



CASE REPORT

Is regression of catheter-related epidural granuloma possible? A case report

*Epidural port kateter sonrası gelişen epidural granülomun iyileşmesi mümkün mü?
Olgu sunumu*

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Summary

Epidural granuloma may develop as a complication during long-term use of intrathecal analgesics. To the best of our knowledge, it is not mentioned in the current literature that discontinuation of therapy may cause a regression of epidural granulation and clinical symptoms. In this case, we aimed to present spontaneous regression of epidural granuloma within 2 months after removal of epidural port.

Keywords: Epidural granuloma; epidural port catheter; magnetic resonance imaging; spinal opioid therapy.

Özet

Analjeziklerin uzun süreli intratekal uygulamalarında bir komplikasyon olarak epidural granülom gelişebilmektedir. Literatürde tedavinin ara verilmesi ile semptomların gerilediği ve gelişen granülasyon dokusunun iyileşebileceğine dair bir bilgiye rastlanmamıştır. Bu yazı ile epidural portu çekildikten iki ay sonra semptomları gerileyen ve epidural granülomun kendiliğinden iyileşme gösterdiği saptanan olgunun sunulması amaçlanmıştır.

Anahtar sözcükler: Epidural granülom; epidural port-kateter; manyatik rezonans görüntüleme; spinal opioid tedavisi.

Introduction

Spinal drug administration is effective in providing effective analgesia, especially in cancer patients, but it can cause serious complications.^[1,2] One of these complications requiring close follow-up is epidural granulation.^[2,3] Epidural granulation can cause retrograde dissection along the catheter, leakage from the port, and neurological deficits.^[3–6]

Significant findings suggesting that the patient develops epidural granulation are decreased treatment efficacy and pain during injection.^[3] The most important method to show the granuloma appears to be magnetic resonance imaging (MRI).^[7]

Local irritation of the drugs, foreign body reaction to the catheter, and local infections may be responsible

for the development of granulation. Histopathological studies show that inflammatory reactions around the catheter cause the formation of granuloma.^[8,9]

To the best of our knowledge, it is not mentioned in the current literature that discontinuation of therapy may cause a regression of epidural granulation and clinical symptoms. In this case, we aimed to present spontaneous regression of epidural granuloma within 2 months after removal of epidural port.

Case Report

A 40-year-old female patient with metastatic cervix cancer and pain on waist and left lower extremity was sent to the Department of Algology at Mersin University for pain treatment. A lumbosacral MRI with contrast revealed metastatic mass lesions in

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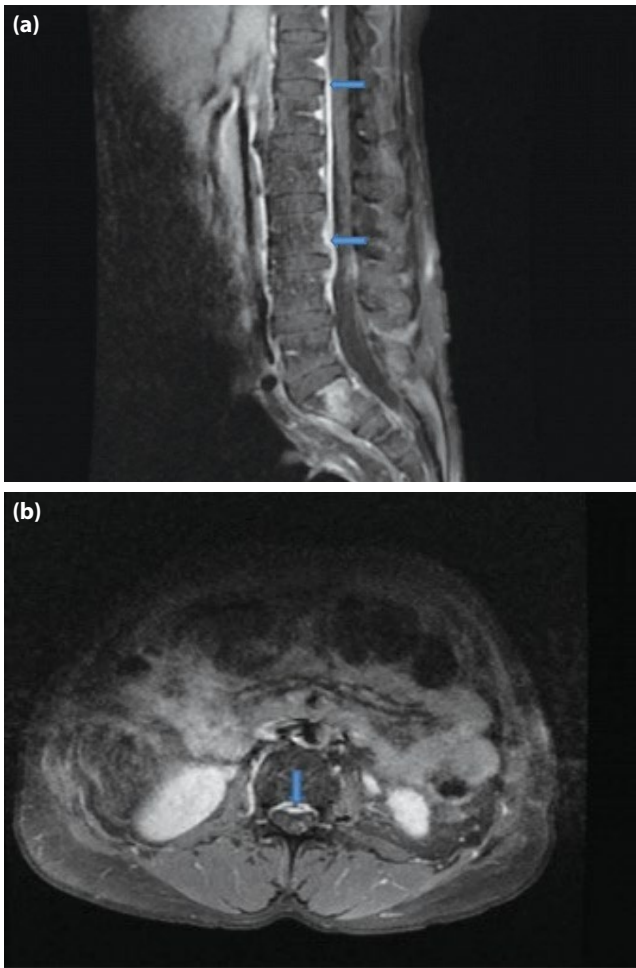


Figure 1. T1-weighted fat-saturated contrast-enhanced sagittal (a) and axial (b) images show enhancing soft-tissue thickening within the anterior epidural space (Arrows).

L5, sacrum, and surrounding tissues. Pain treatment was planned to be given by an epidural port (Celcite/Braun) catheter.

Bupivacaine (25 mg, Marcaine 0.5%/AstraZeneca) and 1.5 mg morphine (Morphine/Osel) in a total volume of 10 cc SF were given every 8 h with an epidural port catheter. The patient complained increased pain due to radiotherapy on the 10th day of epidural port catheterization. Bupivacaine dose increased to 35 mg and oral dexamethasone (4×0.75 mg Dekort/Deva) was added to the initial treatment regime. After 10 days, morphine dose was increased to 2 mg due to the increase in pain. The patient needed pain medications every 12 h at this dose. On the 3rd month of follow-up, it was decided to reduce the total volume of medications to 3 ml using same dose of morphine and no bupivacaine, due to the pain complaint after the volume of 3 ml during injection. Daily morphine need was increased 3 times (12 mg/day) in next 7 days and lumbosacral MRI

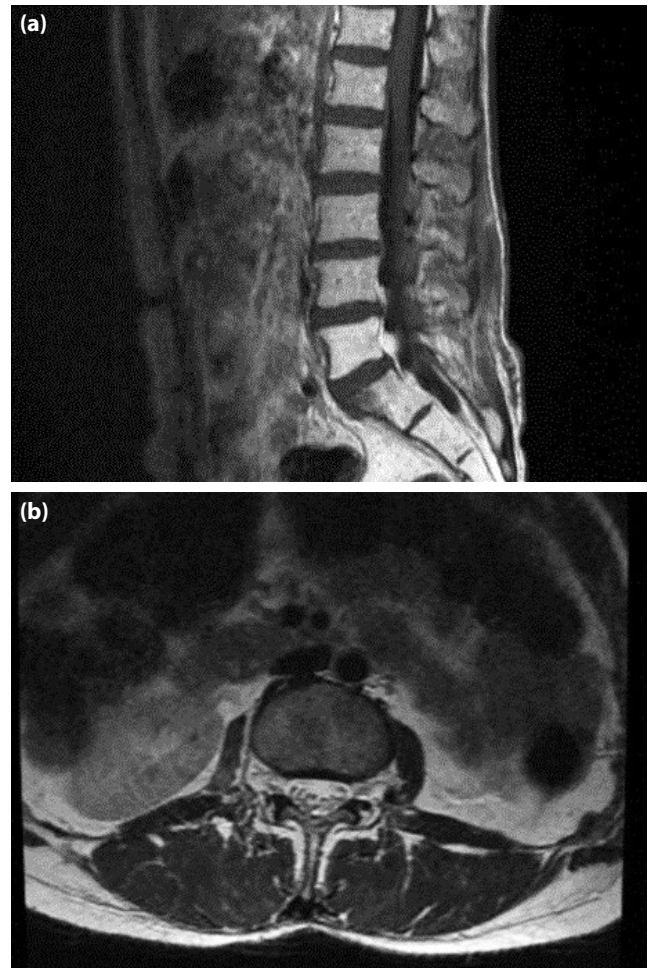


Figure 2. Sagittal contrast-enhanced T1-weighted (a) and axial T2-weighted (b) images demonstrate no granulation tissue within the anterior epidural space.

with contrast was planned. MRI revealed granuloma compatible lesion in the anterior epidural space at the L1-L4 vertebra level (Fig. 1). The port was removed and transdermal fentanyl (100 mcg/h, Durogesic, Jhonson and Jhonson) was started. The dose of transdermal fentanyl was gradually increased to 200 mcg/h due to the increased pain in the next 2 months. Since the patient continued to complain of pain, epidural catheter placement was reconsidered. The patient was referred to the radiology clinic for the evaluation of epidural granulation. The new MRI, only 2 months later than the previous one revealed total clearance of granuloma (Fig. 2). Epidural catheter was inserted with no complication and the patient did not complain of pain during injection of 25 mg bupivacaine and 2 mg morphine combination in a total volume of 10 ml SF. Analgesia was continued for approximately 3 months (until the patient died) with the combination of bupivacaine and morphine. There was no clinical evidence of epidural granulation during the follow-up.

Discussion

It is known that when the factors causing granulation are eliminated, the tissue can show normal improvement.^[10] Our case has the first case feature demonstrated by MR imaging in which the epidural granuloma disappears after removal of the catheter.

Epidural granulation requires increased doses of the administered drug. It can also lead to the appearance of different clinical conditions ranging from radicular pain to paresthesia, paralysis, and cauda equina syndrome.^[2,3,11] In our case, during drug administration, analgesic resistant, gradually increasing radicular pain intensity, was evident. However, these symptoms were not observed during the 3-month treatment with the reinserted epidural catheter.

The first case of granulation after epidural infusion was shown in 1985,^[12] and the inflammatory cell cluster at the end of the intrathecal catheter was shown in 1991.^[4]

Histopathological examination of epidural granulomas revealed macrophages, plasma cells, and eosinophils/lymphocytes around the necrotic tissue.^[6,13] Furthermore, clustered plasma cells around the vasculature were detected. These changes are evaluated as acute/chronic inflammatory response. It is thought that used catheters can activate this inflammatory response.^[2] Both of the epidural catheters that we used were the same brand. For this reason, it was thought that the granulation development in our patient was not dependent on the catheter.

Opioids are known to cause degranulation in mast cells.^[8] Factors that are released from mast cells in the spinal meninges are believed to cause vasodilatation in the meningeal vessels and increase migration of inflammatory cells. In a study of dogs, intrathecal granulation tissue developed after 2–4 weeks of opioid infusion.^[14] These granulomas are thought to be similar to human granulomas. One study reported that 41 patients with intrathecal granuloma had morphine in 31 patients and hydromorphone use in 9 patients.^[15] In another study, it was shown that granulation developed during morphine administration but not after alfentanil infusion.

Discussions continue on why responses to different opioids differ.^[8] There are also some publications

that indicate that opioids cause degranulation in the cutaneous mast cells but not other tissues.^[16,17] In some publications, epidural granulomas have been reported to develop with non-opioid drugs.^[3] It is, therefore, not possible that the underlying mechanism is only mast cell degranulation due to opioids. The same drug combination was applied to our case in both administration periods, but no complaints occurred in the second period.

The development of different tissue responses to the same effect suggests that not only drugs but also other factors that affect the general state of the patient (e.g., chemotherapy, radiotherapy, and infection) may be effective in the development of granulomas. Whether these factors are upset or treated, tissue reactions to catheters and drugs may be changing. We believe that detailed studies are needed to determine these factors.

Informed Consent: *Written informed consent was obtained from the patient for the publication of the case report and the accompanying images.*

Conflict-of-interest issues regarding the authorship or article: *None declared.*

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References

1. Wang JK, Nauss LA, Thomas JE. Pain relief by intrathecally applied morphine in man. *Anesthesiology* 1979;50(2):149–51.
2. Aprilì D, Bandschapp O, Rochlitz C, Urwyler A, Ruppen W. Serious complications associated with external intrathecal catheters used in cancer pain patients: A systematic review and meta-analysis. *Anesthesiology* 2009;111(6):1346–55.
3. Deer TR, Prager J, Levy R, Rathmell J, Buchser E, Burton A, et al. Polyanalgesic consensus conference--2012: Consensus on diagnosis, detection, and treatment of catheter-tip granulomas (inflammatory masses). *Neuromodulation* 2012;15(5):483–95. [\[CrossRef\]](#)
4. North RB, Cutchis PN, Epstein JA, Long DM. Spinal cord compression complicating subarachnoid infusion of morphine: Case report and laboratory experience. *Neurosurgery* 1991;29(5):778–84. [\[CrossRef\]](#)
5. Williams BS, Wong D, Amin S. Case scenario: Self-extraction of intrathecal pump medication with a concomitant intrathecal granulomatous mass. *Anesthesiology* 2011;114(2):424–30. [\[CrossRef\]](#)
6. Pancucci G, Lopez-Gonzalez A, Sanchez-Garvì E, Ramos-Soler D, Pla-Cortina C, Prat-Acin R, et al. Spinal granulomas associated with intradural morphine delivery systems: Early diagnosis and surgical treatment. *Clin Neurol Neurosurg* 2013;115(10):2270–3. [\[CrossRef\]](#)

7. Leong SK, Laing B, Saines N. Magnetic resonance imaging (MR) and computed tomography (CT) findings in intrathecal catheter granuloma: Report of two cases. *Eur J Radiol Extra* 2010;74(2):e17–21. [\[CrossRef\]](#)
8. Yaksh TL, Steinauer JJ, Veasart SL, Malkmus SA. Alfentanil: Correlations between absence of effect upon subcutaneous mast cells and absence of granuloma formation after intrathecal infusion in the dog. *Neuromodulation* 2013;16(5):459–66. [\[CrossRef\]](#)
9. Miele VJ, Price KO, Bloomfield S, Hogg J, Bailes JE. A review of intrathecal morphine therapy related granulomas. *Eur J Pain* 2006;10(3):251–61. [\[CrossRef\]](#)
10. Yalçın Ö, Özoran Y. İnflamasyon ve onarım. In: Tuzalı S, Güllüoğlu M, Çevikbaş U, editors. *Robbins Temel Patoloji*. 9th ed. İstanbul: Nobel Tıp Kitapevi; 2014.
11. Koeck K, Grossauer S, Trummer M, Kleinert R. Epidural granuloma by dislocated catheter tip associated with spinal cord compression in high-dose intrathecal morphine therapy. *Gen Med (Los Angel)* 2013;1:1000117.
12. Rodan BA, Cohen FL, Bean WJ, Martyak SN. Fibrous mass complicating epidural morphine infusion. *Neurosurgery* 1985;16(1):68–70. [\[CrossRef\]](#)
13. Philips JA, Escott EJ, Moossy JJ, Kellermier HC. Imaging Appearance of Intrathecal Catheter Tip Granulomas: Report of three cases and review of the literature. *AJR* 2007; 189:W375–81. [\[CrossRef\]](#)
14. Allen JW, Horais KA, Tozier NA, Wegner K, Corbeil JA, Matrey RF, et al. Time course and role of morphine dose and concentration in intrathecal granuloma formation in dogs: A combined magnetic resonance imaging and histopathology investigation. *Anesthesiology* 2006;105(3):581–9.
15. Coffey RJ, Burchiel K. Inflammatory mass lesions associated with intrathecal drug infusion catheters: Report and observations on 41 patients. *Neurosurgery* 2002;50(1):78–86.
16. Ebertz JM, Hermens JM, McMillan JC, Uno H, Hirshman C, Hanifin JM. Functional differences between human cutaneous mast cells and basophils: A comparison of morphine-induced histamine release. *Agents Actions* 1986;18(5-6):455–62. [\[CrossRef\]](#)
17. Tharp MD, Kagey-Sobotka A, Fox CC, Marone G, Lichtenstein LM, Sullivan TJ. Functional heterogeneity of human mast cells from different anatomic sites: In vitro responses to morphine sulfate. *J Allergy Clin Immunol* 1987;79(4):646–53. [\[CrossRef\]](#)