Obstetrical and Pediatric Anesthesia

Anesthetic management of a labouring parturient with urticaria pigmentosa

[Anesthésie d'une parturiente en travail, atteinte d'urticaire pigmentaire]

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Purpose: To report the anesthetic management of labour pain and Cesarean section in a patient with urticaria pigmentosa at risk for systemic mastocytosis.

Clinical: A 37-yr-old patient with a history of urticaria pigmentosa and an allergic reaction to a local anesthetic agent was seen in consultation at 36 weeks gestation. She previously tested negative for an allergy test to lidocaine. Recommendations to avoid systemic mastocytosis included: avoidance of histamine-releasing drugs, using lidocaine for labour epidural, and regional anesthesia in case of a Cesarean section. The patient presented at term in labour. Intravenous fentanyl was used for early labour, followed by a combined spinal-epidural. The spinal contained lidocaine and fentanyl, but because of pruritus, the epidural infusion contained lidocaine only. Most likely because of tachyphylaxis to lidocaine, an epidural bolus of lidocaine with epinephrine failed to provide adequate anesthesia for a Cesarean section. The block was supplemented with nitrous oxide by mask, with fentanyl postdelivery. Postoperative pain control was managed with an epidural infusion of lidocaine and fentanyl for three days. The patient was discharged without complications four days postsurgery.

Conclusion: Proper allergy testing prior to pregnancy is important to help the management of labour pain and anesthesia for Cesarean section in a patient at risk for systemic mastocytosis.

***Objectif** : Présenter l'anesthésie utilisée pendant la césarienne pour contrer la douleur chez une patiente atteinte d'urticaire pigmentaire à risque de mastocytose diffuse.*

***Éléments cliniques** : Une femme de 37 ans, ayant déjà eu de l'urticaire pigmentaire et une réaction allergique à un anesthésique local, a consulté à 36 semaines de grossesse. Un test antérieur d'allergie à la lidocaïne s'était révélé négatif. Pour éviter la mastocytose diffuse, il faut éviter les médicaments à libération d'histamine, utiliser la lidocaïne pour l'anesthésie épidurale pendant le travail et l'anesthésie régionale en cas de césarienne. La patiente en travail a été hospitalisée au terme de sa grossesse. Du fentanyl intraveineux a été utilisé au début du travail, puis une anesthésie rachidienne et épidurale combinée. L'anesthésie rachidienne comprenait de la lidocaïne et du fentanyl, et l'anesthésie épidurale, de la lidocaïne seulement. Sans doute à cause d'une tachyphylaxie à la lidocaïne, l'anesthésie avec un bolus épidural de lidocaïne et de l'épinéphrine n'a pas suffi pour la césarienne. Le bloc a été complété avec du protoxyde d'azote, administré au masque, et du fentanyl après l'accouchement. La douleur postopératoire a été contrôlée par une perfusion épidurale de lidocaïne et de fentanyl pendant trois jours. La patiente n'a subi aucune complication et a quitté l'hôpital quatre jours après la césarienne.*

***Conclusion** : Des tests d'allergie appropriés, faits avant la grossesse, sont importants pour décider du contrôle de la douleur du travail et de l'anesthésie pour la césarienne de patientes à risque de mastocytose diffuse.*

URTICARIA pigmentosa is the cutaneous manifestation of mastocytosis, a disease characterized by the proliferation and accumulation of mast cells in various organs of the body. The incidence of urticaria pigmentosa has been reported to be between 1 in 1,000 and 1 in 8,000 of the population.[1] As many as 10% of patients with urticaria pigmentosa will have systemic

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No financial support or grant supported this work.

Assessed August 10, 2005.

Revision accepted September 22, 2005.

Final revision accepted October 10, 2005.

manifestations with mast cell degranulation.[2] Factors implicated in mast cell degranulation include trauma or mechanical irritation to the skin, psychological stress, extremes of temperature, spicy foods, alcohol, histamine-releasing drugs and biological polymers found in snake and bee venom.[3] Pharmacological agents can also contribute to mast cell degranulation, independent of their propensity to release histamine.[3] Common minor symptoms of systemic mastocytosis and histamine release include weakness, fatigue, urticaria, pruritus, flushing, abdominal cramps, vomiting, diarrhea, mental confusion, and febrile episodes. Uncommon major symptoms include grand mal seizures, anaphylaxis and cardiovascular collapse.[3,4] It is surprising to note that wheezing rarely accompanies these attacks.[5]

Because of the risks associated with mast cell degranulation, patients with urticaria pigmentosa pose a particular challenge for anesthesiologists,[3,5,6] especially in the context of pregnancy and labour.[4] As many as one third of the women experience worsening of the systemic symptoms during pregnancy.[4] Very few reports are available as a reference for the anesthetic management of pregnant patients with mastocytosis.[4,7,8] We present the case of a pregnant patient with urticaria pigmentosa and the anesthetic management of an epidural for labour followed by an emergency Cesarean section. Approval for publication of personal health information was obtained in accordance with the hospital Research Ethics Board.

Case report

A 37-yr-old G1P0, 84 kg patient was seen for consultation at 36 weeks gestation. The obstetrician was concerned about regional anesthesia considering the patient's history of joint laxicity. Investigations for Marfan and Ehlers-Danlos syndrome were negative. During the consultation the patient indicated having been diagnosed with urticaria pigmentosa in the past. Her medical history also revealed that she experienced an allergic reaction to a local anesthetic agent while at the dentist when she was 22 yr old. She remembered throat swelling and dizziness. Paramedics were called and found the patient with a low blood pressure. Although she did not require hospitalization, the patient remembers taking three days to recover. The agent responsible for the allergic reaction remains unknown since an allergy test for lidocaine was negative. This test result complicated the management of the patient in a number of ways. First, even though it was specified in the consultation that an allergy to another amide was very unlikely, this possibility could not be ruled out with certainty without allergy testing. Second, since lidocaine has been used successfully in the past for labour analgesia,[9] it was reasonable to agree to use it as an infusion for labour pain. Finally, even though allergy testing is possible, and sometimes recommended, during pregnancy and labour,[10,11] it is still somewhat controversial,[12,13] especially if another agent is known to be safe for the patient. In the consultation, we also suggested avoiding medications that release histamine such as morphine and meperidine. In the event of a Cesarean section, we suggested premedication with diphenhydramine and ranitidine, and the use of an epidural with lidocaine. It was also suggested to avoid general anesthesia as much as possible, and to install an epidural earlier than later during labour.

During pregnancy, the patient showed cutaneous manifestations of urticaria pigmentosa on the trunk and thighs, but there was no other exacerbation of the disease. The patient presented in spontaneous labour at 39 5/7 weeks. Intravenous access was obtained and resuscitation equipment was kept nearby for the duration of labour. After seven hours of labour stimulated by oxytocin, the patient asked for labour analgesia. After consulting with the anesthesiologist on call, she received four doses of fentanyl 50 µg *iv* over a period of four hours. Intravenous fentanyl was well tolerated by the patient without pruritus. After 11 hr of labour, at 3 cm dilation, the patient requested epidural analgesia. She was in severe pain and extreme distress at the time, even with *iv* fentanyl. Because *iv* fentanyl had been safely administered, the anesthesiologist on call opted for a combined spinal epidural with lidocaine 10 mg and fentanyl 25 µg intrathecally. The procedure was uneventful except for moderate pruritus at the start, which did not require treatment. In order to avoid mechanical trauma by scratching, diphehydramine and nulbuphine were readily available in the room in the event of worsening pruritus. An epidural infusion with 0.75% lidocaine was started at 12 $mL \cdot hr^{-1}$ 15 min after the spinal, without fentanyl to limit pruritus. After four hours of lidocaine infusion, pain relief was inadequate and 10 mL of the 0.75% lidocaine solution was given. After only 45 min, the patient required 8 mL of 2% lidocaine to relieve the pain. Two similar boluses were given shortly thereafter. The rate of infusion was increased to 14 $mL \cdot hr^{-1}$ and the lidocaine concentration to 1%. The patient was relieved for four hours at this infusion rate, after which, another bolus of 8 mL of 2% lidocaine was necessary to relieve rectal pain.

Two hours later, after 25 hr of labour, at 4 cm dilation, station 0, the obstetrician decided to perform a Cesarean section for failure to progress and non-reassuring fetal heart rate tracings. Each contraction was

painful at this point. In the operating room, 30 mL of sodium citrate was given and 30 mL of lidocaine 2% with epinephrine 1:200 000 was injected in the epidural catheter in divided doses. The sensory block was tested to T4 bilaterally with ice. The patient did not react to skin incision, but complained of pain with peritoneal incision. General anesthesia was avoided by complementing the neuraxial block with nitrous oxide 60% by mask before the delivery of the baby. After, fentanyl 350 μg *iv* was given in divided doses, supplemented with 60% nitrous oxide. We observed no evidence of systemic mastocytosis, and hemodynamic parameters remained stable throughout surgery. Postoperative pain was more or less well controlled with an epidural infusion of 1.0% lidocaine at 12 $mL \cdot hr^{-1}$. Fentanyl, 2 $\mu g \cdot mL^{-1}$, was added to the solution for better pain control, without pruritus. Naproxen 500 mg bid and acetaminophen 975 mg qid were used as analgesic adjuncts. The patient had no complications and left hospital on the fourth day postpartum. We suggested that she be tested for allergy to bupivacaine in the near future.

Discussion

There is no cure for mastocytosis; treatment is aimed at relieving symptoms. Plasma and urinary levels of histamine and its metabolites may help in the diagnosis, but do not correlate with severity of the disease.[3] Antihistamine agents are used to decrease pruritus and to treat gastric symptoms.[14] When surgery and general anesthesia are necessary, premedication with H_1 and H_2 antihistamine agents,[2] and with benzodiazepine to reduce the anxiety level is recommended.[15] Core temperature should be monitored and warming devices should be available throughout the surgery. Repositioning of the patient should be kept to a minimum to decrease the risk of precipitating systemic mastocytosis. Good pain control may contribute to a decrease in overall anxiety and help reduce the risk of exacerbation of the disease. When mast cell degranulation or anaphylaxis are suspected, corticosteroids, antihistamine drugs and epinephrine should be used to prevent further mast cell degranulation and cardiovascular collapse.[2]

The 1991 National Institutes of Health classification of mastocytosis[14] warned that, due to the heterogeneity of the disease, the risks of systemic involvement, mast cell degranulation and anaphylaxis are high in all patients regardless of the presentation of symptoms. In the non-pregnant population, general anesthesia has been associated with mast cell degranulation and cardiovascular collapse.[2,3,15–17] Uncomplicated epidural analgesia for labour and delivery has been described.[4,7] In the case presented here, the combination of known urticaria pigmentosa with the anecdotal story of hypotension following exposure to a local anesthetic agent should raise suspicion of systemic manifestations of mastocytosis. Thus, in order to minimize the risks of anaphylaxis and cardiovascular collapse for this patient, our recommendations included: 1) the use of epidural lidocaine, the only local anesthetic agent known to be safe for her; 2) avoidance of histamine releasing drugs; 3) avoidance of general anesthesia. An extensive list of histamine releasing drugs to be avoided in patients with mastocytosis can be found elsewhere.[3] For our purpose, histamine-releasing drugs commonly used in obstetrical anesthesia include sodium thiopental, succinylcholine, meperidine, morphine, tetracaine, procaine, and vancomycin. Methylparaben, a common preservative agent, should be avoided as well. Nevertheless, sodium thiopental, succinylcholine and vancomycin have been used previously in patients with mastocytosis without adverse effect.[3] These uncomplicated case reports most likely reflect the wide spectrum of the disease and these agents should be avoided unless specifically indicated.[3]

If general anesthesia for emergency Cesarean section is necessary, anesthesiologists should try to avoid histamine-releasing drugs, a neonatologist should be present, and the resuscitation cart should be in the operating room. Propofol and etomidate are good choices for induction, while rocuronium can replace succinylcholine if there are no concerns about the airway. Remifentanil has been shown to be safe for the mother and newborn[18] and could be used pre- or postdelivery as deemed necessary. Fentanyl is a good choice for pain control after delivery as long as pruritus and scratching are well controlled.

The patient in this case report tolerated well *iv* fentanyl in early labour. The use of fentanyl in the spinal canal may be questioned since intrathecal fentanyl has been known to produce pruritus.[19–22] While the incidence of pruritus was related to the intrathecal dose of fentanyl in one study,[22] this was not the case in another.[21] However, both studies showed pruritus to be common at intrathecal doses as low as 5 or 10 μg (33–75%).[21,22] The severity of pruritus, however, does not seem to be related to the dose.[21,22]

The duration of pain relief with intrathecal fentanyl is directly related to the dose up to 25 μg[21] and, because lidocaine is a short-acting local anesthetic, it was decided to maximize the duration of pain relief at the expense of some probable but manageable pruritus.

Paradoxically, since the patient was stable with moderate pruritus after the spinal, and because pru-

ritus has been described with epidural fentanyl in a pregnant patient with urticaria pigmentosa,[15] it was decided not to exacerbate the situation and to avoid fentanyl in the epidural infusion.

Antihistamine prophylaxis was not administered to the patient in a timely fashion prior to the Cesarean section. There was only a short time between the time of the decision to perform a Cesarean section and the surgery because of changes in the fetal heart rate tracings. In retrospect, the decision to give antihistamine prophylaxis should have been made in collaboration with the obstetrical team, and the patient should have received regular doses during her entire labour.

The partial failure of epidural lidocaine for the Cesarean section may have been due to a patchy block, adequate for labour but not for surgical incision. Most likely however, lidocaine tachyphylaxis may have developed in this patient. Tachyphylaxis to local anesthetic agents, including lidocaine, has been described previously.[23–25] Furthermore, postoperative pain control was more or less adequate with epidural lidocaine, so much so that fentanyl had to be added to the infusion solution. This also indicates that tachyphylaxis may have been present.

In conclusion, patients with urticaria pigmentosa should be considered at risk of systemic mastocytosis. In pregnancy, these patients represent a particular challenge for anesthesiologists in the management of labour and possible Cesarean section. Improper allergy testing can complicate the management of such cases. When alternatives are available, intrathecal opioids should probably be avoided, and if general anesthesia is necessary, histamine-releasing drugs should be avoided as much as possible. Anesthesiologists need to collaborate closely with the obstetrical team for the timely administration of prophylactic medications. Finally, as a preventive measure, resuscitation equipment should be available for the duration of labour, delivery and postpartum period to treat unanticipated hypotension and shock.

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