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Pregnancy in a Patient with Spinal Muscular Atrophy and Severe Restrictive Lung Disease

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Abstract

Spinal muscular atrophy (SMA) is a rare autosomal recessive neuromuscular disease that is often associated with chronic respiratory failure. Few cases have described the antepartum and postpartum course in patients with severely compromised respiratory status.

We present a case of a 24-year-old nullipara with a history of SMA type II complicated by surgically corrected kyphoscoliosis and severe restrictive lung disease. Her pregnancy was complicated by progressively worsening dyspnea resulting in increased use of noninvasive positive pressure ventilation, ultimately leading to indicated premature delivery at 28 weeks' gestation via cesarean section under general anesthesia.

Women with SMA and severe restrictive lung disease are at high risk of premature delivery secondary to worsening respiratory status. A multidisciplinary approach is vital in treating these patients.

Keywords
- spinal muscular atrophy
- SMA
- pregnancy
- restrictive lung disease

Spinal muscular atrophy (SMA) is an autosomal recessive neuromuscular disease affecting the survival motor neuron 1 (*SMN1*) gene and has an incidence of 1 in 6,000 to 11,000, making it the second most common fatal autosomal recessive disorder.[1] The disease is characterized by progressive proximal muscle weakness and, ultimately, paralysis caused by degeneration of alpha motor neurons in the spinal cord and brain stem nuclei.[1] Historically, the disease has been classified into five subtypes, SMA 0 to IV, from most to least severe. Restrictive lung disease is often a feature of SMA due to weak inspiratory/expiratory muscles, kyphoscoliosis, poor chest wall growth, poor airway clearance, recurrent infection, and nocturnal hypoventilation.[2] Furthermore, the physiologic respiratory strain of pregnancy with increased oxygen demand, increased respiratory load, and decreased lung volumes poses a significant challenge to management and care of the parturient with SMA.[3]

Case

A 24-year-old G2P0010 presented to our practice at $5^{0/7}$ weeks estimated gestational age (EGA) with a highly desired

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pregnancy. She was known to our practice following a missed abortion the year prior requiring office manual vacuum aspiration.

Her medical history included SMA, which she had been diagnosed with at 8 months of age. She subsequently underwent genetic testing which revealed a homozygous deletion of exon 7 on the *SMN1* gene and the presence of two copies of the *SMN2* gene. She had previously established care with a multidisciplinary team of medical specialists including a pulmonologist, neurologist, and cardiologist who continued to follow her throughout the antepartum course.

The patient's prepregnancy status was significant for severely limited mobility requiring a motorized wheelchair, bilateral facial weakness, profound weakness in both the upper and lower extremities, dysphagia necessitating gastric tube feeding, atonic bladder, and the use of noninvasive positive pressure ventilation (NIPPV) due to severe restrictive lung disease. She was started on nusinersen in November 2018; however, self-discontinued when she became pregnant due to the lack of safety data on this medication in pregnancy. She was also markedly underweight at 35 kg with a body mass index of 16 kg/m^2. Her surgical history was significant for kyphoscoliosis with T4-S1 posterior spinal rod fusion at the age of 10 years.

The patient was noted to have a decline in her respiratory status prior to conception. For the past 12 years, the patient had been using NIPPV via home Trilogy ventilator (Philips, Amsterdam) with nasal pillows for at least 8 hours per night. Repeat pulmonary function tests during pregnancy demonstrated a decreased functional vital capacity (FVC) of 13% from 16% a year prior, and a decreased forced expiratory volume in 1 second of 13% from 16% as well. She was maintained on multiple agents for respiratory optimization including fluticasone, umeclidinium, vilanterol, budesonide, dornase alfa, and levalbuterol.

Given her significant respiratory disease, she was offered termination, but decided to continue the pregnancy. Due to her immobility, she was started on prophylactic anticoagulation with enoxaparin. On routine prenatal workup, she was found to have anti-E antibodies, and titers were drawn monthly for monitoring. A multidisciplinary team was assembled including maternal–fetal medicine (MFM), anesthesiology, neonatology, pulmonology, neurology, cardiology, gastroenterology, nutrition, genetics, and social work.

Cardiology evaluated the patient for persistent tachycardia. The workup revealed sinus tachycardia and unremarkable echocardiogram. She was started on metoprolol 25 mg three times daily.

The patient had thorough genetic counseling regarding the autosomal recessive inheritance pattern of SMA. Her partner had SMA carrier screening which indicated the presence of two copies of the *SMN1* gene. She elected to screen for fetal aneuploidy and was found to have low-risk cell-free DNA. She declined diagnostic genetic testing.

MFM recommended advanced directives for the patient as well as gastroenterology and nutritional consults due to her underweight status. Her obstetric plan of care included early anatomy scan, monthly growth scans, and twice weekly antenatal testing starting at 32 weeks. Throughout her pregnancy, her fetal status was stable at the 51st percentile with a normal anatomy scan. Delivery timing and mode were based on maternal respiratory status in the absence of fetal indications. While vaginal delivery is not contraindicated for patients with SMA, cesarean section was selected for this patient, due to concern for respiratory tolerance in labor, pelvic contractures, and inability to provide neuraxial analgesia secondary to prior spinal surgery.

The patient developed worsened dyspnea requiring the use of her Trilogy ventilator mouthpiece throughout the day at $8^{0/7}$ weeks EGA. By $19^{0/7}$ weeks EGA, eating and reclining were severely limited by dyspnea, a noticeable change from baseline. At $24^{0/7}$ weeks EGA, she began using Trilogy mouthpiece for 50% of the day on at least 2 to 3 days of the week.

At $26^{5/7}$ weeks EGA, she was admitted to the medical intensive care unit (MICU) for ongoing pulmonary care and optimization before scheduled cesarean section at $28^{0/7}$ weeks EGA. She was given betamethasone for fetal lung maturity and was transitioned from enoxaparin to subcutaneous heparin. During this period, her blood pressures were labile without entering into severe ranges, leading to the diagnosis of preeclampsia without severe features due to the presence of protein in her urine (though chronicity of her proteinuria was unclear). She was noted to have anemia with hemoglobin of 6.8 g/dL and was transfused one unit of packed red blood cells with an appropriate rise in her hemoglobin, given her upcoming surgery.

Due to the patient's severe upper extremity contractures, a peripherally inserted central catheter was placed preoperatively in the MICU. Her cesarean section occurred in a labor and delivery operating room, under general anesthesia, without incident. The anesthesia team brought the patient into the operating room, where standard American Society of Anesthesiologists monitors were applied. A preinduction radial arterial line was placed for invasive hemodynamic monitoring. A rapid sequence induction was performed, and the patient was intubated with a 6.0-mm endotracheal tube using a McGrath video laryngoscope for a grade I view. After securing the airway, the obstetric team proceeded with the cesarean section via a Pfannenstiel incision and a low transverse incision in the uterus. A male infant was delivered with Apgar scores of 4, 5, and 7 at 1, 5, and 10 minutes, respectively. The infant was transferred to the neonatal intensive care unit for management of sequalae related to prematurity. A Copper intrauterine device (Paragard, CooperSurgical, Trumbull, CT) was placed for birth control. Estimated blood loss was 500 mL. Ultrasound-guided bilateral transversus abdominis plane blocks were performed for postoperative pain control, in addition to intravenous hydromorphone. The patient remained intubated and was transferred to the MICU where she was weaned from the ventilator and extubated within 3 hours. Following extubation, she was placed back on her home Trilogy device. Her postoperative recovery was unremarkable, and she was discharged home on postoperative day 3.

Comment

This is a case of 24-year-old woman with SMA type II and severe restrictive lung disease who underwent a successful pregnancy with medically indicated preterm delivery secondary to worsening pulmonary function. It is known that pregnancy induces unique physiologic alterations in the pulmonary system via different mechanisms. Some of the most significant changes include displacement of the diaphragm secondary to uterine expansion, as well as decreases in expiratory reserve volume and functional residual capacity. Generally, changes in total lung capacity are negligible.[4] Pregnancy is also associated with an increase in ventilatory requirements, creating an increased burden on patients with preexisting pulmonary disease.[5] Our patient exhibited severe restrictive lung disease as evidenced by baseline FVC 13 to 17% of predicted value since 2017. She had been dependent on NIPPV prior to pregnancy, limited to nighttime use. Her FVC remained stable throughout the pregnancy, 0.38 L in the first trimester, and 0.5 and 0.41 L in the second trimester. Throughout the pregnancy, she continued to maintain adequate O_2 saturations ($>$ 93%), although she complained of worsening dyspnea. Her prolonged immobility may have complicated her respiratory status. In a review by Abati and Corti, it was observed that ventilatory insufficiency occurred more frequently in patients who were wheelchair bound.[3] This is likely secondary to a combination of severe kyphoscoliosis and thoracoabdominal muscle weakness.[3] NIPPV support is the cornerstone of treatment for these patients.[6]

In the setting of severely compromised respiratory function and low weight, there was additional concern for fetal growth restriction. She had a growth scan at $24^{5/7}$ weeks EGA which surprisingly showed an estimated fetal weight in the 51st percentile. Generally, neonatal outcomes tend to be favorable in this population, despite prematurity and a complicated intrapartum course.[3,7]

Her dyspnea and increased dependence on the ventilator led to the decision for delivery at $28^{0/7}$ weeks' gestation. The patient was admitted to the MICU in the week preceding delivery for concern for declining respiratory status. The decision was made to forego magnesium sulfate for fetal neuroprotection in the setting of significant maternal risk should she develop pulmonary edema. Premature delivery is a well-known risk in women with SMA with worsening respiratory function being one of the leading causes.[3,7] To some degree, our patient complained of increasingly worsening abdominal and back pain with progression of the pregnancy. She also had labile blood pressures in the days preceding delivery with a spot protein to creatinine ratio of greater than 0.3, raising concern for evolving preeclampsia without severe features.

Although there is no absolute contraindication to vaginal delivery in patients with SMA, cesarean delivery was elected due to concerns about pulmonary status in the supine position and anticipated cephalopelvic disproportion in the setting of pelvic contractures.[8] Vaginal delivery has been reported in other cases mostly with less severe phenotypes (SMA types III and IV) and often with the use of an assisted second stage.[3,7] While a spinal anesthetic is commonly preferred for cesarean deliveries, this patient's surgically corrected kyphoscoliosis made accessing her subarachnoid space difficult. Furthermore, an adequate level of neuraxial anesthesia for cesarean delivery (T4 dermatomal level) could worsen her respiratory status and necessitate emergent intubation. Therefore, cesarean delivery under general anesthesia in a controlled setting was deemed the safest delivery plan for the patient and her fetus.

Important considerations for general anesthesia in patients with neuromuscular disease include assessment of airway accessibility and cervical spine mobility as well as careful selection of anesthetic agents to decrease the risk of residual muscle weakness.[3] Preoperative cardiac evaluation is prudent, as severe pulmonary disease may predispose to cardiac dysfunction.[3] With regard to extubation, periods of close monitoring in the intensive care unit may be required following general anesthesia.[9]

Genetic counseling is an essential part of prenatal care in patients with inherited disease. This patient had undergone a thorough evaluation during a preconception counseling and in early pregnancy.

Pregnant women with SMA may face multiple intrapartum complications with respiratory compromise being one of the leading causes of maternal and neonatal morbidity. In a patient with severe preexisting restrictive disease, it is important to weigh these risks carefully. This case demonstrates the importance of NIPPV in the management of severe restrictive disease to meet the higher demands of pregnancy. Other important clinical considerations such as anesthetic approach, delivery timing, and mode of delivery can equate to large difference in maternal morbidity and mortality. The management of an SMA-affected pregnancy requires the expertise of a multidisciplinary team which is involved earlier in the pregnancy.

Conclusion

Women with SMA and severe restrictive lung disease are at high risk of premature delivery and require a multidisciplinary approach for treatment.

Conflict of Interest
None declared.

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