

SEVERE PAIN IN A LEIOMYOMA WITH TWIN PREGNANCY- AN ANALGESIC DILEMMA

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Background: Pain is the most common complication of fibroids in pregnancy and can be difficult to treat. The choices of pain relief in pregnancy are limited due to myriad risks including miscarriage, teratogenicity, premature birth, and low birth weight.

Case Report: This paper describes the analgesic challenges faced when managing severe pain in the antepartum period for a woman pregnant with twins who also suffered from uterine leiomyomas. Multiple analgesic regimens were trialled over the course of the pregnancy with large doses of opioids required for long periods. Ultimately the patient underwent a laparotomy and myomectomy at 25 weeks gestation in an attempt to alleviate her pain.

Conclusion: There should be early discussions and planning around the choice of analgesic agents and their planned duration, with the risks and benefits weighed in each instance. A multidisciplinary approach with obstetricians, neonatologists, anesthetists, and pain specialists is likely to result in the most benefit while limiting the risk to the fetus.

Key words: Pain, analgesia, pregnancy, leiomyoma, teratogenicity

BACKGROUND

Uterine leiomyomas are common, benign smooth muscle tumors originating from uterine myometrial cells. They are estimated to affect 40%–80% of women by age 50 and are present in up to 4% of pregnancies (1-3). However, severe localized abdominal pain can occur if a fibroid undergoes degeneration, torsion, or impaction, which usually occurs between the 14th and 20th week when growth of the uterus is most active (2).

Conservative management is the gold standard for pain management, but other options include the early use of epidural analgesia and/or surgical management. We describe a difficult case where analgesia proved challenging in the antepartum period with multiple failed analgesic regimens including an epidural and ultimately requiring a myomectomy.

CASE

A 24-year-old primigravida presented at her first appointment. A pelvic ultrasound scan revealed a twin pregnancy but was otherwise unremarkable. The patient has a past medical history of sickle cell trait. She ceased smoking upon pregnancy.

She first presented to the accident and emergency department (A&E) at 15 weeks gestation with generalized abdominal pain. An ultrasound scan showed a viable twin pregnancy and a “degenerating fundal fibroid”. The patient was admitted, treated with acetaminophen and discharged when the pain improved.

She presented to A&E again at 16 weeks with severe abdominal pain. She required admission and was started on regular acetaminophen, tramadol, and meperidine, with nitrous oxide as required. Despite this analgesia,

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the patient's pain remained severe, and required the continuous use of nitrous oxide.

At this point the acute pain team was consulted, and together the team decided on a regimen of acetaminophen, diclofenac, morphine patient-controlled analgesia (PCA), and nitrous oxide as required. After 6 days the morphine PCA and nitrous oxide was stopped and the patient started on regular acetaminophen, diclofenac, oxycodone modified release (MR) and oxycodone immediate release (IR). On day 8 of the new regimen, the regular diclofenac was stopped and she was discharged home on regular acetaminophen and oxycodone MR.

At 21 weeks gestation she was readmitted with severe abdominal pain. She was restarted on her previously successful regimen of regular acetaminophen, diclofenac, and oxycodone MR and IR. The pain continued to be severe and over the next 10 days the oxycodone doses were increased regularly until the patient was taking more than 100 mg of oxycodone each day.

With limited success, the patient was next restarted on a morphine PCA with regular acetaminophen with all other analgesia stopped. Magnetic resonance imaging confirmed torsion of a pedunculated fibroid, and a decision to proceed to laparotomy was made by the gynecology team with the pregnancy now at 25 weeks gestation and considered viable. A laparotomy and myomectomy were performed with regular intra-uterine fetal monitoring and a neonatal team on standby should an emergency Cesarean section be required.

Pre-operative analgesia was managed with an epidural using bupivacaine, which resulted in excellent pain relief before general anesthesia was induced. Postoperatively, analgesia was initially continued with the sited epidural catheter. However, the epidural became dislodged the next day so the patient was started on a morphine PCA with acetaminophen and lidocaine patches applied to the skin around the laparotomy wound. Three days later the patient was weaned from the morphine PCA onto codeine and oral morphine. On day 5 she was well enough to be discharged home with regular acetaminophen and codeine.

Three weeks later, with the gestation of the twins at 30 weeks, the patient was re-admitted through A&E with severe pain. A pelvic ultrasound scan was performed which did not show any significant pathology or explanation for the reoccurrence of pain. She was restarted on acetaminophen and oxycodone MR and IR. Due to increasing levels of pain, the oxycodone doses were regularly increased without great success

and the patient was becoming increasingly upset and requesting immediate Cesarean section. The importance of delaying delivery as much as possible was explained to the patient, and she was managed in the hospital for 2 further weeks on high doses of oxycodone before improving enough to be discharged home.

At 34 weeks gestation the patient presented with premature rupture of membranes and a Cesarean section was carried out. The procedure was carried out under spinal anesthesia using 2.4 mL 0.5% heavy bupivacaine and 300 µg diamorphine (Although it is considered standard practice in the UK, diamorphine is Schedule I drug in the US). Two healthy twins were born, one of which required a very brief stay on neonatal intensive care for respiratory support. The patient was managed postoperatively with acetaminophen, ibuprofen, and morphine. She was discharged home 6 days later on codeine, acetaminophen, and ibuprofen. Several months later in a pain follow-up clinic, the patient was not taking any regular analgesia and reported no ongoing pain.

DISCUSSION

Pain is the most common complication of fibroids in pregnancy (1). The approach to fibroid analgesia in the nonpregnant population would be to broadly follow the World Health Organization pain ladder. Acetaminophen and nonsteroidal anti-inflammatories would be the mainstay of therapy with weak and strong opioids added in as required for those with more severe pain (4).

Hormonal therapy, radiological embolization or the surgical options of myomectomy or hysterectomy are offered for recurrent and severe pain. Of those above, only the surgical option of a myomectomy can be carried out during a pregnancy, but this carries a significant risk to the fetus and is delayed where possible until pregnancy reaches a viable gestation of at least 24 weeks, and ideally longer (4).

With such limited options for fibroid management in pregnancy, its treatment can be extremely challenging in the atypical cases where pain is severe. The goal must be to adequately control pain to allow the pregnancy to reach full gestation, or in cases such as this one, allowing the pregnancy to progress as far as possible before surgery is attempted. Compounding the difficulty is the very limited choice of analgesia in the pregnant patient due to the potential risk of many medicines to the fetus, which include miscarriage, teratogenicity, premature birth, and low birth weight.

Acetaminophen has a well-established safety profile, is frequently used in pregnancy (3), and was used without concern in this case.

Nonsteroidal anti-inflammatory drugs are a mainstay of fibroid analgesia in the nonpregnant population but are contraindicated in the first and third trimesters. They have been used with caution in the second trimester (5,6). Diclofenac was used during the second trimester of this case in low doses and for short durations to limit the exposure of the fetus to the drug. Of all the analgesia employed by the pain team, the obstetricians were most concerned about the potential risk of diclofenac to the fetus. There were no adverse consequences to using diclofenac in this case.

Opioids are the most commonly used class of analgesic for severe pain in the general population. Prolonged opioid use in the mother can lead to tolerance, hyperalgesia, dependence, and addiction (7) and in the neonate can cause preterm birth, low birth weight, small head circumference, neural tube defects, neonatal abstinence syndrome, and congenital malformations (8-10). In this case the patient was on large doses of oral or intravenous opioids for prolonged periods of the pregnancy due to the severity of her pain. Despite significant concerns from all medical teams involved in this patient's care, there were no major complications attributed to prolonged opioid use. One of the twins required respiratory support for a brief period in the neonatal intensive care unit and neither of the twins showed any signs of withdrawal.

Alternatives and adjuvants to opioids are increasingly used in pain management in the general population in an attempt to limit opioid use and their associated side effects. The use of adjuvant analgesia in the pregnant population is not common however, and guidance on its use is limited. In this case the main adjuvant used was inhaled nitrous oxide but its use in this context is unusual. Outside of anesthetic practice, nitrous oxide is most commonly used in the prehospital setting, in emergency departments for procedural analgesia and sedation, or in childbirth (11,12). Due to its use in labor, the gas was easily available on the obstetric ward where this patient was managed, and nursing staff were comfortable with its administration.

Despite its use during labour however, the drug is

known to interfere with folate metabolism and carries theoretical toxic risk to the fetus and mother with prolonged use (13). After much discussion, it was used in this case for short periods and never for more than 24 hours. There is little in the literature describing nitrous oxide use for fibroid pain but it was felt to be of great use in helping to control acute exacerbations of severe pain for this patient.

Systemic lidocaine administration can produce sodium channel blocking activity leading to analgesia and can be a useful adjuvant to more typical analgesics. Lidocaine patches provide a transdermal mode of delivery for this local anesthetic and were used in this case postoperatively following the patient's laparotomy in an attempt to reduce opioid consumption. While local anesthetics are known to cross the placenta, they are not known to cause fetal harm (14) and their use was felt to be helpful in reducing postoperative opioid consumption.

Other adjuvants such as ketamine, pregabalin, and gabapentin have not been evaluated in large trials and their use in pregnancy is controversial (15-17). They were avoided in this case as the risks were felt to outweigh the benefits.

Nonpharmacological treatments for pain have been described such as massage, acupuncture, and mindfulness (18). With hindsight, this is an area that could have been explored more in this case. The patient's pain was likely to have been exacerbated by her anxiety around the safety of her unborn twins, and while her anxiety was addressed at every visit, nonpharmacological approaches may have been helpful.

CONCLUSION

Management of pain due to fibroids in pregnancy is challenging. A multidisciplinary team approach to pain management is vital in our opinion. There should be early discussions and planning around the choice of analgesic agents and their planned duration with the risks and benefits weighed in each instance. Adjuvants to the analgesics in the World Health Organization pain ladder, such as nitrous oxide and lidocaine patches were helpful in this case and should be considered. Nonpharmacological approaches to acute pain management are often overlooked and may have been of benefit in this case.

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