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Anesthetic Management for Ehlers-Danlos Syndrome, Hypermobility Type Complicated by Local Anesthetic Allergy: A Case Report

Authors' Contribution:
Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
Literature Search F
Funds Collection G

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Conflict of interest: None declared

Patient: Female, 22
Final Diagnosis: Ehlers-Danlos syndrome • hypermobility type
Symptoms: Pregnancy
Medication: —
Clinical Procedure: Cesarean section
Specialty: Anesthesiology

Objective: Unusual clinical course
Background: Ehlers-Danlos syndrome, hypermobility type is characterized by increased extensibility, permeability, and fragility of the affected cartilaginous tissues, including the trachea, larynx, and skin. Anesthetic considerations for patients with this syndrome include intubation difficulties secondary to the collapse of fibro-elastic tissues in the trachea and a reported resistance to local anesthetics.
Case Report: Our patient was a 22-year-old G4P0030 woman with a history of morbid obesity, seizures, Barrett's esophagus, hypermobility being evaluated for Ehlers-Danlos syndrome, and anaphylaxis to an unknown local anesthetic who was scheduled for cesarean delivery. She refused allergy testing. After rapid-sequence induction of general anesthesia, video laryngoscopy facilitated endotracheal intubation. Delivery and recovery were uneventful for the mother and child.
Conclusions: No guidelines for neuraxial or general anesthesia exist for patients with Ehlers-Danlos syndrome, hypermobility type. Increased rates of cervical spine instability and local anesthetic resistance have been reported in this population and should be considered when developing the anesthetic plan.

MeSH Keywords: Anesthesia, Local • Anesthesia, Obstetrical • Ehlers-Danlos Syndrome

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Background

Ehlers-Danlos syndrome (EDS) is a group of connective tissue disorders characterized by mutations in the genes encoding fibrillar collagen or enzymes related to the post-translational modification of collagen [1]. This results in increased extensibility, permeability, and fragility of the affected tissues. Beighton et al. [2] described diagnostic criteria for six distinct EDS subtypes based on the spectrum of tissue involvement; of these, the hypermobility subtype (EDS-HT) is the most common. EDS-HT is defined by skin hyperextensibility and generalized joint hypermobility (major criteria), as well as recurring joint dislocations, chronic joint pain, and a positive family history (minor criteria). A heritable, autosomal dominant collagen gene mutation has been implicated in the pathogenesis of EDS-HT [2]. Although the specific gene responsible for this subtype is unknown, it appears to affect the cartilaginous tissues of the trachea, larynx, and skin. As such, the syndrome presents a unique set of anesthetic challenges. Intubation difficulties can arise secondary to the collapse of fibro-elastic tissues in the trachea. Additional issues relevant to anesthetic care include difficult vascular access and positioning secondary to skin hyperextensibility and fragility, as well as a reported resistance to local anesthetics [3,4].

Although EDS is relatively common, with an incidence of approximately 1 in 5000, no specific recommendations for anesthetic management exist [5]. Some sources advocate the avoidance of neuraxial anesthesia for obstetric patients with EDS due to risk of local anesthetic resistance, but successful cases have been reported [1,3,4,6]. This case report presents the effective anesthetic management of an obstetric patient presumed to have EDS-HT in addition to a local anesthetic allergy. The patient has provided written consent to publish this case report.

Case Report

A 22-year-old G4P0030 woman with a history of morbid obesity (BMI 39), seizures, Barrett's esophagus, joint hypermobility, and anaphylaxis to an unknown local anesthetic was scheduled for elective cesarean delivery at 39 weeks gestation at Penn State Health Milton S. Hershey Medical Center. Upon further questioning during her pre-operative appointment, she could only recall that she "stopped breathing" following administration of local anesthetic for a dental procedure, and she had never received local anesthetic since that time. Her hypermobility syndrome was being evaluated for EDS-HT; her family history was positive for a sister with EDS-HT. The patient's history was also significant for postural hypotension, chronic pain, heroin addiction, bipolar disorder, and difficult intravenous (IV) access.

After discussion of the risks and benefits of formal allergy testing prior to delivery, the patient ultimately refused this procedure. The risks of general endotracheal anesthesia for cesarean delivery and her comorbidities were discussed, and the patient provided informed consent.

EDS-HT placed her at increased risk for intubation difficulties secondary to potential cervical spine hypermobility or instability, collapse of the fibro-elastic tissues and cartilaginous rings of the trachea with minimal pressure, TMJ dysfunction, and spontaneous pneumothorax. Awake fiberoptic intubation was considered and discussed given these risks, but would have been extremely challenging without local anesthetic, and the patient refused. Pre-operative evaluation revealed ASA class III, Mallampati class II, right non-tender jaw click, and a supple neck with normal range of motion including flexion and extension.

General anesthesia was induced with the IV administration of propofol (250 mg) and succinylcholine (200 mg). Intubation was performed using video laryngoscopy (GlideScope) assisted by cricoid pressure. Neutral neck position was maintained throughout the induction and intubation processes. Following endotracheal intubation, anesthesia was maintained with nitrous oxide and sevoflurane (minimum alveolar concentration 0.9). A healthy male infant was delivered shortly thereafter. Intraoperatively, the patient received fentanyl (75 mcg), ketamine (50 mg), morphine (10 mg), and ketorolac (30 mg) IV for multimodal analgesia. IV midazolam (2 mg) was also given to decrease the risk of distressing hallucinations secondary to ketamine. Rocuronium (10 mg) was used to maintain neuromuscular blockade, which was reversed with glycopyrrolate (0.6 mg) and neostigmine (3 mg) IV. During the procedure, phenylephrine (200 mcg) was administered for transient hypotension. She also received dexamethasone and ondansetron (4 mg each) IV for post-operative nausea and vomiting prophylaxis. IV oxytocin (40 units) was given to improve uterine tone. Estimated blood loss was 800 mL. The patient was extubated and transported to the post-anesthesia care unit, where she recovered uneventfully.

Discussion

Pregnancy places EDS-HT patients at increased risk for obstetric complications related to increased stress on abnormal connective tissues. Augmented laxity of the joints, skin, and other connective tissues at baseline is worsened by the increased weight of pregnancy; this can lead to nerve impingement secondary to hypermobile facet joints of the spine, separation of the pubis symphysis during labor, or pre-term delivery secondary to an incompetent cervix [6,7]. Uterine prolapse also occurs with higher frequency in EDS-HT patients during the

post-partum period [6]. Dysautonomia in the form of postural orthostatic tachycardia syndrome (POTS) is particularly common in EDS-HT patients. Orthostatic hypotension usually occurs secondary to abnormal aortic baroreceptor responses and can cause dizziness, nausea, palpitations, fatigue, and tachycardia. During labor, these symptoms are worsened by pain and stress. Additionally, neuraxial anesthesia necessarily results in peripheral vasodilation and hypotension, thus worsening the dysautonomia and furthering hemodynamic instability [8]. Despite these potential complications, pregnancy and delivery appear to be relatively safe in EDS-HT patients compared to patients with other forms of EDS [7].

Endotracheal intubation can be challenging in EDS-HT patients. Difficulties can arise secondary to collapse of the tracheal cartilage or joint hypermobility with respect to the cervical spine instability, and TMJ dysfunction in particular. The application of cricoid pressure in the backward, upward, and rightward directions is frequently used during direct laryngoscopy to aid in visualization of the vocal cords. In a patient with EDS-HT, however, even a minimal amount of pressure may occlude the trachea and further obscure the view. Mechanically ventilated EDS-HT patients are at higher risk of orolaryngeal hematomas and spontaneous pneumothoraxes secondary to increased airway pressures [4]. Cervical spine examination with flexion and extension x-rays are generally sufficient to rule out instability. When available, this can facilitate intubation by allowing for normal manipulation of the cervical spine rather than a requirement to maintain a neutral spine position throughout the process. Patients predisposed to ligamentous laxity, such as those with EDS-HT, are at increased risk of TMJ dislocation. TMJ dislocation can occur when the mandibular condyle prolapses anteriorly during the jaw thrust maneuver necessary for direct laryngoscopy. When the mouth is opened widely, the supportive ligaments are at their highest level of laxity [9]. Generally, these complications can be minimized, but not eliminated, with the use of video laryngoscopy, intubating laryngeal mask airway devices, or fiberoptic bronchoscopes.

In this case, general anesthesia was utilized instead of neuraxial anesthesia due to the patient's reported allergy to local anesthetics, as well as the reported potential for local anesthetic failure in EDS-HT patients. Sood et al. found that this risk can be as high as 1 in 3 [3]. Other studies have found that EDS-HT patients can obtain total analgesia from intradermal lidocaine injection, but the effects do not last as long as in patients without EDS-HT despite the use of epinephrine for vasoconstriction. The underlying mechanism for the shorter duration of local anesthetic effect could be swift removal of the anesthetic from the dermis, most likely via vascular uptake and leakage through highly permeable connective tissues. These patients frequently report a history of anxiety and pain secondary to inadequate analgesia during minor

procedures [10]. Hakim et al. asked a group of hypermobile patients the following question: "If you have ever had a local anesthetic injection (dentist/minor surgery/epidural), did you think that it was as effective as it should have been?" Fifty-eight percent of patients answered in the negative compared to 21% of control subjects [11,12]. Previous cases of successful local and neuraxial anesthetic use have been described, however, and it appears that the success of these interventions varies greatly on a case-by-case basis [4,6,13]. When neuraxial anesthesia is selected for patients with EDS, it is probably best to use either a combined spinal epidural or epidural catheter in order to allow for additional doses of local anesthetic to be administered in case of local anesthetic resistance.

No specific guidelines or indications for specific general anesthetic techniques exist with regard to patients with EDS-HT. Local anesthetics, volatile anesthetics, nitrous oxide, total intravenous anesthesia, depolarizing agents, and non-depolarizing agents are all assumed to be safe and effective unless an additional contraindication exists. Recommendations for local anesthesia are similarly lacking. Dolan et al. published "general recommendations for the anesthetic management of patients with Ehlers-Danlos syndrome" in 1980 [4], but these were non-specific to the type of EDS involved. More recent updates, notably by Wiesmann et al. [1], have made improvements, but do not provide details concerning pharmacologic options. In patients undergoing sub-umbilical surgeries, the combined spinal epidural technique, with the addition of morphine to bupivacaine, has been shown to enhance the efficacy of the neuraxial blockade and allow for fine titrations to a desired sensory level [14]. Similarly, in elderly patients, adjuvants such as epinephrine and clonidine have been shown to prolong the duration of spinal or regional blockade [15]. It is possible that similar strategies could be effective in EDS-HT patients, but further studies are needed to explore these options.

Conclusions

No guidelines for neuraxial or general anesthesia exist for patients with Ehlers-Danlos syndrome, hypermobility type. Increased rates of cervical spine instability and local anesthetic resistance have been reported in this population and should be considered when developing the anesthetic plan. If a local anesthetic resistance is identified, the combined spinal epidural technique and/or pharmacologic neuraxial adjuvants such as epinephrine and clonidine may provide an alternative solution, but more research is needed to explore these options.

Conflicts of interest

None.

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