Delivery and postpartum management of a patient with Pompe disease: Case report and review of the literature

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Abstract

Pompe disease is an autosomal-recessive disorder caused by acid alpha-glucosidase deficiency due to mutations in the GAA gene. There are two forms of the disease: infantile-onset Pompe disease and late-onset Pompe disease. The worldwide incidence of both forms of the disease is commonly reported to be 1 in 40,000. Adult patients are affected by limb-girdle muscular weakness and respiratory insufficiency. Enzyme replacement therapy with alglucosidase- α is available since 2006. There is little knowledge about pregnant woman with Pompe disease. These women should be considered as high-risk pregnant women. Here, we aim to present Cesarean delivery and postpartum management of a case with an interrupted enzyme replacement therapy during pregnancy.

Keywords

Perinatal medicine, complications, Pompe disease, delivery, postpartum management

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Background

Pompe disease (PD) is an autosomal-recessive disorder caused by acid alpha-glucosidase deficiency due to mutations in the GAA gene. There are two forms of the disease: infantile-onset PD (IOPD) and late-onset PD (LOPD). The worldwide incidence of both forms is commonly reported as 1 in 40,000.¹ Adult patients are affected by limb-girdle muscular weakness and respiratory insufficiency.² Enzyme replacement therapy (ERT) with alglucosidase- α has been available since 2006.³ There is little knowledge about pregnancy in women with PD. Pregnancies in these patients should be considered high risk. We present the case of a pregnant patient with PD who chose to interrupt ERT during pregnancy.

Case report

A 38-year-old primiparous woman at week 38 of gestation was admitted to our department for delivery. She was diagnosed with juvenile-onset PD at the age of 15 during admission to hospital because of a tick bite. She had chronic myalgia along with worsening weakness and pain in the legs and hip girdle when climbing stairs. Laboratory results showed high AST and ALT levels. The patient underwent muscle biopsy and genetic testing revealed PD.

She had isolated motor deficiency of her proximal leg muscles. After the diagnosis of PD, ERT was initiated. While on ERT treatment, the patient's condition was stable and she remained free of respiratory problems. Before pregnancy, echocardiography demonstrated a normal left ventricular ejection fraction of 69%; forced expiratory volume (FEV1) and vital capacity (VC) were 80% of normal values. The difference between sitting and supine was 12% and 13% for FEV1 and VC, respectively. Apnoea hypopnoea index and oxygen desaturation index were 1, and average saturation was 97% in polysomnographic sleep study. Maximal expiratory pressure and maximal inspiratory pressure were 44 cm H₂O and 48 cm H₂O, respectively. Proximal muscle weakness was revealed (Medical Research Council grade 4/5 upper limb and lower limb).

The patient stopped ERT from the seventh week of gestation because of fear of any adverse fetal effects. Pregnancy was uncomplicated and the fetus was appropriately grown for gestational age.

Fetal well-being and growth were monitored with serial ultrasound examinations. The patient underwent routine prenatal follow-up. Laboratory testing and ultrasound examinations were normal. At 38⁵ weeks, elective Cesarean section was performed under spinal regional anesthesia, because it was felt that if given a general anaesthetic the patient might not be able to be extubated due to limited diaphragmatic and intercostal muscle strength. The patient gave birth to a 3110 g female baby with APGAR scores of 8/9 at the first and fifth minutes, respectively. Postpartum cefazolin 1 g b.d was prescribed for surgical wound infection prevention. In order to prevent postpartum hemorrhage, oxytocin infusion at a rate of 100 mU/min was given for 16 h continuously. Methylergonovine was prescribed 0.2 mg IM three times a day and after 24 h 0.125 mg orally every 8 h for the next three days. Preoperative Hb was 12.8 g/dL and decreased to 10.4 g/dL 6 h postpartum. The patient was admitted to the ICU for 12 h postpartum. The following three days were uneventful until discharge at day 3. Regarding the initiation of ERT, endocrinology and neurology departments were consulted. Treatment with 20 mg/kg alglucosidase- α (Myozyme) every two weeks was recommended with the strict advice not to breastfeed for 24 h after the completion of drug infusion. At the end of the first postpartum month, physical examination was normal. Her muscle strength and motor functions were even better than pre-pregnancy levels. Respiratory muscle evaluation test, echocardiography, spirometry and muscle power tests were renewed and no significant changes were observed at the end of second postpartum month. The patient started her ERT at the third postpartum month. The patient expressed additional milk before the ERT, because breastfeeding was not allowed for 24 h.

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Discussion

PD is a rare autosomal-recessive disorder. There are two forms of the disease: IOPD (aged <1 year with cardiomyopathy) and LOPD (>1 year of age through to adulthood or <1 year without cardiomyopathy). The worldwide incidence of both forms of the disease is commonly reported as 1 in 40,000¹; however, prospective trials suggest the incidence may be as high as 1 in 9000.^{4,5} It has been treated with ERT since 2006. Since the therapy is new and it is not a common disease, there is a little knowledge on the management in pregnancy with or without medical therapy.

De Vries et al.⁶ indicated that alglucosidase-alfa can be safely administered during pregnancy and lactation. Despite the paucity of available information, alglucosidase alfa is reported as a category B drug.⁷

Karabul et al.⁸ reported the clinical course and obstetric outcome of 66 patients with PD. They used a detailed questionnaire and telephone interviews to obtain information from all participants. The majority of women, recruited from two registries (German and British), became pregnant prior to the occurrence of the symptoms of disease. Only 15.2% of the participants became pregnant after symptoms (such as chronic myalgia and proximal muscle weakness) already existed. These symptomatic women had no higher risk of developing complications during pregnancy and delivery compared to asymptomatic patients and women in the general population. However, muscle weakness and deterioration of respiratory function can manifest during pregnancy. Despite the favorable results presented in the study, authors emphasized that a pregnancy in a woman with PD should be considered potentially high risk and monitored with special attention.

Rohman et al.⁹ reported eight women attending the Royal Free Hospital Lysosomal Storage Disorders Unit. Four of the eight women had seven pregnancies over a period of eight years. ERT was stopped in the first trimester in all four patients and only one of the four patients did not experience any subjective or objective muscle strength decline. ERT was re-started in the postpartum period in five of the seven pregnancies, and in two pregnancies, it was continued after first trimester. In our case, the patient did not resume her treatment due to her preference. Rohman et al.⁹ concluded that Cesarean section should only be performed for obstetric reasons. We decided to perform Cesarean section because we observed that the patient did not have enough muscle power and had anxiety about labor. Although the safety of ERT has not been proven, the authors did not observe any adverse effects due to enzyme treatment during breastfeeding. In our case, we offered our patient to restart treatment immediately after birth, but she only accepted treatment at third month postpartum.

Weida et al.¹⁰ also reported complete management of the pregnancy, delivery, and postpartum period of a symptomatic patient with juvenile-onset PD. Despite detailed counseling on the risks of continuation of pregnancy, the patient and her husband elected to continue the pregnancy, but declined ERT because of its experimental nature at that time. The fetal well-being and all laboratory parameters of the patient were within normal limits. Because of deterioration of the pulmonary status of the patient, delivery via Cesarean section under regional anesthesia was performed due to unfavorable cervix and the possible risks of extubation. During the postoperative period, feeding and respiratory assistance needed to continue for two months. Ten months after delivery, her pulmonary functions returned to pre-pregnancy values and her son has had normal development. The authors pointed out that patients with PD should be strictly monitored for respiratory function, metabolic derangements, and musculoskeletal function. The multidisciplinary approach of obstetric care is mandatory and can serve as a bridge to ERT.

In our uncomplicated case of pregnancy in a patient with a diagnosis of PD, we aimed to stress the importance of careful postpartum management with preventive measures needed to avoid the possibility of uterine bleeding and postoperative infection. Although anticoagulation medication was not been used in our patient due to early ambulation, the tendency of increased intravascular coagulation in these immobilized patients should be taken into consideration. We did not observe any postoperative complications with this approach.

At initial prenatal visit, patients with PD should be counseled on the risks of continuing the pregnancy including: chronic maternal hypoxia resulting in intra-uterine growth restriction or intrauterine fetal death; fetal hypoxia with subsequent long-term neurodevelopmental effects; worsening of maternal pulmonary status; and even maternal death. Nonetheless, they should not be discouraged if the mothers' status is stable. Nowadays, ERT is an established treatment option for the patients suffering from PD and it is compatible with pregnancy and lactation.^{6,7}

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Ethical approval

Written consent was obtained from the patient. As this is a case report, ethical approval was not taken.

Guarantor

BT

Contributorship

BT contributed to the data collection, KK to writing, RA to the literature research and FS to the writing and literature research.

References

1. Muller-Felber W, Horvath R, Gempel K, et al. Late onset Pompe disease: clinical and neurophysiological spectrum of 38 patients including long-term follow-up in 18 patients. *Neuromuscul Disord* 2007; 17: 698–706.
2. van der Beek NA, Hagemans ML, van der Ploeg AT, et al. Pompe disease (glycogen storage disease type II): clinical features and enzyme replacement therapy. *Acta Neurol Belg* 2006; 106: 82–86.
3. Toscano A and Schoser B. Enzyme replacement therapy in late-onset Pompe disease: a systematic literature review. *J Neurol* 2013; 260: 951–959.
4. Chien YH, Lee NC, Huang HJ, et al. Later-onset Pompe disease: early detection and early treatment initiation enabled by newborn screening. *J Pediatr* 2011; 158: 1023–1027.
5. Mechtler TP, Stary S, Metz TF, et al. Neonatal screening for lysosomal storage disorders: feasibility and incidence from a nationwide study in Austria. *Lancet* 2012; 379: 335–341.
6. De Vries JM, Brugma JD, Ozkan L, et al. First experience with enzyme replacement therapy during pregnancy and lactation in Pompe disease. *Mol Genet Metab* 2011; 104: 552–555.
7. Briggs GG, Freeman RK and Yaffe SJ. *Drugs in pregnancy and lactation*, 8th ed. Philadelphia: Lippincott Williams & Wilkins, 2008, pp.53–54.
8. Karabul N, Berndt J, Kornblum C, et al. Pregnancy and delivery in women with Pompe disease. *Mol Genet Metab* 2014; 112: 148–153.
9. Rohman PJ, Scott E, Richfield L, et al. Pregnancy and associated events in women receiving enzyme replacement therapy for late-onset glycogen storage disease type II (Pompe disease). *J Obstet Gynaecol Res* 2016; 42: 1263–1271.
10. Weida J, Hainline BE, Bodkin C, et al. Management of a pregnancy complicated by Pompe disease. *Case Rep Obstet Gynecol* 2012; 2012: 137861.