

PERINATAL/NEONATAL CASE PRESENTATION

Treatment of severe achalasia during pregnancy with esophagoscopy injection of botulinum toxin A: a case report

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A pregnant Thai woman presented with progressive dysphagia starting from the gestational age of 18 weeks. Total parenteral nutrition was administered at 33 weeks of gestation due to severe malnutrition. The fetus was found to be growth restricted. Preliminary diagnosis was esophageal achalasia.

Diagnostic and treatment options, including early delivery followed by surgical intervention, temporizing pneumatic dilation and intrasphincteric botulinum toxin injection, were discussed before endoscopic examination. The patient preferred temporizing treatments to prolong the pregnancy and to allow for an improvement of her nutritional status to facilitate postpartum recovery. Marked dilatation of the esophagus was found during esophagoscopy. Therefore, local injection of 80 U of botulinum toxin A was chosen over balloon dilation. The swallowing function improved soon after the treatment. The patient and the fetus started to gain weight. Subsequent sonographic examinations did not show any evidence of botulinum toxicity in the fetus. The baby was born at 36 weeks of gestation with an active respiration and preserved muscle tones. Breast-feeding was withheld. The patient remained asymptomatic for at least 6 weeks after delivery. There have been reports of an intentional use of botulinum toxin in selected cases of unremitting movement disorder during pregnancy. No deleterious effects to the mothers or the babies were found in local injection with limited dosage after the first trimester. The authors cannot encourage the routine administration of this neurotoxin for the treatment of achalasia during pregnancy. However, this report provides additional information of botulinum toxin use in pregnant women.

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Case report

A 39-year-old Thai pregnant woman, G5P2-0-2-2, was referred to our hospital at 33 weeks of gestation due to progressive dysphagia. The symptom started from 18 weeks of gestation. Her first two

children were delivered by low transverse Cesarean section. On admission, she had lost 9 kg, and severe malnutrition and dehydration were observed. Fetal weight estimation was 1400 g, which indicates fetal growth restriction (10th percentile).¹ Her symptoms were suggestive of esophageal achalasia. Total parenteral nutrition was administered immediately. Diagnostic and treatment options were discussed before endoscopic examination. This included an early delivery of the growth-restricted fetus after steroids administration. The patient could have either definitive or palliative surgical treatments afterward. Temporizing interventions to improve the nutritional status of the fetus and herself were also discussed. The options were pneumatic dilation and intrasphincteric botulinum toxin injection. The temporizing options could prolong the pregnancy, so that the baby would be less likely to suffer from the complications of prematurity. As the route of delivery would be by Cesarean section, the improved nutritional status could also facilitate her recovery. The 2% risk of esophageal rupture after balloon dilation and the unknown effect of botulinum toxin on the fetus were considered. The decision would also then be made according to the esophagoscopy findings. The patient was inclined to choose the temporizing treatment over an early delivery.

The endoscopy showed a marked dilatation of the distal esophagus with a large amount of retained food content. No intraluminal esophageal compression was found. There was no peristalsis detected after mass swallowing. Three small linear mucosal tears were noticed. Multiple mucosal hemorrhagic spots were found at the gastric fundus. The examination through the second part of the duodenum was unremarkable. These findings are consistent with esophageal achalasia. The markedly dilated esophagus made botulinum toxin injection more suitable than balloon dilation. A total of 80 U of botulinum toxin A (Botox, Allergan, Irvine, CA, USA) were injected at 1 cm above the squamocolumnar junction, as shown in Figure 1. The procedure took 30 min without an immediate complication. The patient could take a liquid diet 12 h later. She was discharged 2 days afterward. To monitor the growth-restricted fetus, the patient underwent non-stress test and biophysical profile scoring twice a week. The gross activity and breathing movements of the fetus were reassuring on

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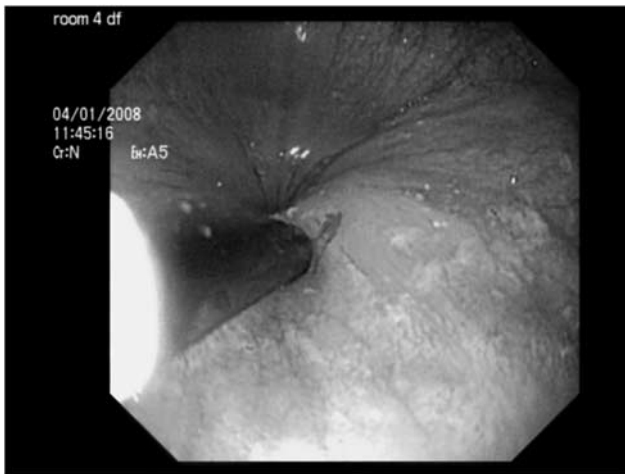


Figure 1 Intrasphincteric injection of botulinum toxin A for the treatment of achalasia during pregnancy.



Figure 2 The growth-restricted, 36-week-old baby born 3 weeks after the intrasphincteric injection of botulinum toxin A in the mother affected with severe esophageal achalasia. Note the preserved muscle tone and active respiration.

every visit. The estimated fetal weight at 35 weeks was 1600 g (10th percentile).¹

The patient gained a total of 5 kg at 36 weeks when spontaneous labor began. An active, 1800-g (10th percentile) female baby was delivered by Cesarean section, as shown in Figure 2.¹ The baby did not express any signs of neuromuscular blockade after close observation for 5 days. Breast-feeding was withheld. The patient's swallowing function was still preserved for at least 6 weeks after delivery.

Discussion

Achalasia is functional esophageal obstruction from loss of motor neurons at the lower esophageal sphincter. During pregnancy, it

could easily be confused with gastroesophageal reflux, and the diagnosis and intervention could have been delayed until the esophagus was remarkably dilated. Severe and persistent vomiting could lead to maternal malnutrition, fetal growth restriction, preterm delivery or fetal demise.² Maternal death has also been reported.³ With a prevalence of eight in a million, this serious disease is not commonly encountered, and evidence-based studies regarding the most suitable treatment during pregnancy are not available.⁴

Diet modification and medical treatment could have been sufficient for a late onset or slowly progressive disease. Minimally invasive procedures, including pneumatic dilation and intrasphincteric injection of botulinum toxin, may provide longer alleviation, at least until delivery. Pneumatic dilation has been a viable option for the treatment of achalasia at any gestational age.⁵ This modality does not pose any risk to the fetus. However, it could be complicated by esophageal rupture, which may require an open surgery.

Botulinum toxin injection can relax the lower esophageal sphincter.⁶ This is a category C medication, and its application should be avoided as far as possible during pregnancy. Treatment with this neurotoxin is justified only when pneumatic dilation is hampered by the markedly dilated esophagus or when the small chance of esophageal rupture is unacceptable to the patient. The patient also has to understand that there are no formal studies regarding the effects of local administration of botulinum toxin to the fetus. With the standard dose for local injection, however, the toxin is not expected to be found in the circulation. It is rather a large molecule (150 000 Da), and a physiologically elevated serum-binding albumin during pregnancy make this toxin unlikely to cross the placental barrier.⁷ Intentional administrations of botulinum toxin during pregnancy have been reported by some authors for selected cases of movement disorders.^{8,9} Anecdotal reports included severe and persistent cervical dystonia that did not respond to conventional medical treatment during pregnancy, and botulinum toxin was intermittently injected intramuscularly with the maximum dosage of 300 U.^{8,9} One patient even received botulinum toxin treatment during all of her four pregnancies.⁸ No deleterious effects to the mother or the fetus were reported if the local injection dosage was between 1.25 and 300 U.¹⁰ The dosage that our patient received was not over this range, and repeated injections were not required. Botulinum toxin use should be strictly prohibited during the first trimester, as there are some references to miscarriages.¹⁰

Theoretically, the administration of this neurotoxin shortly before birth may cause respiratory muscle paralysis in the newborn. The patient was advised that the neonatal resuscitation team would be available at the time of delivery. There has been growing interest in using botulinum toxin as a potent tocolytic agent for patients undergoing fetal surgery.¹¹ Even though the fetus could not improve her weight percentile *in utero*, it did not seem that

botulinum toxin worsened her already established growth restriction. Before this neurotoxin can be more widely used in the pregnant population, it is essential that its potent antidote is available.¹² There have been no studies regarding the excretion of this toxin in breast milk. Even though the blood half-life of botulinum toxin is 230 to 260 min, we decided to withhold breast-feeding.¹³

The authors still cannot encourage the routine use of botulinum toxin in the management of esophageal achalasia during pregnancy. This single case report adds up to the experience of intentional botulinum toxin therapy during pregnancy. Although studies on the safety of botulinum toxin in human fetus cannot be carried out, the physicians who administer botulinum toxin to pregnant women, either intentionally or unintentionally, should be encouraged to report their outcomes.

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