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Case Report

DILEMMAS ABOUT THE SELECTION OF ANESTHESIA FOR ELECTIVE CESAREAN SECTION IN PREGNANT WOMEN WITH MYOTONIC DYSTROPHY TYPE 2 AND SUSPECTED von WILLEBRAND DISEASE: A CASE REPORT

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SUMMARY – With advancement of medicine in the field of diagnostics and treatment of women suffering from certain genetic disorders, more and more women have attained reproductive age and desired fertility. Maintaining pregnancy, as well as bringing it to an end poses a real challenge not only for obstetricians, but also for anesthesiologists involved in the procedure. In our case report, we describe anesthetic management of a female patient suffering from myotonic dystrophy type 2 and suspected von Willebrand's disease, and undergoing elective cesarean section. It is acknowledged that both diseases have their own peculiarities and specificities related to anesthesia and require careful consideration when it comes to selecting it. Bearing in mind the advantages and disadvantages of certain types of anesthesia, we believe that in this case, general anesthesia was a better choice compared to the regional techniques of anesthesia.

Key words: *Pregnancy; Myotonic dystrophy; von Willebrand disease; Anesthesia; Cesarean section*

Introduction

When considering the finest possible treatment algorithm it is necessary to evaluate presentation of a particular disease and its effect on different organic systems. Namely, myotonic dystrophy (MD) belongs to a family of heterogeneous genetic disorders where mutation in chlorine channels results in progressive muscle weakness that is followed by both voluntary and involuntary muscle contractions. MD is a chronic, slowly progressive disease with multisystem repercussions[1-3]. Its onset depends on the type of MD; MD1 is considered to be by far more common than MD2, with earlier onset and more severe clinical picture[4]. According to the variability of MD1 presentation, patients can suffer from mild MD1, which is characterized by minor myotonia, cataracts and normal life span, or classical MD, which is characterized by pronounced muscle weakness and cardiac conduction abnormalities. MD type 2 can be associated with physical limitations and shortened life span. MD should be suspected in individuals based on the symptoms, after which molecular genetic testing is performed to confirm the diagnosis[5,6].

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Comparable with MD, von Willebrand's disease (vWD) is also a genetically and clinically heterogeneous disorder, where diagnosis and management are challenging for a physician[7]. It is caused by qualitative or quantitative abnormalities of von Willebrand's factor (vWF), a plasma protein that mediates platelet adhesion and stabilizes coagulation factor VIII (FVIII), thus impairing primary hemostasis[8]. Three major types of vWD have been described: (1) partial quantitative vWF deficiency; (2) qualitative vWF defects; and (3) virtually complete vWF deficiency[9]. It may also occur as an acquired disorder (von Willebrand's syndrome) in patients with malignancies, autoimmune diseases, or with certain medications[7]. Depending on the vWD type, symptoms may vary from spontaneous hemorrhage (usually nosebleeds, bruising, menorrhagia) to modest or heavy bleeding associated only with medical procedures or injuries[10].

In this report, we present a case of a 27-year-old pregnant woman with MD2 and suspected vWD, scheduled for elective cesarean section under general anesthesia.

Case Report

A 27-year-old, type O RhD positive woman at 23/24 weeks of gestation was admitted to Department of Gynecology and Obstetrics for observation because of her past medical history. She was diagnosed with MD2, and so were her three sisters. At a younger age, she underwent muscle biopsy. During the procedure, which was performed under general anesthesia, she had a severe adverse reaction to inhalation anesthetics.

At the age of 26, she underwent total thyroidectomy due to papillary carcinoma. Abnormal bleeding was recorded afterwards. She also reported an episode of abnormal bleeding following tooth extraction. As she stated, vWD tests were performed and revealed a slightly reduced vWF activity level. No medical records were available.

During her hospital stay, she was seen by a neurologist because of deteriorating muscular weakness. A hematologist was consulted due to her bleeding diathesis, as well as a cardiologist and an endocrinologist to optimize her cardiac and hormonal status. Routine preoperative laboratory investigations were unremarkable. Due to her bleeding diathesis, additional coagulation tests were performed. Investigations revealed increased FVIII activity (175% activity, reference range: 70%-150% activity) and von Willebrand ristocetin cofactor test (vWF Ri:Co; >150% activity, reference range: 70%-150% activity).

At 38 weeks of gestation, elective cesarean section was performed because of the expected labor abnormalities related to MD. As suggested by a hematologist, she had desmopressin administered intranasally two days before the planned procedure. Preoperatively, she received ranitidine 50 mg i.v., levothyroxine 100 mcg *per os*, normal saline 1000 mL i.v., and elastic compression stockings. Difficult airway was expected due to her previous neck surgery. General intravenous anesthesia was induced using propofol injection (150 mg). After intubation, rocuronium 30 mg i.v., a short-acting muscle relaxant, was applied. After delivery, sufentanil, an opioid analgesic, up to 25 mcg i.v., was administered. General anesthesia was maintained using continuous propofol infusion (10 mL/h, until reaching the maximal dose of 300 mg) and 50/50 (6 L/min) oxygen and air mixture. Anesthesia was maintained without volatile anesthetics. During the emergence from anesthesia, sugammadex (200 mg) i.v. was administered to achieve quick reversion of the neuromuscular blockade. No residual blockade was observed. The procedure was uneventful. The patient delivered a healthy baby (Apgar score 1' and 5': 9 and 10, respectively). Five days later, the mother and the baby were discharged home.

Discussion

Women with an inborn coagulopathy also suffering from an ongoing neurological condition present a substantial challenge during pregnancy and in the peripartum period[1]. There were several modalities we had to take in consideration, with first decision being made upon what type of delivery would be optimal to perform. Chung *et al.* specified the complications related to natural birth in patients with MD. During prolongation of the first labor stage, as well as poor voluntary effort in the second stage, the inability of the uterus to contract after delivery was well recognized due to inadequate response of the uterine and abdominal musculature[2]. The data presented clearly addressed the risks underlying natural childbirth and we decided to perform elective cesarean section.

In the subsequent stage, great importance of appropriate preoperative anesthesiologic evaluation was emphasized, in order to achieve an optimal psychophysical condition of a patient undergoing surgery, as well as to decide on the preferable kind of anesthesia.

According to Argov and de Visser, general anesthesia is expected to have an increased risk of postoperative pulmonary complications in patients with MD[11]. On the other hand, Ferschl *et al.* from the Myotonic Dystrophy Foundation state that there are case reports which describe shivering sufficient to stimulate myotonic contractures with neuraxial anesthesia, as well as incomplete blocks in patients with MD[12]. The reviewed data indicated that in a parturient suffering from MD2, regional anesthesia had an advantage over general anesthesia[13,14].

Of equal importance for every anesthesiologist is understanding the impact that vWD has on the safety profile of the anesthetic techniques. With an overall risk of epidural or spinal hematoma after neuraxial anesthesia in the obstetric population estimated at 1:168 000 and an increased incidence of anesthesia-related spinal hematoma in parturient with coagulopathies (68%), it is not surprising that anesthesiologists are often hesitant to administer neuraxial anesthesia to patients with vWD[15-17]. Although there are numerous case reports that demonstrate the safe use of neuraxial anesthesia in this population, guidelines based on well-controlled trials cannot be offered[18]. This was supported by the described complications related to the use of neuraxial anesthesia in patients with hemorrhagic diathesis, where the occurrence of hematoma with consequential spinal lesions emerged in several cases due to the unreliable interpretation of coagulation tests in pregnancy[19-21].

Given the incidence of vWD along with MD, the preoperative plan on the prophylactic care for possible peripartum or postpartum hemorrhage was correspondingly considered. Excessive bleeding is not only a problem in patients suffering from coagulopathy, but postpartum bleeding is the leading cause of women's morbidity and mortality globally[22-24].

As indicated in the study by Govorov *et al.*, women with vWD appear to show a significantly increased incidence of postpartum hemorrhage compared to healthy controls, putting aside that the quantity of FVIII and vWF increase during pregnancy[25].

In pregnancy, the activity of both FVIII and vWF can increase by 200%-375%, which is in support of our findings where 175% FVIII activity, >150% vWF:RCo activity, and 194x10^9/L platelets were found (Table 1). Despite the increased coagulation activity, parturients who present with known bleeding disorders or bleeding history according to Sood *et al.* are still at an increased risk of bleeding complications during pregnancy, in labor, and postpartum, as the true integrity rests in the fact that their mutations are qualitative in nature[26,27].

Taking into consideration our patient's bleeding history and inconclusive coagulation tests, we could have only suspected vWD as a diagnosis. For a precise diagnosis of coagulation disorders, it is important to undergo genetic testing in order to estimate the type of vWD. The exact diagnosis of the vWD type would reduce the risk of surgery and define the possibility of child inheritance.

No less important is to emphasize that the increased vWF levels caused by pregnancy usually return to baseline within 4-6 weeks after delivery, hence extended care should be taken in women with vWD[28].

Table 1. Preoperative laboratory findings

RBC count (4.2-5.5x10^{12}/mL)	Hemoglobin concentration (115-150 g/L)	Hematocrit level (37%-47%)	Platelet count (140-450x10^9/L)	WBC count (4-11x10^9/L)
3.8	118	38	194	15.1

Values are expressed as mean; RBC = red blood cell; WBC = white blood cell

PT (11-13.5 s)	PT INR <1.25	aPTT (25-38 s)	TT (9-35 s)	Fibrinolysis (150-210 min)	Plasminogen (70%-150%)	vWF:Rco (70%-150%)
13.4	0.84	27	14	210	>175	>150

Values are expressed as mean; PT = prothrombin time; INR = international normalized ratio; aPTT = activated partial prothrombin time; TT= thrombin time; vWF:RCo = von Willebrand ristocetin cofactor test

Considering the abovementioned, the three main approaches to the treatment of vWD in peripartum period would include increasing plasma concentration of vWF through stimulation of endothelial cells with desmopressin (DDAVP); replacing deficient vWF with human plasma-derived concentrates; and promoting hemostasis using hemostatic agents with mechanisms other than increasing vWF[29]. Despite the fact that guidelines based on well-controlled trials could not be offered, close follow-up performed by Chi *et al.* suggested the benefits of using desmopressin. It was stated to be safe and effective in preventing significant bleeding during delivery in most women with vWD, with a very low rate of immediate and late bleeding complications in such women[30].

The abovementioned severe side effects incurred after admission of inhalation anesthetics and succinylcholine in patients suffering from MD2 were one of the guiding principles in the process of choosing a proper combination of anesthetics for the surgery. Indeed, many researchers point out that there is considerable occurrence of malignant hyperthermia while utilizing both the inhalation anesthetics and/or succinylcholine, a representative of depolarizing neuromuscular blocker[31-34]. Namely, malignant hyperthermia is a genetic disorder that manifests itself in the hypermetabolism of the body, in which metabolic acidosis and hyperkalemia are accompanied by muscle rigidity which if not taken care of results in rhabdomyolysis of muscles and respiratory failure[35-40]. Taking into account all of the possible complications that may occur, the administration of succinylcholine and volatile anesthetics has been vigorously contraindicated[41,42].

When we considered the selection of neuromuscular blocker reversal, sugammadex was shown to be beneficial, although much more expensive, due to its strength, whereas neostigmine proved to be weaker with underlying muscarine side effects. Subsequently, in some cases, severe adverse effects were observed following the administration of neostigmine in patients with MD[43].

Conclusion

Considering the serious situation regarding the presumed range of possible complications, we re-evaluated the anesthesiologic approaches from the available literature and developed detailed anesthesiologic framework for performance of elective cesarean section in a parturient with MD and vWD.

Anesthetic management in this specific case presented quite a challenge. An unpredictable response to drugs used in general anesthesia and serious perioperative complications in patients diagnosed with MD have been described. However, in our case, we opted for general anesthesia due to suspected vWD and the associated increased risk of spinal and epidural hematoma. A multidisciplinary approach and careful planning proved to be essential for a successful perioperative management in this particular situation.

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Sažetak

DILEME OKO IZBORA ANESTEZIJE ZA ELEKTIVNI CARSKI REZ U TRUDNICA S MIOTONIČNOM DISTROFIJOM TIP 2 I SUMNJOM NA von WILLEBRANDOVU BOLEST: PRIKAZ SLUČAJA

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Napretkom medicine u dijagnostici i liječenju određenih genetskih poremećaja sve više žena postiže reproduktivnu dob i željenu plodnost. Očuvanje trudnoće kao i njen završetak predstavlja pravi izazov ne samo za opstetričare, nego i za anesteziologe uključene u skrb takvih bolesnica. U našem slučaju prikazujemo anestezijski postupak za elektivni carski rez kod trudnice koja boluje od mišićne distrofije tipa 2 i suspektne von Willebrandove bolesti. Poznato je da obje bolesti imaju svoje osobitosti i specifičnosti vezane uz anesteziju te zahtijevaju pažljivo razmatranje oko odabira iste. Razmatrajući prednosti i nedostatke određene vrste anestezije smatramo da je u ovom slučaju opća anestezija bolji izbor u odnosu na regionalne tehnike izvođenja anestezije.

Ključne riječi: *Trudnoća; Miotonična distrofija; von Willebrandova bolest; Anestezija; Carski rez*