Anesthetic management of a parturient with Ehlers Danlos syndrome type IV

[L'anesthésie d'une parturiente atteinte du syndrome d'Ehlers Danlos de type IV]

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Purpose: To describe the anesthetic management of a parturient with Ehlers Danlos syndrome (EDS) type IV.

Clinical features: A 29-yr-old pregnant woman with EDS type IV was seen in the Obstetric Anesthesia Pre-assessment Clinic at 30 weeks gestation. She had a history of vertebral artery dissection, resulting in a transient neurological deficit at 22 yr of age. She had a normal vaginal delivery with continuous epidural analgesia for the delivery of her first child at 27 yr of age, before the diagnosis of EDS was made. Recent fibroblast culture demonstrated the production of abnormal procollagen type III, which is pathognomonic for EDS type IV. The patient and obstetrician preferred a repeat vaginal birth with instrumental delivery in the second stage. Analgesia for labour and delivery was provided with a continuous epidural infusion of ropivacaine and fentanyl. She delivered a healthy female infant with the use of outlet forceps, without complications.

Conclusion: A pre-delivery, multidisciplinary, individualized management plan is required in patients with EDS, a rare disease with variable clinical features. In the case described, continuous epidural analgesia was effective and associated with excellent maternal and fetal outcomes.

Objectif : Décrire l'anesthésie réalisée pour une parturiente atteinte du syndrome d'Ehlers Danlos (SED) de type IV.

Éléments cliniques : Une femme de 29 ans, enceinte, atteinte du SED de type IV a été examinée à l'Obstetric Anesthesia Pre-assessment Clinic à 39 sem de grossesse. À l'âge de 22 ans, elle avait été victime d'une dissection de l'artère vertébrale, suivie d'un déficit neurologique transitoire. Elle avait eu un accouchement normal par voie vaginale sous analgésie épidurale continue à la naissance de son premier enfant à 27 ans avant que le diagnostic de SED ne soit posé. Une récente culture de fibroblaste a démontré la production de procollagène anormal de type III, ce qui est pathognomonique du SED de type IV. La patiente et l'obstétricien ont préféré une seconde naissance par voie vaginale avec l'utilisation d'instruments pendant le deuxième stade du travail. L'analgésie pour le travail et l'accouchement a été

fournie par une perfusion épidurale continue de ropivacaine et de fentanyl. La patiente a donné naissance à une petite fille en bonne santé, sans complications avec l'application de forceps à la partie basse.

Conclusion : Un plan de traitement pré-accouchement, multidisciplinaire et individualisé est nécessaire pour les patientes atteintes du SED, une maladie rare aux caractéristiques cliniques variables. Dans le cas présent, l'analgésie épidurale continue a été efficace et associée à des résultats positifs pour la mère et l'enfant.

EHLERS Danlos syndrome (EDS) is a group of inherited connective tissue disorders, which are characterized by the production of abnormal procollagen and collagen. We report the uneventful labour and instrumental vaginal delivery of a parturient with EDS type IV, utilizing a continuous epidural infusion of ropivacaine and fentanyl for pain relief.

Case report

A 29-yr-old woman was referred to the Obstetric Anesthesia Pre-assessment Clinic by her obstetrician, during the second trimester of her third pregnancy, for advice regarding anesthesia management during labour and delivery. She had previously been diagnosed with EDS IV, spina bifida occulta at L5 and mild asthma.

She originally presented at 22 yr of age with a history of left-sided neck pain, right-sided facial paresis, ptosis and unsteady gait. This was found to be due to localized vertebral artery dissection. She was prescribed warfarin *po* for anticoagulant therapy, which was substituted with acetyl salicylic acid (ASA) after six months. She did not receive any further diagnostic testing or genetic counseling at this time.

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She received continuous epidural analgesia during labour for the uncomplicated spontaneous vaginal delivery of her first child five years after this event. There were no complications associated with epidural insertion and no neurological sequelae. Subsequently, her 32-yr-old, first paternal cousin developed a dissecting abdominal aortic aneurysm. This raised the possibility of an inherited connective tissue disorder. She was referred for further diagnostic investigation. Fibroblast culture demonstrated the production of abnormal type III collagen. However, her genotype did not correspond with any of the known mutations in the gene for procollagen III (COL3A1).

Her asthma was not symptomatic during the pregnancy, and there was no neurological deficit associated with the spina bifida at L5. She reported easy bruising and slow healing associated with prominent scar formation. She had previously received several uneventful general anesthetics, and had no family history of complications with general anesthesia. She was receiving enteric-coated ASA 325 mg daily and had no drug allergies. On physical examination, she had a long narrow nose, slightly tight facial skin and a pointed chin. She had long thin fingers and hyper-extensibility of the fingers and elbows. Her blood pressure was normal. Examination of the airway revealed a Mallampati grade 2 oro-pharyngeal view, full dentition and good neck movement. Neurological examination was normal. Coagulation studies (prothrombin time, activated partial thrombin time, platelet count, protein C, protein S and anti-thrombin III) performed in the second trimester were all within normal range. Bleeding time was not performed.

She presented to the labour and delivery unit at 41 weeks gestation for induction of labour. Vaginal examination revealed that the cervix was 4 cm dilated. An amniotomy was performed to induce labour. One hour later, when labour was established, a 20 G Portex® (Keene, NH, USA) polyurethane epidural catheter was inserted at the L2–L3 interspace, using a midline approach, with a 16 G Tuohy needle and a loss of resistance to air technique. Analgesia was initiated with three incremental doses of 3 mL lidocaine 1.5% with 1:200 000 epinephrine and was maintained by continuous infusion of ropivacaine 0.1% with 2 µg·mL⁻¹ fentanyl at 15–20 mL·hr⁻¹. Labour progressed uneventfully and a live female infant was delivered 12 hr later using outlet forceps with no maternal effort. There was no significant perineal trauma. Mother and baby were discharged on the third postpartum day after an uneventful hospital stay.

Discussion

EDS

EDS is a heterogeneous group of inherited diseases characterized by abnormal procollagen and collagen production. There are nine variants of this syndrome, with considerable variation in clinical features and prognosis. EDS IV is also known as the vascular, ecchymotic or Sack Barabas EDS and is characterized by the production of abnormal type III procollagen. The diagnosis of EDS type IV is made on the basis of four clinical criteria: easy bruising, thin skin with visible veins, characteristic facial features and rupture of an artery or a hollow viscus.¹ There is no treatment for the condition. Vessel walls, the bowel and uterus are all rich in type III collagen. Therefore, these patients are at increased risk of arterial rupture and false aneurysm formation, bowel and uterine rupture. The abnormal vessel wall predisposes to easy bruising. Coagulation is usually normal, although abnormal platelet function and coagulopathy have been described in some patients with EDS IV.^{2,3}

At least 72 different mutations in the gene that codes for type III collagen (COL3A1) have been recognized.¹ There may be deletions⁴ or substitutions in the gene.^{5,6} The condition is inherited in an autosomal dominant manner, although up to one third of the mutations occur spontaneously. No single genotype is associated with one clinical picture.^{1,5} The diagnosis of EDS IV is confirmed in the laboratory by dermal fibroblast culture. The fibroblasts produce abnormal type III procollagen which is secreted in reduced amounts, causing swelling of the endoplasmic reticulum. The structurally abnormal collagen is less thermally stable and its secretion is reduced at 37°C. Secretion of the abnormal collagen is increased at 32°C. The increase in abnormal extracellular constituents at lower temperatures is thought to account for the more pronounced skin changes in cooler areas of skin.⁷

Complications of EDS IV

Patients with EDS IV have a reduced life expectancy; median survival is 48 yr of age. Complications in childhood are infrequent, but 25% have experienced a complication by 20 yr of age.¹ More than 80% of patients with EDS IV have experienced at least one complication by the age of 40.¹ The most frequent cause of death is arterial rupture.¹

Pregnancy related complications of EDS IV

A recent review¹ described the outcome of 183 pregnancies in 81 women. There were 167 live-born infants and 12 peripartum maternal deaths. Five par-

turients died in labour of uterine rupture, two of vessel rupture at delivery and five of vessel rupture after delivery. An earlier study, by Rudd *et al.*,⁸ identified a maternal mortality rate of 25% among patients with EDS IV. Georgy *et al.*⁹ described a parturient with EDS that developed a large central perineal tear after active pushing during second stage of labour without epidural analgesia.

Planned management for delivery

There is little information regarding preferred mode of delivery for these women.^{1,8-12} A vaginal delivery exposes the parturient to the risk of uterine rupture during labour. The increase in blood pressure associated with painful contractions and increased intra-abdominal pressure, particularly during the second stage of labour with valsalva manoeuvres, may alter the vascular transmural pressures and therefore predispose to vessel damage and subsequent rupture. Instrumental vaginal delivery may cause perineal trauma and bleeding. Continuous electronic fetal monitoring is recommended during labour, to ensure fetal well-being, because of the increased risk of uterine rupture.

Cesarean delivery may be associated with increased risk of perioperative hemorrhage.¹⁰ Wound healing may be impaired, and there is an increased likelihood of wound dehiscence. Administration of 1-desamino-8-D-arginine vasopressin (DDAVP) prior to Cesarean delivery has been described in a woman with EDS IV to enhance coagulation.¹²

In that case, the DDAVP was given after consultation with a hematologist, despite a normal coagulation profile, because of an increased bleeding tendency, the patient having developed hemarthrosis following a trivial fall and subconjunctival hemorrhage after sneezing. We elected not to administer DDAVP to our patient prior to the epidural catheter insertion because coagulation studies were within normal limits and there was no history or signs of increased bleeding tendency.

The choice of anesthesia for a Cesarean delivery is controversial. General anesthesia exposes the parturient to the risk of aspiration and difficult tracheal intubation. Some patients with EDS IV have an unstable cervical spine,¹³ which would make laryngoscopy and intubation hazardous. The hypertensive response to intubation may predispose to vessel wall damage because of the increased intraluminal pressure. Neuraxial techniques using epidural anesthesia and combined spinal-epidural anesthesia may be associated with an increased risk of epidural hematoma formation because of catheter insertion in a patient with increased fragility of the epidural veins. However, both techniques offer the advantage of extending the

anesthesia for the duration of the surgery and thus avoiding conversion to general anesthesia. The Portex® polyurethane catheters used at our institution are more flexible than nylon catheters, thus minimizing the risk of intravascular placement.¹⁴

Subarachnoid block with a small gauge needle (e.g., 27 g) minimizes the risk of bleeding within the epidural space, but the surgery for Cesarean delivery may be protracted because of bleeding and difficulty in securing hemostasis. The finite duration of spinal anesthesia may make this technique inappropriate.

The obstetrician and patient had proposed vaginal delivery with the use of outlet forceps to prevent pushing in the second stage of labour. This was felt to be more appropriate than elective Cesarean delivery because she had undergone an uneventful vaginal delivery for her first child, before the diagnosis of EDS IV was made. The patient was anxious to receive epidural pain relief for this delivery, since she was very satisfied with epidural analgesia previously. However, we also discussed other pain management options with her during the consultation in the Obstetric Anesthesia Pre-assessment Clinic. It was our opinion that the benefit of epidural analgesia would outweigh the potential risks associated with epidural catheter insertion. Epidural analgesia would reduce the likelihood of hypertension associated with painful uterine contractions and reduce the urge to push during the second stage of labour. Epidural analgesia would also provide pain relief and perineal relaxation for vaginal delivery.

In summary, we have described the anesthetic and obstetric management of a patient with EDS IV using continuous epidural analgesia for labour and instrumental vaginal delivery, with excellent maternal and fetal outcomes. EDS IV is a rare disease with variable clinical features; hence the obstetric and anesthetic management should be individualized.

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