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Twin–Twin Transfusion Syndrome and Twin Anemia–Polycythemia Sequence in a Monochorionic Triamniotic Pregnancy

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Twin–twin transfusion syndrome (TTTS) is an antenatal complication of monochorionic multiple gestations. There have been few studies exploring the role of laser photocoagulation or outcomes following treatment in monochorionic triplet pregnancies with TTTS. We present a case where TTTS and twin anemia–polycythemia sequence (TAPS) complicated a monochorionic triplet pregnancy. Following the laser photocoagulation to treat the TTTS between the triplets, an intra-uterine death occurred in one triplet and TAPS developed in the remaining two triplets. Intervention in this case resulted in a 2-week prolongation of pregnancy and a positive outcome for the remaining fetuses. This case and other published data reviewed in this article suggest that laser photocoagulation has a potential role for TTTS in monochorionic triplet pregnancies.

■ **Keywords:** triplet, laser, twin–twin transfusion, feto-fetal transfusion, anemia, polycythemia, monochorionic, multiple pregnancy

Monochorionic triplet pregnancies occur in 1 to 4 per 100,000 pregnancies (Enzetami et al., 1997; Ghulmiyyah et al., 2003; Imaizumi, 2003). Twin–twin transfusion syndrome (TTTS) can occur between twin pairs in monochorionic triplet pregnancies (Jain & Fisk, 2004). We present a case of TTTS in a monochorionic triamniotic pregnancy treated with laser photocoagulation. To our knowledge, this is the first reported case of twin anemia–polycythemia sequence (TAPS) in a pair of monochorionic triplets after laser photocoagulation for TTTS in a triplet pregnancy.

Case Report

A 37-year-old woman with a monochorionic triamniotic pregnancy presented with TTTS between triplets 1 and 2 on ultrasound scan at $19^{3/7}$ weeks gestation. TTTS was diagnosed on the basis of oligohydramnios (maximal vertical pocket [MVP] of 1.7 cm) in triplet 1 and polyhydramnios (MVP = 8 cm) in triplet 2. The umbilical artery (UA), middle cerebral artery (MCA), and ductus venosus (DV) Doppler waveforms were normal for all triplets.

Three amnioreductions were performed at $20^{5/7}$, $22^{1/7}$, and $24^{1/7}$ weeks from triplet 2 (1,500 mL, 1,250 mL, and 1,250 mL). Placental laser photocoagulation was performed at $24^{3/7}$ weeks due to rapid progression from stage 1 to stage 3 TTTS between triplets 1 and 2, with normal MCA peak systolic velocities in all triplets and deep 'a' waves in triplet 2. The procedure was technically challenging due to the large anterior placenta and fetal positions. All anastomoses between triplets 1 and 2 and triplets 2 and 3 that were identified were photocoagulated (Dornier Medilas D SkinPulse S Class IV Diode Laser). At completion of the procedure, an amnioreduction was performed from triplet 2 (2,250 mL) reducing the MVP to 3 cm. All triplets were alive at the end of the procedure. The following day fetal demise of triplet 1 was identified on ultrasound scan. Triplets 2 and 3 had normal UA, MCA, and DV Doppler waveforms.

At $26^{1/7}$ weeks, an ultrasound scan found discordant amniotic fluid volumes in the surviving triplets (triplet 2 MVP = 4.8 cm, triplet 3 MVP = 0.8 cm). The UA and MCA were normal for both surviving triplets. Three days later at

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$26^{4/7}$ weeks, ultrasound demonstrated TAPS between the surviving triplets (triplet 2 MCA peak systolic velocity [-PSV] 77.5 cm/s, triplet 3 MCA-PSV 16 cm/s). Furthermore, triplet 2 had an elevated UA systolic–diastolic (S/D) ratio (3.9) and the DV had deep 'a' waves. Triplet 3, who had oligohydramnios (MVP = 0.8 cm) 3 days earlier, now had an MVP of 3 cm and a large fetal bladder.

Betamethasone was administered and the triplets were delivered by caesarean section.

Triplet 2 (905 gram) and triplet 3 (945 gram) were born in good condition with normal Apgar scores and normal umbilical cord blood gas results. Triplet 2 was found to have a hemoglobin of 68 g/L and a hematocrit of 0.21 and triplet 3 had a hemoglobin of 216 g/L and a hematocrit of 0.66. Triplet 2 required ventilation for 3 weeks, continuous positive airway pressure (CPAP) ventilation for 6 weeks, surfactant for hyaline membrane disease and four top-up transfusions for anemia. Triplet 2 also had a patent ductus arteriosus but had no evidence of retinopathy of prematurity (ROP), intraventricular hemorrhage (IVH), or any other white-matter abnormalities on any of the postnatal ultrasound scans. Triplet 3 required ventilation for 3 weeks, CPAP for 8 weeks and surfactant for hyaline membrane disease. Similar to triplet 2, triplet 3 had no evidence of ROP, IVH, or other white-matter abnormalities on any postnatal imaging.

Triplet 2 was discharged on day 111 and triplet 3 was discharged on day 90 of life. Both triplets were discharged in good condition.

Discussion

Monochorionic triplet pregnancies are rare (Enzetami et al., 1997; Ghulmiyyah et al., 2003; Imaizumi, 2003). Since 2005, to our knowledge, there have been five reported cases of monochorionic triplet pregnancies in Western Australia. As there are approximately 25,000 births a year, the incidence of monochorionic triplet births in Western Australia is approximately 1 in 125,000.

TTTS is an antenatal complication of monochorionic multiple gestation pregnancies (Ling et al., 2000). TTTS is diagnosed by the presence in the mid-trimester of oligohydramnios (MVP $<$ 2 cm) in one fetus and polyhydramnios (MVP $>$ 8 cm) in the other fetus (Jain & Fisk, 2004). Although the pathogenesis of TTTS is not fully understood, it is thought to result from arterio-venous anastomoses in the placental bed (Jain & Fisk, 2004).

The rate of TTTS in monochorionic triplet pregnancies is unknown (Sepulveda et al., 2005), while in monochorionic twin pregnancies the incidence is 15% (Sebire et al., 2000). Previous studies have demonstrated high rates of morbidity and mortality associated with TTTS in monochorionic triplet pregnancies (Adegbite et al., 2005; Enzetami et al., 1997; Fisk et al., 1990; Hayashi et al., 2005; Ishii et al., 2006; Leung et al., 2003; Ling et al., 2000; Pons et al., 1990; Rehan et al., 1995). Expectant management (Enzetami et al., 1997; Fisk et al., 1990; Pons et al., 1990), termination of pregnancy (Chasen et al., 2002; Diemert et al., 2010), amnioreduction (Adegbite et al., 2005; Chasen et al., 2002; Hayashi et al., 2005; Leung et al., 2003; Ling et al., 2000; Rehan et al., 1995), and laser photocoagulation (Chmait et al., 2009; Diemert et al., 2010; Ishii et al., 2006; Sepulveda et al., 2005; Van Shoubroeck et al., 2004) have been reported to treat these pregnancies.

Our case demonstrated the failure of conservative management in TTTS in a triplet pregnancy and a 2-week prolongation of pregnancy following laser photocoagulation. Laser photocoagulation for TTTS in monochorionic twins has been strongly supported in clinical trials (Roberts et al., 2008; Rossi & D'Addario, 2008; Salomon et al., 2010; Senat et al., 2004). In a recent study of monochorionic twins with TTTS, laser photocoagulation was associated with improved survival and improved neurologic outcome (Ages and Stages Questionnaire) compared with amnioreduction at 6 years of age (Salomon et al., 2010). There have been few studies exploring the role of laser photocoagulation or outcomes following treatment in monochorionic triplet pregnancies with TTTS (Chmait et al., 2009; Diemert et al., 2010; Ishii et al., 2006; Sepulveda et al., 2005; Van Shoubroeck et al., 2004). Chmait et al. (2009) described the largest case series with six women with monochorionic triplets. In this report, the overall survival was 61% following laser photocoagulation, which was not different from the survival after amnioreduction (Chmait et al., 2009). Poor outcomes from laser photocoagulation reported in other studies (Ishii et al., 2006; Sepulveda et al., 2005) may be attributed to the technical difficulty and complexity of laser photocoagulation in monochorionic triplet pregnancies (Chmait et al., 2009; Diemert et al., 2010; Sepulveda et al., 2005; Van Shoubroeck et al., 2004).

TAPS is a form of inter-twin transfusion characterized by a significant difference in hemoglobin level between twins without amniotic fluid discordance (Lopriore et al., 2007). In utero, this usually presents with increased MCA-PSV in one fetus, suggesting anemia, and reduced MCA-PSV in the other, suggesting polycythemia (Robyr et al., 2006). There has been one reported case of TAPS in a monochorionic triplet pregnancy (Lopriore et al., 2007), but no reported cases of both TTTS and TAPS between pairs of monochorionic triamniotic triplets.

TAPS may occur following laser photocoagulation for TTTS, as in this case, or spontaneously in uncomplicated monochorionic pregnancies (Lopriore et al., 2007). It is reported to occur in up to 13% of cases following laser photocoagulation (Robyr et al., 2006). There are currently no guidelines for the management of TAPS, but management options include expectant management, repeat laser photocoagulation, intrauterine transfusion, or selective feticide (Lopriore et al., 2008). In our case, the triplets were managed by prompt delivery.

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Conclusion

In conclusion, monochorionic triamniotic pregnancies are rare and high risk (Adegbite et al., 2005; Enzetami et al., 1997; Fisk et al., 1990; Hayashi et al., 2005; Imaizumi, 2003; Ishii et al., 2006; Leung et al., 2003; Ling et al., 2000; Pons et al., 1990; Rehan et al., 1995). The invasive management of TTTS in monochorionic triplet pregnancies with laser photocoagulation bears the risk of intra-uterine death (Chmait et al., 2009; Diemert et al., 2010; Ishii et al., 2006; Sepulveda et al., 2005; Van Shoubroeck et al., 2004) and TAPS (Lopriore et al., 2007; Robyr et al., 2006). Laser photocoagulation is technically challenging in these pregnancies (Chmait et al., 2009; Diemert et al., 2010; Sepulveda et al., 2005; Van Shoubroeck et al., 2004) and is best performed by teams with extensive experience in the treatment of TTTS in monochorionic twin pregnancies. In our case, the relatively good outcome of triplets 2 and 3 at short-term follow-up suggests the potential role of laser photocoagulation in similar cases in the future. Monochorionic triamniotic pregnancies should be managed in a tertiary setting with frequent ultrasound assessment due to the possibility of rapid changes in the condition of the triplets as the pregnancy progresses.

Disclosure of Interests

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

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