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Selective Birth in a Case of Twins Discordant for Tay Sachs Disease

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Abstract. The authors have performed selective birth in two twin pregnancies in the same patient. The couple's first pregnancy resulted in the birth of a male with Tay Sachs disease: their Pergonal-induced second pregnancy was a twin gestation discordant for Tay Sachs disease. A fetal intracardiac puncture, exsanguination, and fetal intracardiac air embolization were then performed. The patient went into premature labor 9 days later and delivered a normal immature infant, who died, and the macerated cotwin. The third Pergonal-induced pregnancy was a singleton with Tay Sachs disease and the pregnancy was terminated. Their fourth Pergonal-induced pregnancy was a twin gestation discordant for Tay Sachs disease. At 20 weeks gestation, fetal intracardiac air embolization was performed with immediate demise of the affected fetus. The pregnancy was followed closely with ultrasonography and coagulation studies and proceeded to term without complication. A normal female and a fetus papyraceous were delivered by cesarean section.

Key words: Selective birth, Twin pregnancy, Tay-Sachs disease, Abortion

INTRODUCTION

The prenatal diagnosis of twins discordant for genetic disease will inevitably occur with increasing frequency, because of an increase in the utilization of antenatal genetic studies and of an increase of twin pregnancies in women of advanced maternal age. Until recently patients found to be carrying twins discordant for genetic disease had only two options: continuing the pregnancy or abortion of both the normal and abnormal fetus. The fear of this dilemma alters parents attitude about genetic studies [3]. Since 1978, a third alternative has been offered to patients in a few centers. This alternative is termed selective birth and involves the destruction of the genetically abnormal fetus with the preservation of the normal cotwin. The author's previous experience with this procedure

resulted in the loss of both fetuses. However, the same patient returned with a second twin pregnancy discordant for Tay Sachs disease and a report of that pregnancy follows.

CASE REPORT

The patient is a 29-year old gravida, para 1, abortus 2, Jewish female, whose first pregnancy was uneventful and terminated in a spontaneous vaginal delivery of a male child who had Tay Sachs disease and died in 1980. Seven months before the death of her first child, her second pregnancy was initiated after Pergonal^{R}-induced ovulation. She was referred to the Medical College of Virginia Antenatal Testing Program for intrauterine genetic studies. At the time of the initial visit, at 14 weeks gestation, it was discovered that she had a twin gestation, and amniotic fluid specimens were obtained from both sacs. Hexosaminidase A determinations revealed that fetus A was affected with Tay Sachs disease and fetus B was a carrier. Chromosome analysis was normal and both were male. After the results were confirmed at 22 weeks gestation, an attempt at selective birth by destruction of the fetus with Tay Sachs was performed. This was technically difficult and after three unsuccessful attempts at fetal exsanguination by cardiac puncture, fetal death was achieved by embolizing the fetal heart with 5 cc of air. Nine days later the patient went into labor with suspected chorioamnionitis and was delivered by cesarean section of immature twins, one stillborn and one that died in the neonatal period and was shown to be a Tay Sachs carrier. In 1981, the patient's third pregnancy, a singleton, was terminated by intraamniotic saline injection after it had been determined to be affected by Tay Sachs disease.

The patient's fourth pregnancy resulted from Pergonal^{R}-induced ovulation. At her first visit for genetic studies she was 14 weeks pregnant, and ultrasound examination revealed a twin gestation. Fluid was obtained from both sacs for chromosome analysis and hexosaminidase A determination. The results demonstrated that twin A was a normal female noncarrier and that twin B was a male affected by Tay Sachs disease. The parents were informed and amniotic fluid was sent to another laboratory for confirmation of the diagnosis. After detailed consent of the patient and her husband, they again decided on selective termination of the affected fetus. They refused to continue the pregnancy with the affected fetus, and stated that their only alternative to selective birth was termination of the pregnancy. At 22 weeks gestation, fluid was obtained from the sac of the affected fetus (twin B) and indigo carmine dye instilled. Rapid hexosaminidase A assay confirmed the diagnosis that twin B was affected. After confirmation, a fetal intracardiac puncture was performed on twin B under real-time ultrasound guidance. With a 20-gauge needle in the fetal heart, very little fetal blood could be aspirated. Five cc of air were injected into the heart through a millipore filter. Although the ultrasound images were then of poor quality because of the air in the fetal tissues, fetal movement immediately ceased. Ultrasound of twin A showed a normal fetal heart rate and normal activity. Ultrasound examination the following day revealed no movement in twin B and normal activity and heart rate in twin A. Real-time ultrasound one week after the procedure confirmed these findings. Ultrasound six weeks after the procedure (28 weeks gestation) revealed a living twin A with a BPD of 73 mm and remnants of the dead fetus. Serial maternal serum fibrinogen and platelet counts were normal throughout pregnancy. The patient was delivered at 40 weeks gestation by repeat cesarean section of a living, 3.0 kg female infant with Apgars of 9, 10, and a small male fetus papyraceus.

DISCUSSION

As amniocentesis for intrauterine genetic studies has become a routine part of antenatal care, the presence of a twin gestation is a rather common finding. The discovery of the twin gestation is often made at the time of the ultrasound prior to amniocentesis. Patients have routinely been counseled about the routine risks of amniocentesis as well as their specific risk for genetic disease. However, the presence of twins considerably changes the counseling.

In the general population, 70% of twins are dizygotic, 30% monozygotic. However, in a group of patients heavily skewed toward advanced maternal age, the proportion of DZ twins is higher. Since the conception of DZ twins implies genetically two separate events, the risks of abnormality in each twin are independent but additive. In the specific case of advanced maternal age, for example, where the risk of a chromosome aneuploydy is 1-2%, the risk that one or the other fetus would be affected by a chromosome aneuploidy is 2-4%.

In the case of autosomal recessive disease the risk of abnormality is 25% for each conception; the risk that one of DZ twins will be affected thus approaches 50%. The presence of a twin gestation at the time of antenatal diagnosis, therefore, radically changes the counseling and changes the reaction of the parents toward antental testing. A negative reaction originates from the fear of having both a normal and an abnormal fetus.

Parents who have a twin pregnancy discordant for a major abnormality have three options. The first is obviously to continue the pregnancy. The second option is to terminate the pregnancy, sacrificing the normal cotwin. The third option is selective birth.

The first case of selective birth was reported in 1978 and involved exsanguination by cardiac puncture of a fetus affected by Hurler's syndrome [1]. This pregnancy proceeded to 32 weeks with premature labor and delivery of the normal cotwin. In 1981, the first case of selective birth in twin pregnancy discordant for Down's syndrome was performed in the United States [4]. The feticide was performed by intracardiac puncture at 22 weeks gestation with removal of 20 cc of fetal blood, following which there was fetal death of the affected twin and continuation of the pregnancy. This patient was delivered at term of a normal male infant. The second case in the United States was reported later in 1981 by us [6]. Fetal death in two of the reported cases was accomplished by exsanguination via intracardiac puncture, and in two others by intracardiac air embolization. Another recent report described air embolization of the umbilical vein of a microcephalic twin using the fetoscope [2].

There are many remaining questions about the technical aspects of selective birth. The first is the efficacy of the procedure. Of the six cases known to the authors, two have resulted in loss of both twins and one resulted in a failure to accomplish the death of the affected twin and continuation of the pregnancy (private communication).

The risk of fetal morbidity, rather than mortality, secondary to the procedure, is of great concern, particularly if the neonate survives with a permanent disability. Our experience in the previous case has demonstrated that one can "exsanguinate" a fetus in utero and have it survive. In our experience, air embolization seems to be the more efficacious procedure.

The effect of the death of the affected twin on the normal cotwin must also be considered. Brain damage due to intravascular coagulopathy in the surviving twin of a

MZ twin pair has been reported [5]. Although arteriovenous anastomosis is common in MZ twins, it is thought to be almost nonexistent in DZ twins. Therefore, since the vast majority of twins discordant for genetic disease are DZ, this should be a rare complication.

The risk of potential harm to the mother is not known. Disseminated intravascular coagulation is a recognized risk in cases of intrauterine retention of a dead fetus. However, maternal disseminated intravascular coagulopathy in a twin gestation after spontaneous or induced death of one fetus has not been reported.

The serious complication of this procedure would be destruction of the wrong fetus. Since in most defects amenable to antenatal genetic diagnosis there are no quick markers (Tay Sachs being the rare exception), it is imperative that the fetuses have been correctly identified at the time of the first amniocentesis and that the exact anatomical position of the amniotic septum and fetuses be carefully observed and recorded. In cases in which the twins are also discordant for sex, it is possible to identify the fetal sex by ultrasound and/or sex chromatin staining from cells in the amniotic fluid, to assure that the affected twin has been correctly identified.

Selective birth may be an option which is difficult for patients and physicians to consider. However, the traditional options have significant disadvantages. Our patient had four pregnancies involving six fetuses, four of whom were affected by Tay Sachs disease, and she was able to at last have a normal child by means of selective birth.

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