

## A Selective Feticide in Discordant Twins with Niemann Pick Type C Disease and a Delayed Interval Delivery

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### Abstract

We report a twin pregnancy with a selective feticide of the first foetus with a Niemann Pick disease type C and a delayed interval delivery. The presented case confirmed that a delayed interval delivery is possible and successful. However, a close monitoring of the mother and the retained child after the birth of the first child is essential. A delayed delivery seems to be save for the mother, but the success for the neonatal outcome cannot be predicted.

**Keywords:** Delayed delivery; Feticide; Neonatal outcome; Niemann Pick type C; Twin pregnancy

### Introduction

Morbus Niemann-Pick disease (NPD) is a rare autosomal recessive genetic disorder occurring in 1/120.000 live births described by Vanier et al. [1]. Based to clinico-pathological findings five different subtypes of NPD have been described (A-E).

The Niemann-Pick disease type C (NPC) is a neurovisceral lysosomal lipid storage disorder harbouring a mutation of either the *NPC-1* gene (95%) or the *NPC-2* gene (5%) of cases [2]. NPC is characterized by abnormalities of intracellular transport of endocytosed cholesterol leading to an accumulation of cholesterol and sphingolipids in neuronal endosomes and lysosomes [2]. Manifestation time point of NPC ranges from the perinatal period to adult age [3] but 60% to 70% of all cases occur in the late infantile and juvenile period [4].

Clinical presentations of NPC are heterogeneous varying from hepatic, splenic and pulmonary disorders to neurologic or psychiatric manifestations. While splenomegaly or neonatal icterus are often diagnosed within the first month of life [2,4], psychotic symptoms, paranoid delusions, visual or auditory hallucinations as well as behavioural disorders are mostly diagnosed in elderly patients [5]. Prominent neurological signs include cerebellar ataxia, dysarthria, dysphagia, gait problems, cataplexy, dystonia, progressive dementia and characteristic vertical supranuclear ophthalmoplegia [2,5].

To date miglustat, a small iminosugar molecule that reversibly inhibits glucosylceramide synthase, is the only approved specific therapy for NPC being efficient in stabilizing or slowing disease progression for NPC [6]. However, early diagnosis of NPC is essential for a successful therapy, moreover the latter should be initiated at the earliest signs of neurological problems to delay or stabilize the progression of irreversible neurological damage [2].

We report a case of a selective feticide in a pregnancy with discordant twins after the diagnosis of NPC of one fetus and a delayed interval delivery of the twins.

### Case Report

A 35-year-old woman was referred to our department in the 13<sup>th</sup> week of gestational age with a diamniotic dichorionic pregnancy. It was the fourth pregnancy of the woman resulting in one healthy child, one with infantile NPC 1 and one miscarriage. As both marriage partners were known as heterozygote carrier of the NPD-mutation, an antenatal diagnosis of NPD was offered to the couple.

Amniocentesis of both foetuses performed (Figure 1) at the 16<sup>th</sup> gestation week revealed that the first twin was homozygote for NPC

mutation and the second twin had a heterozygote mutation. In addition, a chorionic villus sampling to confirm the diagnosis was performed. After extensive interdisciplinary counselling the couple decided to undergo a selective feticide of the foetus with the homozygote gene defect, which was performed in the 23<sup>rd</sup> week of gestational age using intracardial potassium chloride without any complications.

In the 30<sup>th</sup> week of pregnancy the patient was referred to our hospital with an acute cervical insufficiency accompanied by a cervical dilation



Figure 1: Amniocentesis performed under ultrasound control.

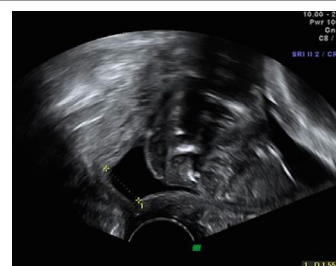


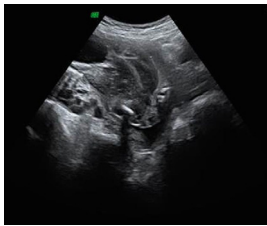
Figure 2: Acute cervical insufficiency and dilated cervix.

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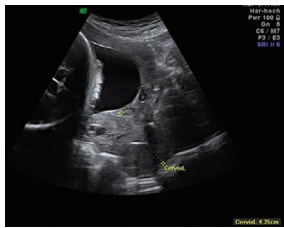
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**Figure 3:** Prolapse of the amniotic sac from the first, death twin, presented by the Breech.



**Figure 4:** Cervical length after the emergency cervical cerclage.

of two centimetres (Figure 2). Two days later the amniotic sac of the dead twin prolapsed through the partially dilated cervical os. The ultrasound scan showed a bulging of the fetal membranes and the fetal breech into the widened cervical os (Figure 3). Consequently, there was urgent need to extract the first twin from the uterus.

To prevent a premature delivery of the second foetus we performed subsequent an emergency cervical cerclage (Figure 4). There was no contraction at the uterus when performing the cerclage using the McDonald technique, after a prophylactic tocolytics was administrated. At the time of cerclage placement there were no clinical or laboratory signs of infection and hence the aim was to prolong the pregnancy and therefore improving the clinical outcome of the second twin.

The postoperative management included daily clinical assessments (blood pressure and temperature controls) as well as laboratory tests including serum level of C-reactive protein and white blood cell count. Ultrasonographic assessments of the cervix and fetal monitoring at regular intervals confirmed the wellbeing of the foetus.

Six days after cerclage placement therapy the woman experienced a premature rupture of the membranes (PROM) associated with a significant increase of laboratory infection parameters. Since the presumption of an infection of the amniotic sac was an obvious reason of systemic infection, the cerclage was surgically removed immediately.

A few hours later spontaneous labour started resulting in a spontaneous delivery of a male new-born in the 32<sup>nd</sup> week of gestational age. The APGAR score was 9/10/10 and the child had an uneventful postnatal course. After the delivery also, the mother was in a good performance status.

## Discussion

Over the last years the number of multiple pregnancies has increased due to the rising age of the pregnant women and hence the increased use of assisted reproductive technologies [7]. According to literature cases of delayed interval delivery in twin pregnancies are very rare and therefore there is no consensus about the best practice in management of twin pregnancies after birth of the first twin.

An intrauterine fetal death, or like in our case a selective feticide, is a rare obstetric complication and it is a challenge in respect of the

management of continuing pregnancy and delivery. Regular fetal monitoring of the second child including cardiotocography, doppler flow velocimetry and ultrasound are important analyses to prevent and recognize any complications [7].

When delaying a twin delivery is considered to know the following criteria: monochorionicity, placenta praevia, fetal distress, preeclampsia, placental abruption or the need of a cesarean delivery of the first foetus [8]. Some reports even show a higher rate of chorioamnionitis in delayed delivery twin pregnancies, but even though they describe a significant advantage in delaying delivery. In addition, infection appears to be an important relative contraindication [8,9].

After delivery of the first child the prophylactic treatment with antibiotics, cervical cerclage and tocolysis are reasonable options and part of a modern management procedure [7,8].

However, it is important to start the administration with parenteral broad-spectrum antibiotics for 72 hours during or immediately after delivery of the first foetus. Afterwards the oral monotherapy, with adaption to bacteriological results, can normally be used for 7 days [8]. Nevertheless, contradictory opinions about the exact treatment are discussed in literature. For example, some authors recommend the use of culture-directed antibiotics until the birth of the second child [10], others advise to use broad-spectrum antibiotics until cervical cultures are negative [11]. Moreover, it might be also essential to avoid vaginal examinations to prevent infections.

Another point discussed in literature is the use of prophylactic tocolysis. Most authors recommend tocolysis [12] due to an increased delivery interval, moreover an immediate start of tocolysis after the first birth seems to prolong pregnancy [8]. However, for example Cozzolino et al. used the tocolytic therapy only when the risk for the preterm delivery of the second child was high, however the authors of this study claim that tocolysis should never be used before 24 weeks of pregnancy [12].

In general, cervical cerclage is the most debated treatment after the delivery of the first child in a twin pregnancy. Some studies suggest that cervical cerclage leads to a longer delivery interval [8,13], on the other hand the indications for using a cerclage are not clear defined as it does not significantly improve survival rates of the second twin [14]. In addition, a cervical cerclage seems to increase the risk of chorioamnionitis through rupture of the membranes and infections are observed more often [8]. Therefore, it has to be pointed out, that in case of cervical cerclage being used after the first birth, it should be performed in penible aseptical conditions within the first two hours after delivery of the first child after exclusion of a floride infection [14].

## Conclusion

In the presented case, we were able to extend the pregnancy for one week before a rupture of the membranes occurred. Because of increasing laboratory signs of infection, we had to remove the cerclage. In this context it is an interesting fact that a cervical cerclage by itself is a significant risk factor for preterm rupture of the membranes and for infections, especially in emergency procedures (51%), as Kurup described [15].

In summary the present case report clearly reveals that there is no standard procedure underlying the importance of an individualized case management in delayed delivery in a twin pregnancy.

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