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Case Report
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A case of priapism following intrathecal morphine injection in a dog

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Abstract

Background: Priapism refers to prolonged erection unrelated to sexual stimulation, with severe sequelae unless treated. In humans, it is a rare complication associated with epidural or spinal opioid administration. Its pathophysiology is unclear. This is the first report of priapism following neuraxial anesthesia in dog.

Case Description: An intrathecal morphine injection (30 mcg/kg) at L5–L6 for postoperative analgesia was given at the end of surgery for removal of cutaneous mastocytomas of the abdomen and left axillary lymphadenectomy. Painless penile erection occurred 2 hours later and lasted 6 hours, before spontaneously resolving 7–8 hours after the injection. No pain or other adverse events (e.g., nausea, urinary retention, and itching) were recorded. Recovery was complete without treatment.

Conclusion: Painless, self-resolving priapism is a rare complication associated with intrathecal morphine injection in dogs.

Keywords: Dog, Intrathecal morphine, Priapism.

Introduction

Priapism refers to a prolonged erection usually unrelated to sexual stimulation; it may result in severe sequelae unless treated. Its pathophysiology is unclear. Priapism is classified as either high flow (nonischemic) or low flow (ischemic) (Burnett, 2003). Nonischemic priapism results from direct trauma to the genitals and perineum or during transurethral surgery (Pautler and Brock, 2001), while ischemic priapism is caused by medications, hematological, or neurological disease. Priapism is among the most common urologic emergencies in humans. Ischemic priapism is associated with intrathecal or epidural anesthesia administered during urological procedures involving genital manipulation (Chin and Sharpe, 1983; Shantha *et al.*, 1989; Baltogiannis *et al.*, 2006; Das *et al.*, 2010). Here, we report a case of priapism, a rare complication of spinal morphine administration observed in a dog.

Case Details

A spayed, mixed-breed male dog (age 12 years, body weight 21 kg) was placed under general anesthesia for excision of multiple cutaneous mastocytoma of the abdomen and left axillary lymphadenectomy. The medical history was unremarkable, except for the tumor; the preanesthetic physical exam and complete blood analyses revealed no abnormalities. The dog was premedicated with an intramuscular (IM) injection of 1 µg/kg dexmedetomidine (Dexdomitor; Orion) and methadone 0.2 mg/kg (Semfortan; Dechra), followed 15 minutes later by placement of an 18-gauge intravenous (IV) catheter (Surflo; Terumo) in the right saphenous vein. General anesthesia was induced with an IV injection of propofol 2.8 mg/kg (Proposure 1%; Merial). After endotracheal intubation, the dog was placed in dorsal recumbency and connected to a rotatory breathing system. Mechanical volumetric ventilation was started at an initial tidal volume of 250 ml/kg, pressure inspiratory peak of 11 cm/H_2O, and 12 respiratory breaths per minute (Primus, Draeger, Lubeck, Germany). Anesthesia was maintained with a median 1.4 end tidal isoflurane tension (FE'_{iso}) (Isoflo; Esteve) in a mixture of 0.4 oxygen and air. An infusion of Ringer's Lactate (lactated Ringer's; Fresenius Kabi) was administered at 5 ml/kg/hour. Vital parameters were monitored on a multiparameter-anesthetic monitor (Infinity Delta; Draeger): noninvasive systolic, diastolic, and mean arterial blood pressure, a three-lead electrocardiogram, peripheral oxygen saturation, inspired fraction of oxygen, end tidal carbon dioxide, FE'_{iso}, and esophageal temperature (T,°C). The surgery was successful, and the 2-hour anesthesia was uneventful. Before discontinuing isoflurane, meloxicam (0.2 mg/kg IV Metacam; Boehringer) was injected and the dog was placed in lateral recumbency. After aseptic preparation of the lumbar skin, an intrathecal morphine injection (Morfina cloridrato 1%; Molteni, Italy) was administered with a 25 G 50 mm Quincke needle (Becton, Dickinson and Company, USA) at L5–L6 to ensure adequate postoperative analgesia via a paramedian technique. Needle entrance into the subarachnoid space was verified by outflow of cerebrospinal fluid in the

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hub of the needle. Preservative-free morphine (30 µg/kg) was diluted with 0.6 ml of sterile saline solution and administered in a single bolus over 20–40 seconds. Recovery was uneventful without initial complications, and the dog was brought into the ward. 2 hours after tracheal extubation, a painless penile erection began and lasted 6 hours, before spontaneously resolving 7–8 hours after the spinal injection. No pain or other adverse events (e.g., nausea, urinary retention, or itching) were recorded. Recovery was complete without sequelae and the dog was discharged from hospital the morning after the surgery. The follow-up physical examination 1 week later revealed no abnormal findings and the owners reported no sequelae.

Discussion

This is the first case report of priapism after intrathecal morphine injection in a dog. The parasympathetic nervous system (PNS) controls erection, while the sympathetic nervous system (SNS) influences ejaculation and termination of an erection (Pybus *et al.*, 1984). Erection is produced by blocking sympathetic vasoconstriction, whereas detumescence results when parasympathetic vasodilatory action is impaired. Priapism refers to full or partial penile erection that lasts for several hours and is unrelated to sexual arousal. Its pathophysiology is unclear but is thought to stem from hemodynamic dysfunction of the penis, resulting in persistent erection. One explanation for its cause is that there is a sort of autonomic imbalance between the SNS and the PNS that leads to excessive, persistent blood engorgement (Pelavski *et al.*, 2006). The underlying cause of postoperative priapism remains elusive. Theoretically, any drug or drug combination that affects the neurovascular system or the central nervous system may cause priapism (Appell *et al.*, 1977; Gottlieb and Lustberg, 1977; Chin and Sharp, 1983).

In the human medical literature, priapism has been reported as a complication of central regional anesthesia with local anesthetics (Van Arsadelen *et al.*, 1983; Tsai and Hong, 1990; Burnett, 2003; Pelavski *et al.*, 2006; Nair *et al.*, 2019). Epidural anesthesia is thought to produce a potential sympathetic blockade at the lumbar level, without simultaneous complete parasympathetic blockage of the sacral spinal cord. This may result in high flow (nonischemic) priapism (Van Arsadelen *et al.*, 1983; Tsai and Hong, 1990; Burnett, 2003; Pelavski *et al.*, 2006). The same mechanism may explain the occurrence of priapism after spinal injection: the local anesthetic is diluted by the cerebral spinal fluid, resulting in less concentration in areas distal to the injection site. Another possible mechanism is selective inhibition of sympathetic innervation of the penis by spinal anesthesia, which results in unopposed parasympathetic activity and ultimately penile erection (Nair *et al.*, 2019).

As largely described in humans, epidural (Torda *et al.*, 1980; Rawal *et al.*, 1983) and intrathecal opioids (Pybus *et al.*, 1984; Wiesenfeld-Hallin and Soderstern, 1984; Cunicelli *et al.*, 2021) seem to have a key role in priapism. Sustained erections and incapacity to ejaculate have been reported after single-shot epidural administration (Torda *et al.*, 1980; Rawal *et al.*, 1983) and via catheter in healthy men (Ruan *et al.*, 2007). Wiesenfeld-Hallin and Soderstern (1984) noted that as intrathecal morphine increased, naloxone decreased the number of intromissions prior to orgasm in male rats. To our best knowledge, there are no reports of systemic morphine-causing priapism. Furthermore, neither prolonged penile erection nor inability to ejaculate was reported in males following IV or IM opioid injection (Torda *et al.*, 1980; Rawal *et al.*, 1983; Wiesenfeld-Hallin and Soderstern, 1984). These findings corroborate the opioid-induced spinally mediated mechanism that decreases sympathetic response to sexual stimulation (Pybus *et al.*, 1984). However, sexual functioning is variably affected by opioids. Reduction in testosterone levels, decreased libido, erectile dysfunction, and delayed ejaculation are noted to occur frequently in chronic opioid users (Mirin *et al.*, 1980; Gulliford, 1998), and impotence and decreased libido are often seen in patients under long-term intrathecal morphine therapy (Ruan, 2007).

Our hypothesis is that the anesthetic protocol we used did not lead to the occurrence of priapism in this patient. Dexmedetomidine was shown to have protective effects against ischemia-reperfusion injury in an experimental rat model of priapism (Kölükçü *et al.*, 2021), and it has been successfully used in the treatment of intraoperative penile erection in men (Guler *et al.*, 2021). Although priapism is sometimes associated with propofol-based anesthesia in men (Corten *et al.*, 2017), it is improbable that the propofol timing and dosage we used for anesthesia induction could have been responsible for this complication. In our opinion, the cause of priapism is ascribable to the intrathecal morphine the dog received as postoperative analgesia. A probable cause was the blockage of sympathetic outflow from the sacral spinal cord through a spinally mediated mechanism. Another possible mechanism was an increased nitric oxide (NO)-mediated vasodilation. NO is released from vascular endothelium and mediates the increase of blood flow and the relaxation of smooth muscle in the corpora cavernosa, causing erection. Morphine is believed to cause an increase in endothelial production of NO (Pourshanazari *et al.*, 2011) and might contribute to the development of priapism. These conclusions are concordant with studies in humans (Ruan *et al.*, 2007; Cunicelli *et al.*, 2021).

The morphine dosage we used has been reported in previous studies on orthopedic surgery with bupivacaine (Sarotti *et al.*, 2013, 2016, 2019) without the occurrence of priapism. The same dose of morphine (without local anesthetics) was effective in managing perioperative pain in dogs undergoing major thoracic or cranial abdominal surgery (Lardone *et al.*, 2022)

and it is known to reduce the need for rescue analgesia in dogs undergoing cervical and thoracolumbar spinal surgery (Novello *et al.*, 2008). Considering all the above, the cranial spread was expected to be sufficient to produce adequate analgesia in terms of quality and duration. Although its frequency is extremely rare in dogs and uncommon in men, many anesthetists, including ourselves, often add a low dose of morphine to lumbar epidural or spinal injection without risking the complication of priapism. It is unclear what could have increased the susceptibility of the patient to developing such a complication. It seems that the site of injection in relation to the autonomic outflow from the spinal cord plays an important role in priapism development as all previously reported cases, including ours, involved lumbar central regional anesthesia where the injection or the catheter tip could potentially be adjacent to the sympathetic outflow of the L1–L2 nerve roots.

We were unable to find published data on spinal morphine at recovery. In our experience, intrathecal morphine is more often associated with adverse effects when administered at the end of surgery as postoperative analgesia. While general anesthesia may hide some complications (e.g., itching or nausea) timing could be another crucial factor. We speculate that a high spinal concentration of opioids (without local anesthetic), together with sudden sympathetic activation during recovery from the general anesthesia, may have contributed to the priapism in this patient. Although pain is commonly reported during low-flow priapism in men (Corten *et al.*, 2017), no pain was observed in our patient and no analgesics were administered. The complication self-resolved without any treatment. Although priapism is rare, veterinarians should be aware of this complication and initiate prompt therapy as needed.

Conflict of interest

The authors declare that the study was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Authors' contributions

EL: data management and manuscript preparation; VG: data collection; and PF: interpretation and correction of the manuscript.

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