDS replacement due to end-of--battery-life, the patient experienced new severe pain radiating diffusely to the left leg and accompanied by slight weakness. *Results:* MRI disclosed multilevel degenerative spondylogenic stenosis and an intradural extramedullar mass at the T11 level with spinal cord compression. The patient underwent decompressive hemilaminectomy and removal of adherent fibrotic tissue attached to the spinal cord and to the tip of the intrathecal catheter. *Conclusions:* In this patient, a narrow spinal canal, which may have created unfavorable conditions for proper CSF circulation, may have facilitated morphine-associated granuloma formation despite a short-term low dose treatment.

Souhrn

Cíl: V práci uvádíme pacientku s multietážovou degenerativní stenózou páteře, u které došlo k časnému vytvoření granulomu na konci katétru i přes to, že byla léčena krátkou dobu a byla jí podána nízká dávka intratékálního morfinu. *Materiál a metodika:* Osmapadesátiletá pacientka s diagnózou chronických bolestí zad v rámci FBSS (Failed Back Surgery Syndrome) byla úspěšně léčena morfinovou pumpou na nízké dávce morfinu 5 mg/den. Osm měsíců po běžné výměně pumpového systému pro jeho končící životnost se u pacientky objevila slabost levé dolní končetiny spojená s krutou vystřelující bolestí do končetiny. *Výsledky:* Na magnetické rezonanci se prokázala multietážová degenerativní stenóza a intradurálně extramedulárně uložená hmota, která způsobovala kompresi míchy ve výši obratle Th11. Pacientka podstoupila neurochirurgickou dekompresi s hemilaminektomií a s odstraněním adherující fibrotické tkáně, která vycházela z konce intratékálně uloženého katétru. *Závěr:* Domníváme se, že úzký páteřní kanál přispěl u naší nemocné ke zhoršení cirkulace mozkomíšního moku v této oblasti, což umožnilo časnou tvorbu granulomu navzdory podávané nízké dávce morfinu.

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Introduction

Intrathecal opioids have been used for management of chronic pain for more than 20 years. Despite generally favorable outcomes, complications associated with intrathecal administration are common [1]. Formation of granuloma at the tip of intraspinal catheters is one of the severe complications of intrathecal drug delivery systems (IDDS) [2–4]. An increasing number of reported cases suggest that this problem requires more attention by physicians than previously thought and concluded by an expert panel of physicians in their recommendations for the rational use of intrathecal analgesics [5]. Morphine is the most common intrathecal drug associated with granuloma development [3–5]. There has been an ongoing and controversial discussion about baclofen triggering granuloma formation, but this has not been confirmed to date [6].

Here we report granuloma formation in a patient who received low dose morphine for a short period of time and in whom degenerative spinal stenosis may have facilitated granuloma formation by creating unfavorable conditions for proper circulation of the cerebrospinal fluid (CSF).

Case Report

We present a 58-year-old woman with a history of chronic low back pain and chronic radiculopathy L5 on the left side due to failed back surgery syndrome in 1996. Previous neurosurgical treatment included lumbar hemilaminectomy L4/5, decompression and removal of herniated disc L4/5, repeated epidural steroid injections, high dose of oral opioids and intensive physiotherapy with insufficient effect. She approved of us reporting her case.

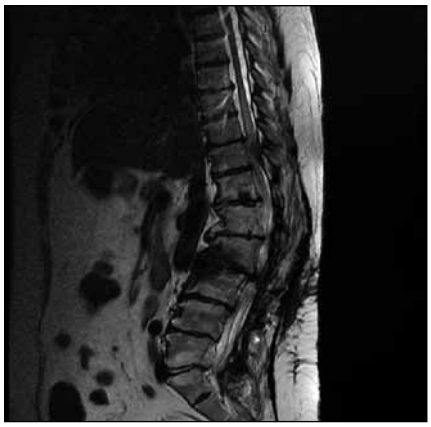


Fig. 1. MRI disclosed an intradural--extramedullar lesion at the level of Th11/12 with compression of spinal cord that confirmed myelopathy, accompanied by multilevel degenerative spondylogenic stenosis and hypertrophy of intervertebral joints and ligaments, with maximum at L1/2 and L2/3 vertebral levels. Sagittal T2 weighted MRI scan.

An IDDS (Synchromed EL, Medtronic, Inc., Minneapolis, USA) was then implanted with the tip of the catheter located at the level of L2/3. Pain was adequately controlled with pharmacy-compounded morphine hydrochloride at a flow rate of 0.25 ml/day for 7 years. Due to end of battery life, the IDDS was replaced (Synchromed II, Medtronic, Inc., Minneapolis, USA) together with the spinal catheter. Before pump replacement, the patient underwent magnetic resonance imaging (MRI) that showed mild degenerative spondylotic changes and multilevel spinal stenosis with a maximum at L1/2 and L2/3 vertebral levels. After pump replacement, the patient did well with the previously effective dose of morphine, 5 mg/day, without any fluctuations. Eight months after IDDS replacement, the patient experienced re-emerging severe pain radiating diffusely to her left leg and rated by the patient 9 on a numeric pain rating scale (0–10). She later noticed slight weakness of her left leg. Clinical examination revealed decreased range of motion of the low back, intensive pain in the thoracolumbar spine with exacerbation during inclination to the left, left patellar hyperreflexia, and dysesthesias with mild hypesthesia in the left lower extremity distal to the inguinal ligament. Achilles tendon reflexes were weak bilaterally. C-reactive protein, blood count, antibodies against borrelia and other routine biochemical serum studies were within normal range. The tip of the catheter was located at the T11 level by plain radiographs. Conventional motor nerve conduction studies were normal in peroneal and tibial nerves including normal F waves. Sural nerve conduction velocity was normal. There was no spontaneous activity in left quadriceps, tibialis anterior, soleus, and T11/12 paraspinal muscles on concentric needle EMG. Discrete chronic neurogenic changes (increased polyphasicity and high amplitude motor unit potentials) in left tibial anterior muscle concurred with chronic L5 radiculopathy. Tibial nerve stimulation elicited cortical SEPs of abnormal latency and amplitude bilaterally (right side stimulation: P37 latency, 46.0 ms; P37–N45 amplitude, 1.1 μV; left side stimulation: P37 latency, 50.8 ms; P37–N45 amplitude, 0.9 μV) consistent with dorsal column dysfunction.

Repeat MRI on a 1.5 Tesla scanner (Symphony, Siemens, Germany) using a special surface coil disclosed an intradural extramedullar lesion at the Th11/12 level with spinal cord compression and T2 signal hyperintensity that confirmed myelopathy (Fig. 1). Modest degenerative spondylogenic stenosis, hypertrophy of intervertebral joints and ligaments were present at the thoracolumbar region, with maximum at the L2/3 level. The patient underwent decompressive hemilaminectomy and resection of an adherent fibrotic mass attached to the spinal cord and to the tip of the intrathecal catheter (Fig. 2). Histological investigation of the removed specimen revealed an inflammatory mass with lymphoplasmocytic infiltration without neutrophilic granulocytes in fibrous tissue with fibrin--rich background. There was no evidence of malignancy, and no pathogenic micro--organisms could be identified. The spinal catheter was shortened so as to end 2 cm below the level of compression. The patient recovered well after surgery, pain subsided promptly, while the mild weakness in her left lower limb have improved only slowly over time.

Postoperative MRI at 3 and 6 months showed no residual fibrotic mass but the in-

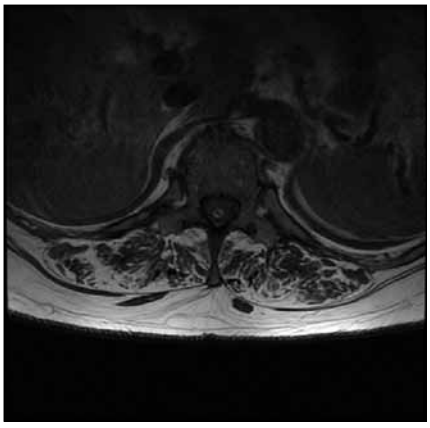


Fig. 2. Axial T1 weighted MRI scan shows granuloma formation at the tip of intrathecal catheter.

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traspinal T2 signal hyperintensity at the level of spinal cord compression was still present. The patient was successfully continued on morphine, flow rate of 0.25 ml/day.

Discussion

The present case report illustrates an inflammatory mass formation at the tip of an intrathecal catheter in a patient treated with a lower dose of morphine for a short period of time. Modest localized degenerative spinal stenosis could be an additional unfavorable factor precipitating granuloma growth by restricted CSF circulation that may have led to increased local morphine concentration.

Intrathecal morphine has been reported to be an efficient treatment modality of chronic non-malignant pain. The number of successfully treated patients will certainly increase in the future [1]. IDDS complications may occur frequently and throughout the life span of the system, usually involving the catheter [5,7]. Granuloma formation at the tip of a spinal catheter has been a rare complication [3]. The reported incidence is 0.04% during the first year of treatment, and 1.15% after 6 years [8]. True incidence and prevalence are likely to be higher due to undiagnosed and asymptomatic cases. This observation has recently been supported by Deer [4] who reported granuloma formation in 6 of 208 subjects (3%) treated with intrathecal morphine in whom the presence of asymptomatic spinal granulomas was sought by MRI or CT. Only one patient was symptomatic and complained of radicular pain at the catheter tip level.

An intrathecal granuloma is supposed to be an inflammatory reaction to opioids [2,8]. Antispastic drugs, such as baclofen, have been accused of precipitating granulomas [6] but others opposed this opinion. Different theories have been proposed: allergic reaction to a silicone catheter, infectious agents, reaction to impurities of a compounded drug but all these etiologies have been excluded [4,5]. High concentrations of opioids and their long-term administration over more than 2 years are the two main factors now considered to be responsible for inflammatory reactions [3]. Allen et al [4] found that, in dogs, an infusion of morphine at different concentrations and a fixed rate resulted in a dose-dependent increase in concentration, with granuloma-producing, dose-yielding lumbar cerebrospinal fluid morphine concentrations around 40 µg/ml. Dogs receiving morphine at a dose of 12.5 mg/ml at 40 µl/h were found to have pericatheter-enhancing tissues as early as at 3 days, whereas removal of morphine reduced the mass volume within 7 days. Yaksh et al [9] reported granuloma formation in one dog at a dosage of 1.5 mg per day. However, beagles are prone to spinal canal stenosis that may have facilitated granuloma formation even in this experimental animal model.

Coffey and Burchiel [2] recommended a morphine dose of 4 to 10 mg/day, and suggested to limit the maximum dose to 20 mg/day in order to avoid granuloma formation. In the present case, the patient was satisfied with a low dose of morphine of 5 mg/day, yet the granuloma developed within eight months of intrathecal morphine delivery only. Although we do not have a proof, one possible explanation could be spinal canal narrowing that may have caused restricted CSF circulation and thus high local morphine concentration around the catheter tip. In fact, retracting the catheter by only 2 cm, so that the catheter tip was localized at a level with a wider diameter of the spinal canal, may have allowed for more drug diffusion and hence less morphine concentration around the catheter tip. Although this was the only change we are aware of, it seems to have been sufficient for prevention of repeated granuloma formation over more than a year now.

Intrathecal granulomas may be asymptomatic or may cause significant neurological deficit due to spinal cord compression. Prompt verification of the problem based on clinical signs and symptoms and localization of the intrathecal catheter tip is crucial. An inflammatory mass of the catheter tip can be documented by imaging techniques and is typically visible on MRI or CT scan. Surgical decompression with inflammatory mass resection is strictly recommended together with catheter removal or replacement [10]. As detailed above, we adhered to these recommendations: MRI disclosed an intradural extramedullar mass with spinal cord compression; surgery revealed a catheter tip granuloma without evidence of pathogenic micro-organisms; the spinal catheter was shortened and placed below the level of compression.

Catheter malfunctions are the most frequent complication associated with IDDS [7]. Fortunately; inflammatory granulomas at the spinal catheter tip are still rare. However, the frequency of this complication will likely increase with increasing numbers of implants and longer duration of intrathecal drug administration. We emphasize early recognition of such a devastating complication with good clinical, diagnostic and surgical management coordinated by a dedicated and experienced professional team. The present case report does not prove but strongly suggests that spinal canal narrowing may contribute to granuloma formation in patients receiving intrathecal morphine. Therefore, we recommend appropriate imaging studies before and after IDDS implantation in order to avoid intrathecal catheter tip placement at the level of a particularly narrow spinal canal segment.

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