Case Report

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Atypical twin-to-twin transfusion syndrome case managed in a single centre in Indonesia with fetoscopic laser photocoagulation and amniopatch: 'Case Report'

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Introduction and importance: The diagnostic criteria for Quintero staging in twin-to-twin transfusion syndrome (TTTS) are not applicable in all cases of TTTS, such as those in which the symptoms overlap with other monochorionic twin complications such as selective intrauterine growth restriction (sIUGR).

Case presentation: A 25-year-old woman, G1P0A0, at 22–24 weeks' gestational age was diagnosed with TTTS, with no outstanding history of medication use during pregnancy, and no family history of genetic disorder or twin pregnancy. In the donor twin, persistently absent end-diastolic flow in the umbilical artery was observed using Doppler velocimetry. Polyhydramnios was observed in the recipient twins. The fetal weight discordance between the twins was 39%. After 2 weeks of follow-up, the authors performed fetoscopic laser photocoagulation and successfully ablated five vascular anastomoses and amnioreduction by 2.5 l. Five days after the laser surgery, the patient developed amniotic fluid leakage, and an amniopatch was performed. The authors did the caesarean section at 34 weeks because of severe preeclampsia, the donor and recipient birth weights were 1,120 g and 1,837 g, respectively (weight discordance 39%). The APGAR scores were 3/4 and 6/8, respectively. The donor twin died 6 days after delivery due to respiratory failure, and the recipient twin survived. Neonatal echocardiography of the surviving twin showed no tricuspid regurgitation. No long-term follow-up was performed.

Clinical discussion: The traditional diagnostic criteria for TTTS stage 3 were not met and overlapped with the diagnostic criteria for sIUGR type 2. This is the first procedure reported in Indonesia for atypical TTTS with the outcome, one twin survived.

Conclusion: Some TTTS cases do not meet traditional diagnostic criteria and overlap with other monochorionic twin complications.

Keywords: amniopatch, amnioreduction, atypical TTTS, case report, fetoscopic laser photocoagulation

Introduction

Multifetal pregnancies are considered high-risk pregnancies and are associated with more fetal and neonatal complications than singleton pregnancies. Monochorionic diamniotic twin gestation is associated with a 10–15% risk of twin-to-twin transfusion syndrome (TTTS), the mainly caused of this condition is vascular anastomoses connecting the two fetal circulations, which are almost always present and are responsible for pregnancy complications, causing damage to the surviving twin in the event of the intrauterine demise of its cotwin. Monochorionic twins share a single placenta that is not always equally shared between twins, which may lead to severe birthweight discordance[1,2].

The traditional diagnosis of TTTS requires ultrasound confirmation of polyhydramnios and oligohydramnios. However, up to 7% of TTTS cases may show ultrasound signs of fetal deterioration, even in the absence of amniotic fluid index discordance. A different clinical scenario involves TTTS overlapping with other monochorionic twin complications, such as selective intrauterine growth restriction (sIUGR). Any TTTS case that fails to meet the established diagnostic criteria is classified as atypical TTTS[3,4]. The aim of this case report to present a TTTS case does not meet the standard TTTS criteria, which is usually and the

HIGHLIGHTS

- In this case report, we report a unique case that does not fulfil the usual twin-to-twin transfusion syndrome (TTTS) criteria.
- TTTS did not always fulfil Quintero's criteria.
- This is the first case reported in Indonesia.

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Sponsorships or competing interests that may be relevant to content are disclosed at the end of this article.

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work has been reported in line with the Surgical CAse REport (SCARE) 2023 criteria[5].

Case presentation

Clinical history

A 25-year-old Bataknese woman, G1P0A0, at 22–24 weeks pregnant was referred to our fetal diagnosis and therapy unit with a suspected diagnosis of TTTS. This was her first spontaneous pregnancy, and she had no remarkable history of medication use during pregnancy, no family history of genetic disorders or twin pregnancies, and no history of psychosocial disorders.

Examination findings

The patient complained of breathlessness and normal blood pressure (120/78 mmHg), and aspirin was not routinely used in our institution for pregnant patients. Physical examination revealed a uniformly enlarged uterus with a fundal height was 38.7 cm. The fetal parts were not palpable, and uterine contractions were palpated, but not observed. Laboratory values were as follows: complete blood count (CBC) examination showed hemoglobin (Hb), 12.6 g/dl (12–16); Ht, 38.0% (36–47); leukocytes (WBC), 8.990/µl (4.000–11.000); and thrombocytes (PLT), 343.000/mm^3 (150.000–450.000).

Imaging data

Ultrasonography revealed a monochorionic diamniotic (MCDA) pregnancy. The placenta was anteriorly located. A thin, intertwined membrane (T-sign) was observed. The donor twin amniotic fluid maximal vertical pocket (MVP) was 2.74 cm. Bladder filling was also observed. The middle cerebral artery peak systolic velocity (MCA-PSV) was 34.97 cm/s (1.244 times the median/MoM). Persistent-absent end-diastolic flow (AEDF) was observed in the Doppler umbilical artery (UA) waveform, a positive a-wave was observed on the Doppler ductus venosus (DV) waveform, and the estimated fetal weight was 322 g. No fetal hydrops was noted in the recipient twin, with an MVP of 14.19 cm, polyhydramnios, bladder hypertrophy, Doppler MCA-PSV of 28.67 cm/s, 1.02 MoM, normal Doppler UA waveform, positive a-wave on the DV waveform, and EFW of 529 g[4] (As shown Fig. 1A, B), fetal weight discordance was at 39.1%. Cervical length (CL) 35.12 mm. The Tei Index (TI) and myocardial performance index (MPI) in the recipient twin's heart were 0.77, the left and 0.79, respectively. After 2 weeks of follow-up, the findings overlapped with diagnostic criteria for sIUGR type 2, discordancy of EFW (>25%) and persistent Absent End Diastolic Flow (AEDF) in Doppler UA donor, hence we decided to diagnose this pregnancy with 'Atypical TTTS'[5]. As shown in (Fig. 2A, B)

Informed consent

As polyhydramnios became more severe, we explained to the patient in detail the natural progression of TTTS, as it is necessary to perform selective fetoscopic laser photocoagulation (SFLP) and amnioreduction at 26 weeks' gestational age, the complications that may arise from the procedures, such as persistent/recurrent TTTS, iatrogenic preterm premature rupture of membranes (iPPROM), preterm labor, chorioamniotic separation, placental abruption, and amniotic fluid embolism in the mother. The patient and her family understood, signed the informed consent form, and agreed with our decision to perform SFLP followed by amnioreduction. Before the laser procedure, we intravenously administered two ketoprofen suppositories as tocolytics and cefotaxime (1 g) for antibiotic prophylaxis.

Therapeutic intervention

The operation was performed by the fetal therapy and diagnostic's team leading by Dr Dudy Aldiansyah, M.Ked (OG), Sp. OG, Subsp.KFm. The patient was placed in a right lateral recumbent position. To maximize the view of the placenta, the left side of the maternal abdomen was selected as the entry point. Under epidural anesthesia, the procedure was ultrasound-guided (GE Voluson P6 BT 16, Seongnam, GE, Ultrasound Korea, LTD), and an 8 Fr curved operating sheath was introduced into the uterine cavity. A 600 µm Nd-YAG laser fiber with a power of 60 watts in continuous mode in the laser source setting was used in this procedure. We found that in the anterior placenta, five vascular anastomoses were successfully ablated, and we continued to perform amnioreduction about 2,5 l untill the MVP in the recipient sac was 7 cm. The surgical time was 35 min[6–8] (Fig. 3A, B).

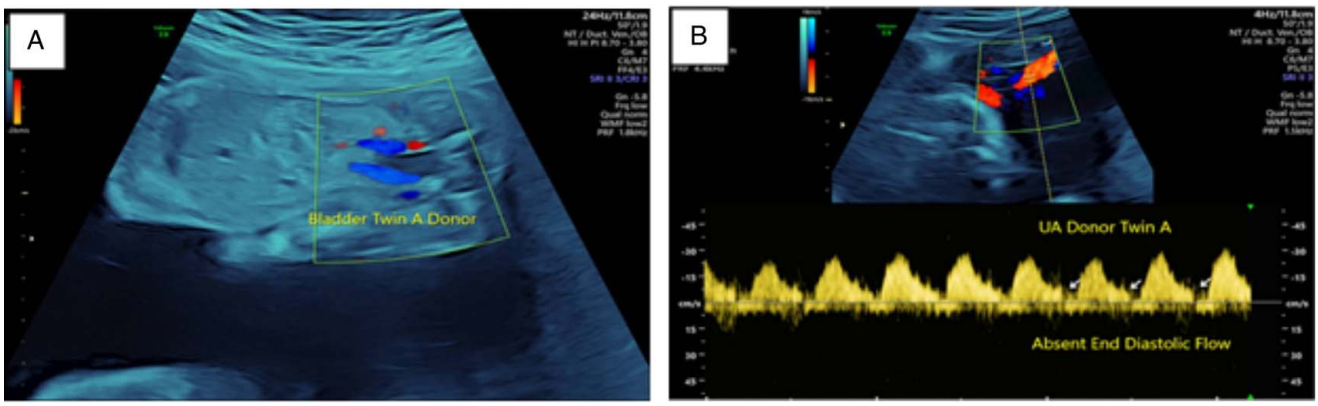

Figure 1. A. Bladder filling in the donor twin was observed. B. Absent end-diastolic flow (AEDF) shown by Doppler umbilical artery velocimetry.

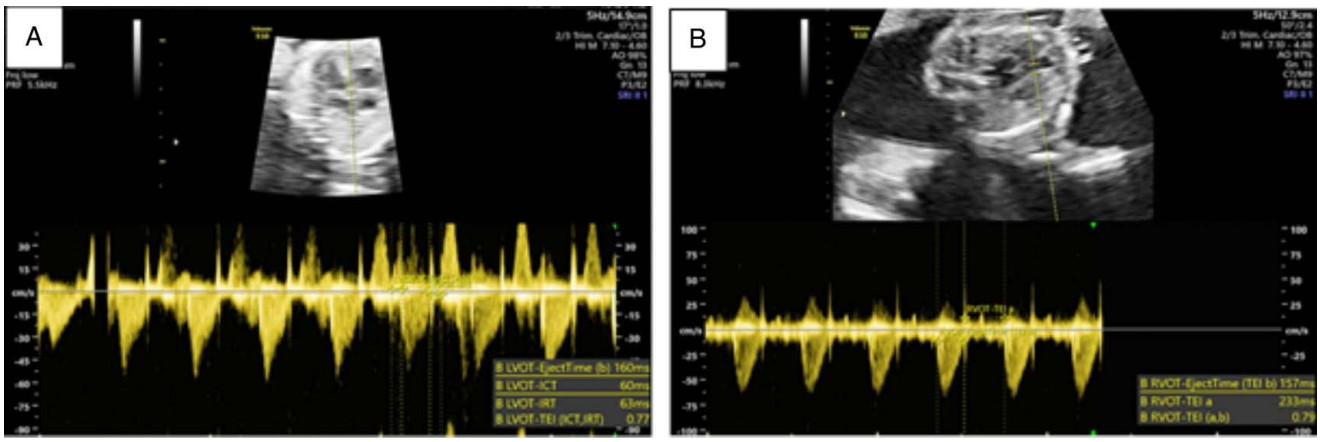

Figure 2. A. The Tei Index (TI) or Myocardial Performance Index (MPI) in the recipient's left. Ventricle (LV) was 0.77. B. TI or MPI in the recipient's right ventricle (RV) was 0.79. Both findings classified this TTTS as Cincinnati be sure to include a legend for each figure. Sure to note prominent features.

For postsurgical tocolytics, we used 100 mg ketoprofen suppositories and 400 mg micronized progesterone vaginally every 12 h until uterine contraction resolved, which occurred in 1 week. The patient received oral cefixime 200 mg every 12 h for 14 days and vitamin C tablets 100 mg daily until delivery. Twenty-four hours after SFLP and amnioreduction, the donor twin developed transient bradycardia (107 BPM) but stabilized the next day (range, 115–125 BPM). Five days after laser surgery, the patient developed amniotic fluid leakage or iPPROM but with normal amniotic fluid (MVP of the recipient twin, 6.29 cm), which was uncomfortable and very afraid because she reported feeling a vaginal discharge, with little by little flowing out continuously, and she asked if there was a way to stop it. An amniopatch was offered to the patient to seal amniotic fluid leakage. The risks of the amniopatch procedure, such as infection, labor, iatrogenic amniotic bands, and fetal death, are discussed. The patient was also informed of the risks of infection from blood product administration and that spontaneous sealing of the membranes could occur without amniopatch, but the rate is not known. After signing the informed consent form, the patient and the patient's family agreed to continue the procedure. We decided to perform amniopatch using autologous blood products, with 350 cc of blood extracted 24 h before the amniopatch procedure. Our institute protocol included 30 ml thrombocyte concentrate and 30 ml cryoprecipitate injected directly into the recipient twin's amniotic sac under local anesthesia (20 cc of lidocaine, 1% noradrenaline) and US guidance. The leak ceased at 7 days after the amniopatch procedure, with normal recipient and donor MVP during follow-up between 4.20 and 6.29 cm and 2.74 to 3.61 cm, respectively. There were no signs of chorioamnionitis. The patient and fetus were then followed by antenatal care and ultrasound weekly[9,10].

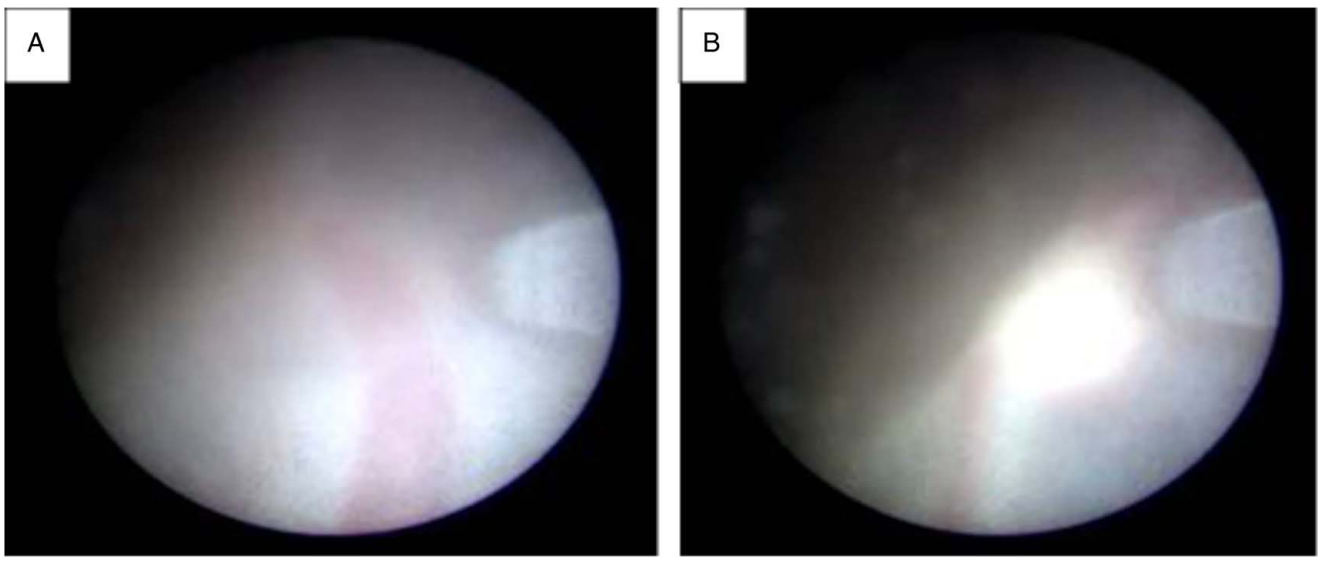

Figure 3. A. Fetoscopy images, before laser coagulation, the laser tip (right picture) about 1 cm, from the vessel surface. B. After laser coagulation; the macroscopic whitening of the coagulated vessel was observed if you use arrows, letters, or other indicators in your figures, be sure that they are permanently affixed in place, and referenced in the legend.

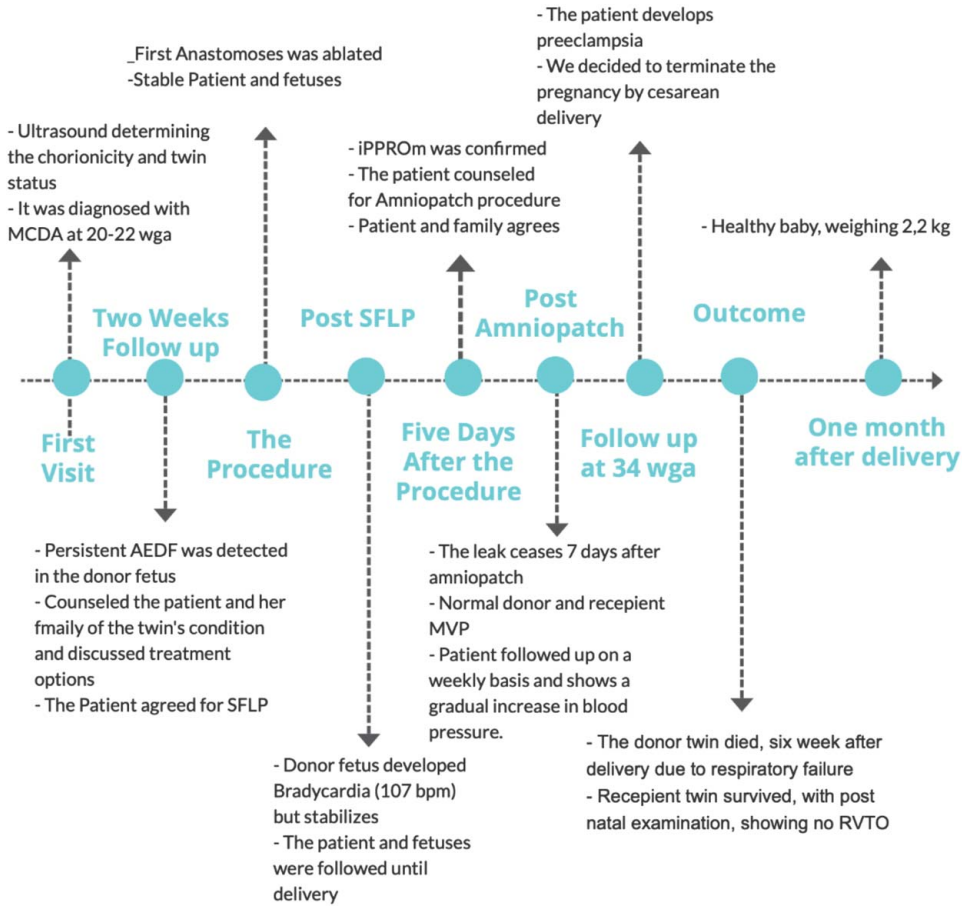

Figure 4. Timeline in the management of this patient.

Follow-up and outcomes

The patient's blood pressure showed a gradual increase over a week-by-week observation period, and 80 mg of low-dose aspirin once daily and 10 mg of calcium channel blocker were added to the patient's treatment regimen. The patient developed severe headache at the gestational age of 34 weeks. The donor twin develops a reversed a-wave in the Doppler DV waveform. Pregnancy was terminated by caesarean section due to pre-eclampsia with severe features, but elective caesarean section was recommended routinely between 36 + 0 and 36 + 6 weeks of gestation after laser surgery for TTTS in uncomplicated pregnancies[11]. The donor and recipient twin weights were 1,120 g and 1,837 g, respectively (EFW discordance 39%, which was greater than 25%). The APGAR scores for donor and recipient twins were 3/4 and 6/8, respectively. The donor twin died 6 days after delivery due to respiratory failure, and the recipient twin survived. Neonatal echocardiography of the surviving twin showed no tricuspid regurgitation or right ventricular outflow tract (RVOT) obstruction[12] (Fig. 4).

We cannot describe the long-term outcomes because the patient and the surviving baby did not return for follow-up for unknown reasons, even though we told them to come to our hospital.

We want to know if any different atypical versus typical TTTS placenta, so we examine the morphology of placenta in our case, the placenta was MCDA measuring 16.0 × 12.5 × 2.2 cm and weighing 686.2 g. The recipient's placental territory appeared much darker, and the donor's placental territory was paler and greenish due to meconium staining and fetal distress. Examination of the umbilical cord showed the recipient cord insertion at the marginal part of the placenta recipient territory, it measured 30.0 cm in length and 2.6 cm in diameter, and had three vessels. The donor twin's cord insertion was at the center part of the placenta donor territory, the cord ismeasured 24.0 cm in length and 2.2 cm in diameter, and had three vessels. There was no velamentous cord insertion, which is found in ~12% of monochorionic twin placentas. The estimated placenta sharing was ~60% for the recipient and 40% for the donor, unlike small sharing placenta in the donor territory, as in the sIUGR twin. We found five coagulation sites in the chorionic plate of the placenta.

Discussion

The diagnosis of twin-to-twin transfusion syndrome (TTTS) in monochorionic diamniotic twin pregnancy usually relies on the presence of polyhydramnios in one sac with concomitant oligohydramnios in the other sac. However, TTTS does not always exhibit linear progression and may present with cardiac compromise or critically abnormal Doppler velocimetry in either fetus before amniotic fluid discordance measurements meet the typical

TTTS criteria. A retrospective study in 2016 showed that 25 cases did not follow linear progression in a cohort of 345 monochorionic twin pregnancies. A center in Maryland reported 35 cases of atypical Quintero Stage III (abnormal Doppler flow with a visible donor bladder) spanning a 9-year period. Another case report from Germany showed a phenotype reversal in TTTS, which changed from absent end-diastolic flow of the donor to normal values in both twins. The new recipient showed transient ascites, and the smaller donor (former recipient) developed progressive cardiomegaly, hypertrophy of the myocardium, and mitral and tricuspid insufficiency at 29 weeks. Doppler sonography in the new donor deteriorated to a highly pathologic flow in the venous system, leading to a caesarean section. These cases show that rigid diagnostic amniotic fluid criteria may underestimate the severity and incidence of TTTS, underscoring the importance of careful surveillance, including arterial and venous Doppler velocimetry, in all monochorionic pregnancies[3,13,14].

Congenital cardiac disease can occur up to 87 times per 1000 live births in TTTS survivors, which is a 12-fold increase above the prevalence in singletons. However, the processes causing the development of congenital cardiac disease during TTTS are not completely understood; a number of factors, including hemodynamic defects in the twins of the donor and the recipient.

Some individuals are predisposed to genetic twinning and an aberrant placentation. Right ventricular outlet obstruction (RVOTO), such as in pulmonary stenosis (PS) and pulmonary atresia (PA), is the most common type of congenital cardiac disease, with recipient twins reporting a frequency of 6.7–12.9%. This danger is increased because recipient twins are predisposed to right heart dysfunction, cardiomegaly, and tricuspid valve regurgitation, which may result in a reduction in the flow through the pulmonary valve, possibly resulting in narrowing and stenosis of the recipient twin's fetal pulmonary valve. We also observed volume overload differences that increased the prevalence of recipient twin RVOTO, with volume overload occurring more frequently in recipient twins than in donor twins due to intermittent absent or reversed umbilical artery end-diastolic flow. Habli et *al*. reported a 10% MPI improvement in the left and right ventricles after SFLP. Prenatal MPI in our case showed severe cardiomyopathy in the recipient fetus, which was classified as Cincinnati Stage 3C. Postnatal echocardiography by a pediatric cardiologist showed no sign of any abnormalities of the fetal heart. Hence, there is an improvement in cardiac function in the recipient twin after SFLP[15–17].

Unlike spontaneous preterm premature rupture of membranes (PPROM), amniotic fluid leakage in iPPROM is caused by direct trauma to healthy fetal membranes during prior fetal therapy instrumentation. Sealing of fetal membranes via amniopatch is a feasible option in patients with iPPROM and, if successful, is associated with favorable perinatal outcomes. The exact mechanisms behind the sealing of the amniotic membrane are unclear, and it is presumed that platelets gather at the sites of the damaged membrane, undergo activation and aggregation, and become platelet plugs stabilized by cryoprecipitate. Chmait et *al*.[18] analyzed 19 cases with iPPROM and reported that gestational age less than 20 weeks was associated with higher success of amniopatch compared with a gestational age greater than 20 weeks (83 versus 14%, $P = 0.0063$). They attributed these findings to two hypotheses: First, the etiology of amniotic membrane rupture before 20 weeks and after 20 weeks of gestational age can be quite different. Second, in the fetal center, the same amniopatch dosage was used regardless of gestational age, indicating that a possible increase in dosage was needed for a more advanced gestational age. We considered the amniopatch procedure to be a success in this patient and attributed the success to the fact that no sign of chorioamnionitis was detected before the amniopatch procedure. We hypothesized that only a small portion of the membrane would rupture[19].

Conclusion

The Quintero staging system suggests a linear deterioration of TTTS, which occurs in cases of isolated or traditional TTTS but not in cases of nonisolated or atypical TTTS, which may present a rapid and progressive hemodynamic deterioration. There is a lack of data on atypical TTTS and no definite criteria currently exist. Here, we report a case of atypical TTTS with one surviving twin. We hope that, in the future, many centers in the world will report such cases, and there will be multicenter trials to determine the best management and treatment for atypical TTTS.

Ethical approval

The ethical approval was obtained from the institutional ethical review board of HSA Hospital (Reference number: 178/KEPK/USU, dated 2 March 2022).

Consent

Written informed consent was obtained from the patient for publication and any accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

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Author contribution

D.A., B.H., and S.N.L: substantial contributions to the conception or design of the work; or the acquisition, analysis, or interpretation of data for the work; E.M.A. and M.F.: draughting the work or revising it critically for important intellectual content; D.A., H.H., and T.T.: final approval of the version to be published; D.A. and S.N.L.: agreement to be accountable for all aspects.

Conflicts of interest disclosures

No conflicts of interest declared by the authors.

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Guarantor

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Data availability statement

The authors declare that they have followed the protocols of their work center on the publication of patient data. Right to privacy and informed consent: The authors declare that no patient data appear in this article.

Provenance and peer review

Not commissioned, externally peer-reviewed.

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