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Twin-To-Twin Transfusion Syndrome (Ttts) Associated With Single Intrauterine Fetal Death: Report Of A Clinical Case.

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Abstract

Approximately 20–25% of twin pregnancies are monochorionic, meaning that the twins share a single placenta.[1] Out of these monochorionic twin pregnancies, about 10–15% are complicated by twin-to-twin transfusion syndrome (TTTS), which arises from unequal sharing of the placental blood supply. TTTS generally manifests during the second trimester of pregnancy, most commonly between 16 and 26 weeks. It occurs due to the net transfer of fluids and hormones from one twin to the other through vascular connections on the placenta. If left untreated, TTTS can have a very poor prognosis. While stage I of the condition may stabilize or even improve in up to 30% of cases managed with observation, there is a risk of progression, fetal demise, or previable birth.[2–12]

The Quintero staging system, is widely accepted as the standard to communicate the severity of disease. However, these indicators are not always reliable for early detection, as TTTS can develop unpredictably.[2–5]

- *Twin-to-twin transfusion syndrome (TTTS) occurring in 8-10% of cases*
- *Selective fetal growth restriction (sFGR) in 10-15% of cases*
- *Single intrauterine fetal death (sIUFD) at a rate of 6%*
- *Twin anemia-polycythemia sequence (TAPS) in about 3-13% of cases*
- *Twin reversed arterial perfusion sequence (TRAP), which occurs in approximately 1% of cases.[9]*

Most of these complications are primarily due to a single shared placenta with intertwined vascular

connections. A subset of monochorionic diamniotic twin (MCDA) pregnancies may exhibit advanced TTTS without earlier stage indicators, a condition known as "atypical TTTS."

Additionally, the atypical TTTS may include coexisting conditions such as TAPS, sFGR, or cardiac compromise. This group also encompasses cases complicated by spontaneous septostomy(a rare complication that occurs when the dividing membrane in a multiple pregnancy ruptures, resulting in a pseudo-monoamniotic environment) or TTTS in monochorionic monoamniotic twins (MCMA).[7]

Outcomes and Prognosis for Twin-to-Twin Transfusion Syndrome (TTTS): Contemporary outcome data after laser surgery suggests survival for both fetuses can be anticipated in up to 65% of cases and survival of a single fetus in up to 88% of cases. Without treatment, FFTS carries a high risk of stillbirth or disability if undetected, with up to 90% fetal loss. [1,2]

However, preterm birth remains a significant contributor to postnatal morbidity and mortality. Long term outcomes of TTTS survivors indicate that up to 11% of children may show signs of neurologic impairment.[2]

A 37-year-old patient came to the unit experiencing abnormal uterine bleeding, and she was subsequently diagnosed with a monochorionic-biamniotic twin pregnancy. After being denied access to tertiary-level care, she received treatment within our unit, resulting in the delivery of one healthy newborn and a papyraceous fetus that weighed 60 grams.

Keywords: twin-to-twin transfusion syndrome (TTTS), feto-fetal transfusion syndrome (FFTS), Vanishing twin, single intrauterine fetal death (sIUFD), intrauterine fetal death (IUFD), monochorionic twin pregnancy. Twin reversed arterial perfusion sequence (TRAP).

INTRODUCTION:

Monozygotic twins are typically formed from the division of a single embryo and make up about 30% of all twin pairs worldwide. In nearly all cases, the fetal blood vessels of each twin converge along the boundary of their respective placental territories. These vessels may connect directly, forming superficial vascular anastomoses, or they may supply a shared placental cotyledon through deeper arteriolar and venular anastomoses. The line on the placental surface that links these anastomoses is referred to as the vascular equator. This portion of the shared placenta can account for 5–10% of the combined vascular volume for each twin, also known as the "third circulation."[2] Balance in this system can be disrupted by volume shunting through arteriovenous vascular anastomoses, leading to a condition known as twin-to-twin transfusion syndrome (TTTS). If not treated, TTTS can result in fetal mortality rates exceeding 80%.[1–5]

The initial diagnosis of Twin-to-Twin Transfusion Syndrome (TTTS) is made through ultrasound by identifying polyhydramnios in the recipient twin, which is indicated by a maximum vertical pocket (MVP) of amniotic fluid greater than 8 cm. In contrast, the donor twin typically exhibits oligohydramnios, characterized by a reduced MVP. Due to

this lack of amniotic fluid, the donor twin may appear to be "stuck" to the placenta or the uterine wall. Occasionally, the fetus may seem to hang from the uterine wall, a phenomenon known as the "chandelier sign," where it is ensconced in the membrane that may appear thicker due to folding. The Quintero staging criteria are the accepted standard for communicating the severity of TTTS. This classification involves assessing bladder filling, performing Doppler evaluations of the umbilical artery, ductus venosus, and umbilical vein, and determining the presence of hydrops or fetal demise (Table 1). Each component of this classification system is evaluated categorically. [1]

Stage	Recipient	Donor
1	MVP >8 cm	MVP <2 cm
2	Visible bladder	No bladder filling
3	UA A/REDV, DV absent/reversed a-wave, UV pulsations in either twin	
4	Hydrops of either twin	
5	Single or double fetal demise	

A/REDV, absent/reversed end diastolic velocity; DV, ductus venosus; MVP, maximum vertical pocket; UA, umbilical artery; UV, umbilical vein.

Table 1. Staging criteria for a twin to twin transfusion syndrome.

One of the complications associated with Twin-to-Twin Transfusion Syndrome (TTTS) is single intrauterine fetal death (sIUFD), which affects up to 6% of all twin pregnancies. This complication is more common in monochorionic (MC) twins, with an occurrence rate of 7.5%, compared to just 3% in dichorionic twins. The morbidity affecting the surviving twin is also higher in MC pregnancies. Many sIUFDs occur before 14 weeks of gestation and may present as a 'vanishing' twin during a dating ultrasound. However, sIUFDs that occur after 14 weeks are linked to serious perinatal consequences for the surviving co-twin. These consequences may include intrauterine fetal death (IUFD), preterm birth, long-term neurological issues, and neonatal death. Furthermore, there is an increased incidence of maternal morbidity following sIUFD, including higher rates of pre-eclampsia, coagulopathy, and sepsis. [13]

The vanishing twin phenomenon can lead to several physiological outcomes, including the condition known as fetus papyraceus. This occurs when a mummified, compressed, or flattened fetus is associated with a viable twin. It is a rare occurrence, most commonly seen in multiple pregnancies. The deceased fetus becomes flattened between the membranes of the viable fetus and the uterine wall. Typically, the demise of the fetus happens early in the second trimester. If the twin dies early in the pregnancy, it may be completely resorbed. However, as the pregnancy progresses towards term, the deceased twin may become macerated, which can potentially affect the surviving twin. These changes can be monitored through regular ultrasonographic examinations.[5]

CLINICAL CASE: A 37-year-old woman who denies substance abuse and was diagnosed with type 2 diabetes mellitus approximately five years ago. Her obstetric history includes four pregnancies and three deliveries.

Her first child, born 13 years ago, was healthy, with no complications during the pregnancy or birth. During her second pregnancy, four years ago, she was diagnosed with gestational diabetes and was treated with metformin; however, she discontinued the medication. Tragically, the child passed away after birth due to heart problems. The third pregnancy, three years ago, ended in stillbirth.

The weights of her previous new borns ranged from

3,000 to 3,200 grams. She was unsure about her last menstrual period (LMP) but has received good prenatal care, attending six check-ups during this pregnancy.

In March 2021, she was referred to our unit due to abnormal uterine bleeding, which was suspected to be related to an ovarian cyst. Upon her arrival at the emergency department, active bleeding was ruled out, and an ultrasound indicated a 7-week intrauterine pregnancy and an abortive fibroid. Additionally, her metabolic control was inadequate, as her blood glucose level measured 300 mg/dL.

She was admitted for the first time for a procedure that involved applying traction and torsion to the fibroid. The diagnosis was confirmed by pathology, and she was managed as a case of threatened abortion, receiving progesterone treatment.

Relevant evaluations and tests were conducted during her stay, revealing an HbA1c level of 7.2%, serum glucose level of 250 mg/dL and glucosuria of 100 mg/dL. An evaluation by ophthalmology found no signs of diabetic retinopathy in her right eye; however, they did identify a hyperpigmented chorioretinal lesion measuring two-disc diameters, consistent with a toxoplasmic scar. A TORCH test was ordered, which did not indicate any active infections.

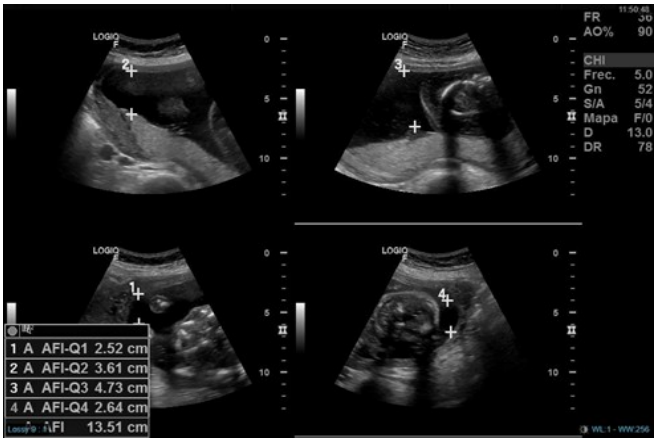
Endocrinology initiated treatment with NPH and rapid-acting insulin, but adjustments were made by the internal medicine team due to continued poor glucose control. Upon discharge, her insulin regimen was set at 10/6-0/0-8/5 units.

She was admitted a second time in May 2021 (20.4 -weeks pregnancy at that time) after an external ultrasound reported an enlarged uterus with two amniotic sacs, one occupying nearly the entire placental cavity (the patient only presented with the written report of the ultrasound without the images), with the following findings:

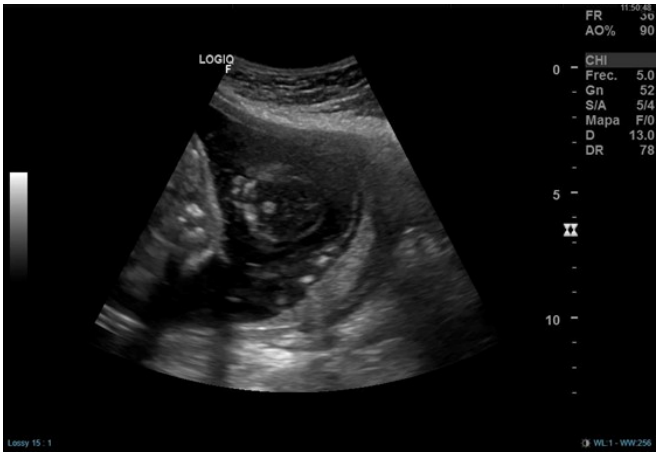
- **Fetus A**: Alive, with a fetal heart rate (FHR) of 158 bpm, estimated weight of 262 grams, and average biometrics for 18.6 WG. Fundal placenta, grade I, with sonographically normal amniotic fluid (Pheelan 18 cm).
- **Fetus B**: The second amniotic sac contained a live fetus with an FHR of 152 bpm, located in the upper area, smaller in size, with poor differentiation of anatomical structures, raising suspicion of multiple malformations, making adequate biometry difficult. Cystic images were seen in the cephalic area of this fetus, suggesting malformations.
- **Cervical length:** 42 mm.
- **Conclusion:** Monochorionic diamniotic twin pregnancy.

During the physical examination of the patient's second admission, a green, foul-smelling vaginal discharge was noted. Acute-phase reactants and cultures were ordered, and all results returned negative. Initially, she was started on a dual antimicrobial regimen of ceftriaxone and metronidazole. However, due to a lack of progress, the treatment was changed to a combination of ceftriaxone, clindamycin, and clarithromycin. During her hospital stay, the patient's blood glucose levels dropped as low as 57 mg/dL, which led to the discontinuation of insulin therapy. Dietary management was initiated, resulting in adequate control of her blood glucose levels. An institutional ultrasound was also performed, confirming a monochorionic diamniotic twin pregnancy with discordance of amniotic fluids (figure 1, figure 2) , with increased cellularity in

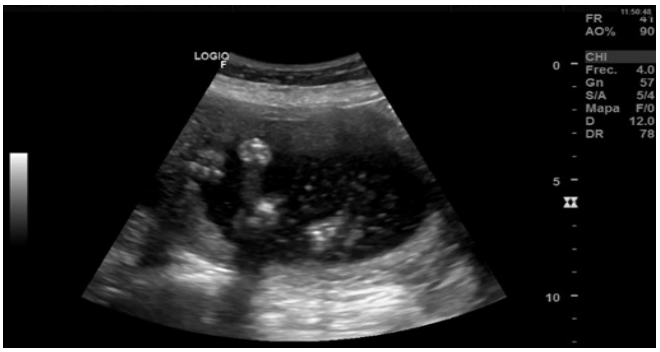
the amniotic fluid (Figure 3); however, fetal demise of one (Figures 4 and 5).



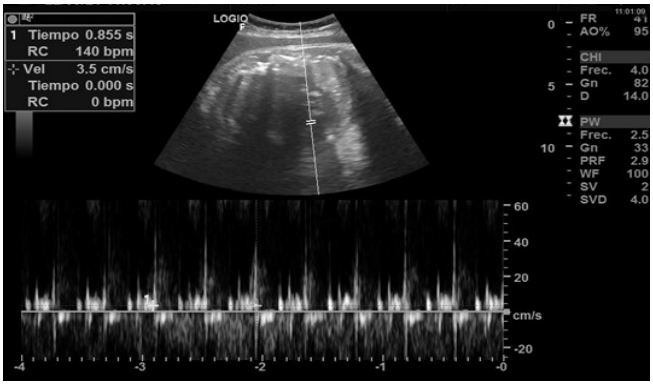
1) Fetus A. Alive. Amniotic Fluid Index 13.5cm



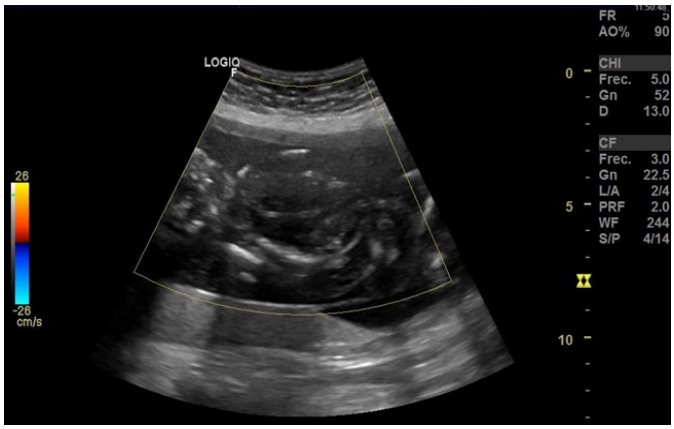
2) Fetus B. Demised. Low amniotic fluid index



3) Increased cellularity in the amniotic fluid



4) Fetus A. Fetal heart rate 140 beats per minute.

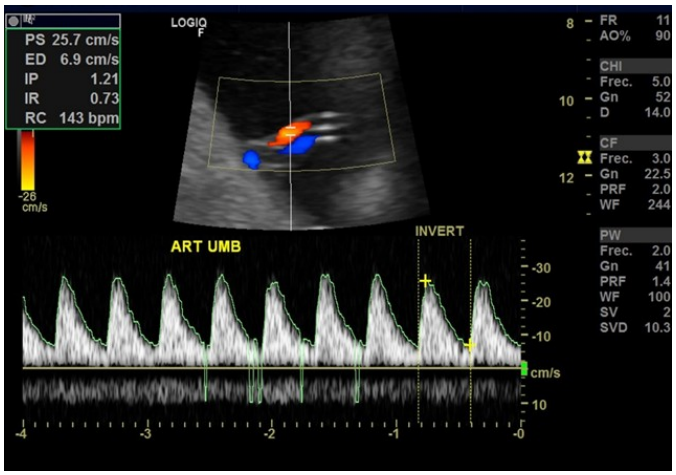


5) Fetal demise.Fetus B

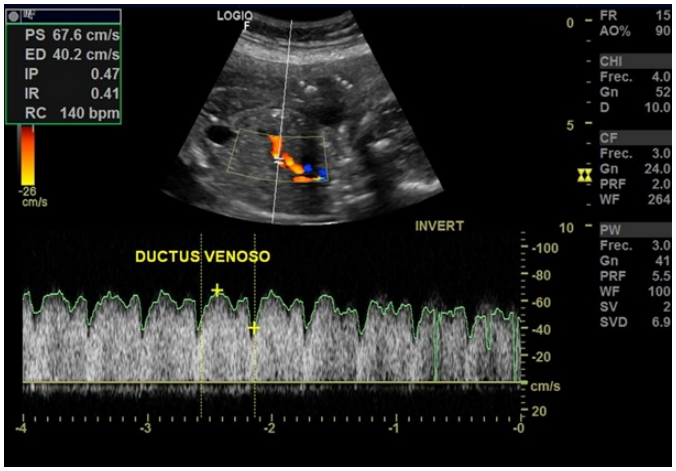
A referral to maternal-fetal medicine for tertiary-level care was requested but ultimately declined, as the situation was not deemed an immediate emergency. The patient was discharged after showing clinical and biochemical improvement, with the following results: fibrinogen levels at 288, negative acute-phase reactants (ESR 13, CRP negative), controlled HbA1c at 4.52%, leukocyte count at 5.96, hemoglobin at 12.3, and platelets at 272. Upon discharge, the patient received instructions for follow-up in the emergency department, which included monitoring fibrinogen levels and conducting serial Doppler ultrasounds.

During follow-up visits starting in July 2021, metformin 850 mg (half a tablet every 12 hours) was initiated due to borderline high blood glucose readings, with no associated complications.

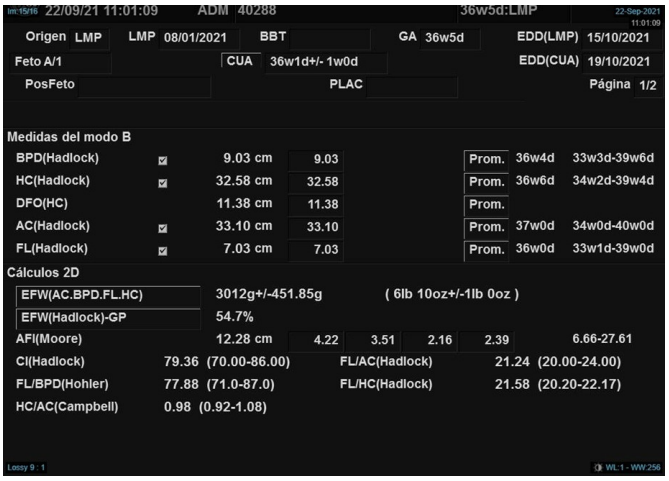
At September, 2021 the following diagnoses were established: 37-week pregnancy/ late single intrauterine fetal death (twin demise at week 16), pregestational type II diabetes mellitus, high maternal age, and completed parity. Given that prenatal control had been adequate up to that point, the last follow-up ultrasound with complementary doppler flujometry (Figures 6, 7, 8) reported the following:



6) Umbilical Artery PI 1.21



7) Ductus Venosus PI: 0.49.



8) Final exam report.

Twin 1: Heart rate of 140 beats per minute. Corresponding somatometry to 36.1 weeks, with an estimated weight of 3,012 grams. Fundal posterior placenta, lateralized to the left, grade 2. Amniotic fluid with increased cellularity (++), with a Phelan index of 12.

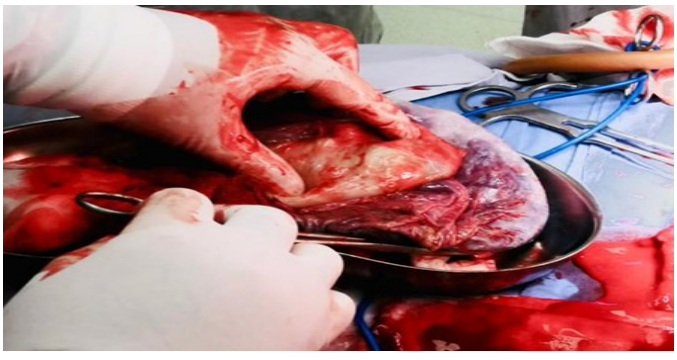
- **Middle Cerebral Artery PI**: 1.69, 52th percentile
- **Umbilical Artery PI**: 1.21, 83th percentile
- **Ductus Venosus PI**: 0.49, 49th percentile.
- **Cerebroplacental Ratio**: 1.4

Twin 2: No evidence of vitality. Poorly defined ossified structures, apparently compatible with bones of the head and lower extremities.

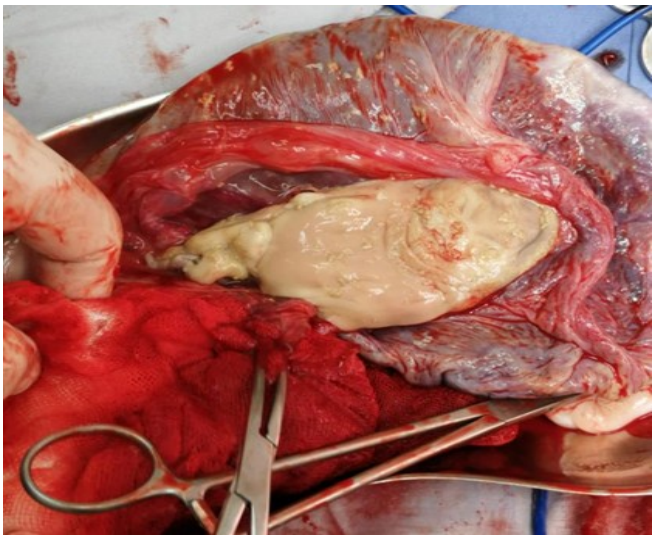
Surgery was scheduled and performed on September 24, 2021 (cesarean section plus Kroener fimbriectomy), resulting in:

- A male newborn weighing 3,275 grams, 49 cm in length, with a Capurro score of 38 weeks of gestation and an APGAR score of 8/9.
- Endometriosis in the right ovary and the posterior bleeding wall.
- During surgery, the patient experienced uterine atony, which required stepwise management, including the application of ergometrine, followed by B-Lynch suturing and a transfusion of one unit of packed red blood cells, with an estimated blood loss of 1,500 cc.

Twin 2: Fetal demise at approximately 14 weeks of gestation, weighing 60 grams, confirmed on September 24, 2021, at 10:22 a.m. (Figure 9,10)



9) Fetal demise at approximately 14 weeks of gestation, weighing 60 grams.



10) Fetal demise at approximately 14 weeks of gestation, weighing 60 grams.

Final Diagnosis: Immediate postoperative pathological puerperium, type II diabetes mellitus, resolved parity, obstetric hemorrhage.

She remained under observation for 48 hours with stable clinical and hemodynamic status and was discharged home without complications.

DISCUSION:

Due to placental vascular anastomoses connecting the two fetal circulations, monochorionic (MC) twin pregnancies are complicated and at risk for certain problems.

Twin-twin transfusion syndrome (TTTS), which most frequently occurs in the second trimester of pregnancy and is characterized by unbalanced amniotic fluid levels and the potential for fetal death if left untreated, is one such problem. TTTS-related complications include:

(TAPS): 5% of instances, identified by the twins' different hemoglobin levels.

In 15% of MCDA pregnancies, selective fetal growth restriction (sFGR) occurs.

(TRAP) sequence: An uncommon disorder in which one twin is dependent on the other for circulation since they both lack hearts.[9–13] The arcadiac twin's structure can range from well-differentiated to anatomically unrecognizable. When they lack a cardiac structure, they are referred to as holoacardiacs; when they do, they are called pseudoacardiacs. The acardiac twin is typically acephalic, lacking upper limbs, but still having a spine and central trunk. By using color Doppler to rate reverse flow in the umbilical artery toward the acardiac twin and by measuring cephalad flow in the aorta, the diagnosis is made. This anomaly is also characterized by blood flow within a bulk that does not have a heartbeat.[3]

Unfortunately, in this instance, the lack of tertiary care made it impossible to prove these findings. Rather, only hospital resources were employed, such as radiologists and gynecologists who were not specialists in maternal-fetal medicine, which resulted in biases and delays in the diagnosis of this pathology.

The prognosis for untreated TTTS is extremely dismal. Progress, fetal death, or previable birth may still occur even if Stage I illness may be stable or regress in as many as 30% of cases that are handled during pregnancy.[2] Considerations for surveillance include: Doppler studies, cervical length, polyhydramnios, and fetal bladder monitoring are crucial, and biweekly ultrasounds are advised starting in the sixteenth week to identify issues early.

By closing placental vascular anastomoses, fetal laser ablation improves survival rates for TTTS by up to 70%. After 26 weeks of pregnancy, amnioreduction is seen as a feasible substitute in cases when laser competence is not accessible. For TTTS

before 26 weeks, laser therapy is the recommended course of action because of its superior results[9_10] Regretfully, our institution does not have access to any of these resources.

In the case of this patient, who displayed a vanished twin (known as fetus papyraceous), a physiological condition characterized by a mummified and compressed fetus alongside a viable one, there are instances—though their frequency in the literature remains unclear—where no poor prognostic signs are present. In cases of early diagnosis and minimal blood flow to the acardiac twin, this situation can lead to a reduction in size and spontaneous resolution. In the case of this patient, who displayed a vanished twin (known as fetus papyraceous), a physiological condition characterized by a mummified and compressed fetus alongside a viable one, there are instances—though their frequency in the literature remains unclear—where no poor prognostic signs are present. In cases of early diagnosis and minimal blood flow to the acardiac twin, this situation can lead to a reduction in size and spontaneous resolution.

It is nevertheless necessary to perform prenatal follow-up throughout gestation to monitor the surviving twin, even though the majority of pregnancies with a vanishing twin conclude without cns, as in this instance. Potential difficulties for the mother and the surviving fetus must be taken into account, depending on the gestational age of diagnosis.[3] Elective deliveries between the ages of 36 and 37 are advised by current guidelines in order to reduce the hazards related to shared circulation. [(9_10_12)]

SYNOPSIS: Follow-up case of a 37-year-old woman diagnosed with monochorionic bianmiotic pregnancy complicated by twin-to-twin transfusion syndrome associated with intrauterine death. The control was carried out in a second level care unit, the which included ultrasonographic follow-up, metabolic control culminating in a healthy and alive single newborn.

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