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Dichoirial triamniotic triplets after in vitro fertilization, complicated by twins to twins transfusion syndrome and the death of two fetuses at 19 weeks of gestation: a clinical case of successful pregnancy and full-term delivery

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Triplet pregnancy after assisted reproductive technologies (ART) carries risks of complications for both the woman and the fetuses. Multiple pregnancies are becoming more common due to the widespread use of ART, particularly *in vitro* fertilization. Although single blastocyst transfer has become the standard, cases of monozygotic twin pregnancies and complicated multiple pregnancies remain relevant.

Aim – to present a rare clinical case of dichorionic triamniotic triplets after the use of ART, complicated by twin-to-twin transfusion syndrome (TTTS) and intrauterine death of two fetuses, as well as to analyze management tactics and perinatal outcome.

Clinical case. A 29-year-old patient underwent in vitro fertilization. After the transfer of two blastocysts, dichorial triamniotic triplets were diagnosed. At 19 weeks of pregnancy, TTTS developed in a pair of monochorionic fetuses. They died in utero, but one fetus continued to develop in its amniotic sac. The pregnancy was successfully carried to 37 weeks, delivery was by cesarean section, and the newborn was healthy. This case highlights the clinical complexity of managing dichorionic triamniotic triplets with TTTS complications and the death of two fetuses at 19 weeks. The main dilemma was whether to continue the pregnancy after the intrauterine death of two fetuses. Given the stable condition of the mother and positive dynamics of ultrasound, D-dimer, and blood counts, the pregnancy was continued. The perinatal outcome indicates the use of a personalized approach.

Conclusions. Despite the risks, the strategy of maintaining pregnancy with intrauterine monitoring showed positive results. This case may be useful for obstetricians and gynecologists who encounter similar cases.

The study was conducted in accordance with the principles of the Declaration of Helsinki. The informed consent was obtained from all participants. The authors declare no conflict of interest.

Keywords: dichorionic triamniotic triplets, monochorial twins, fetal demise at 19 weeks, treatment, progesterone, management.

Дихоріальна тріамніотична трійня після екстракорпорального запліднення, ускладнена фето-фетальним синдромом та інтранатальною загибеллю двох плодів на 19 тижні вагітності: клінічний випадок успішної вагітності та доношених пологів

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Вагітність трійнею після допоміжних репродуктивних технологій (ДРТ) несе ризик ускладнень як для жінки, так і для плодів. Багатоплідні вагітності стають дедалі поширенішими через широке застосування ДРТ, особливо екстракорпорального запліднення. Хоча перенос одинарної бластоцисти став стандартом, випадки монозиготних вагітностей близнюків і складних багатоплідних вагітностей залишаються актуальними.

Мета: представити рідкісний клінічний випадок дихоріонічної тріамніотичної трійні після застосування ДРТ, ускладненого фето-фетальним трансфузійним синдромом (ФФТС) та внутрішньоутробною смертю двох плодів на 19 тижні гестації, а також проаналізувати тактики ведення та перинатальний результат.

Клінічний випадок. 29-річна пацієнтка пройшла ДРТ, після переносу двох бластоцист їй було діагностовано дихоріальну тріамніотичну трійню. На 19-му тижні вагітності у парі монохоріонічних плодів розвинулася ФФТС з інтранатальною загибеллю двох плодів, але один плід продовжував розвиватися. Вагітність була успішно доношена до 37 тижня, пологи відбувалися шляхом кесаревого розтину здоровим новонародженим хлопчиком. Цей випадок підкреслює клінічну складність ведення дихоріальної трійні з ускладненнями ФФТС та інтранатальною загибеллю плодів на 19 тижні. Головна дилема полягала в тому, чи продовжувати вагітність після внутрішньоутробної смерті двох плодів на такому терміні. З огляду на стабільний стан матері та позитивну динаміку ультразвуку, Д-димеру, показників крові,

вагітність продовжували. Перинатальний результат успішного ведення даної клінічної ситуації свідчить про використання персоналізованого підходу.

Висновки. Попри ризики, стратегія підтримки вагітності за допомогою внутрішньоматкового моніторингу показала позитивні результати. Цей випадок може бути корисним для акушерів і гінекологів, які стикаються з подібними випадками.

Дослідження проводилося відповідно до принципів Гельсінської декларації. Від усіх учасників було отримано інформовану згоду.

Автори заявляють про відсутність конфлікту інтересів.

Ключові слова: дихоріальна тріамніотична трійня, монохоріальна двійня, інтранатальна загибель плодів на 19 тижні, лікування, прогестерон, управління.

Introduction

Over the past decade, Ukraine has seen an increase in the number of infertility treatments using *in vitro* fertilization (IVF), reflecting a global trend [16]. Multiple pregnancies are becoming more common due to the widespread use of assisted reproductive technologies (ART), in particular *in vitro* fertilization, which increases the risk of multiple pregnancies and is accompanied by significant perinatal risks for both the mother and the fetus. Although the transfer of a single blastocyst has become the standard, cases of monozygotic embryo events and complicated multiple pregnancies remain relevant [10].

At the same time, there are known cases where even with a single embryo transfer, monozygotic twins were born [6,14]. Depending on the time of embryo cleavage after fertilization, a dichorial diamniotic (up to the 3rd day) or monochorial diamniotic (on the 4th–7th day) pregnancy is formed [2,11]. In Japan, for example, the frequency of monozygotic twins is 0.4%, and triplets is 0.004% [21].

Literature data (Table) indicate the effectiveness of selective reduction in the early stages, but in this case, reduction was not performed, which necessitated prolonged careful monitoring and medical support of the pregnancy until full term [13,19,22]. An assessment of twin-to-twin transfusion syndrome (TTTS) cases in a study by Y. Sato et al. showed a frequency of 17.1% in triplets, which corresponds to the time of fetal death in our case (19 weeks) [18]. However, confirming the diagnosis was tricky because of the changing interpretation of the triplet structure during pregnancy – first as biamniotic, then as triamniotic.

A clinical case of a triplet pregnancy after the transfer of two embryos is presented below. This case was complicated by TTTS and the death of two fetuses in the second trimester at 19 weeks. Treatment was provided to correct the condition of the fetus and the woman. The case resulted in the birth of a healthy child at 37–38 weeks.

The aim of the study is to present a rare clinical case of dichorionic triamniotic triplets after the use of ART, complicated by TTTS and intrauterine death of two fetuses, as well as to analyze management tactics and perinatal outcome.

Clinical case

A 29-year-old patient with 4 years of secondary infertility of tubal, peritoneal, and uterine origin successfully became pregnant after an ART program with the transfer of two embryos at the blastocyst stage. Two embryos were transferred after stimulation (Bemfol 225 – 5 days, then Bemfol 150 + Puregon 50). In medical history, 1 missed pregnancy 7 weeks, 2012 year), infections (gonorrhea, ureaplasma, chlamydia), surgical interventions for endometriosis, and cured chronic

Table

Published cases of TTTS in triplet pregnancies with at least one intrauterine demise

Author, year	Chorionicity	Gestational age at demise	Management	Outcome	DOI
Sato Y. et al. (2019) [18]	Dichorionic triamniotic	20 wks	Expectant	1 survivor	10.1111/jog.13887
Lewi L. et al. (2010) [12]	DC/MC triplets	18 wks	Selective feticide	2 survivors	10.1016/j.ajog.2009.11.019
Ville Y. et al. (2003) [20]	MC triplets	16 wks	Fetoscopic laser	2 survivors	10.1046/j.1469-0705.2003.01002.x
Bebbington M. et al. (2005) [1]	DC/MC triplets	22 wks	Expectant	1 survivor	10.1002/pd.1093
Current case	DC/MC triplets	19 wks	Expectant	1 survivor	—

endometritis. Long-term hormonal preparation was carried out, including the use of dienogest.

2nd pregnancy after present IVF at 5–6 weeks of gestation, twins were confirmed: one embryo was a monochorionic diamniotic (MCDA) pregnancy. At 7–8 weeks of gestation, triplets were diagnosed: one embryo was a monochorionic diamniotic twin, the second was a singleton. The pregnancy was complicated by bleeding and required hormonal support. At 19–20 weeks, two monozygotic fetuses died. A dichorionic triamniotic (DCTA) structure of pregnancy was determined, probably due to the development of TTTS. Only one fetus remained viable (Fig.).

Subsequently, until week 37 – monitoring of one live fetus that corresponded to the gestational age, the other two were mummified.

Genetic testing revealed mutations in the MTHFR, PAL-1, and MTR genes, which could be risk factors for pregnancy complications. At the same time, no signs of intrauterine infection were detected at any stage of gestation.

From 19 weeks, the pregnancy was accompanied by active medical monitoring, correction of the coagulation profile (Enoxaparine, D-dimer control, coagulogram), prescription of progestogens, tocolytics, and antibiotic therapy (amoxicillin, ceftriaxone). High D-dimer levels (15,000) required intensive anticoagulant therapy (Enoxaparine 0.8×2/day).

Treatment:

• vaginal progesterone 200–600 mg, tocolytics, antibiotic therapy (amoxicillin, ceftriaxone). The patient received progestogens from the first weeks of pregnancy until 36 weeks of gestation. Tocolytics, sedatives, and nitric oxide donors were recommended from 19 weeks until delivery. Twice during pregnancy, she received antibiotic therapy with amoxicillin 625 twice a day for 10 days and ceftriaxone 1.0 twice a day for 10 days;

• anticoagulant therapy for coagulopathy;

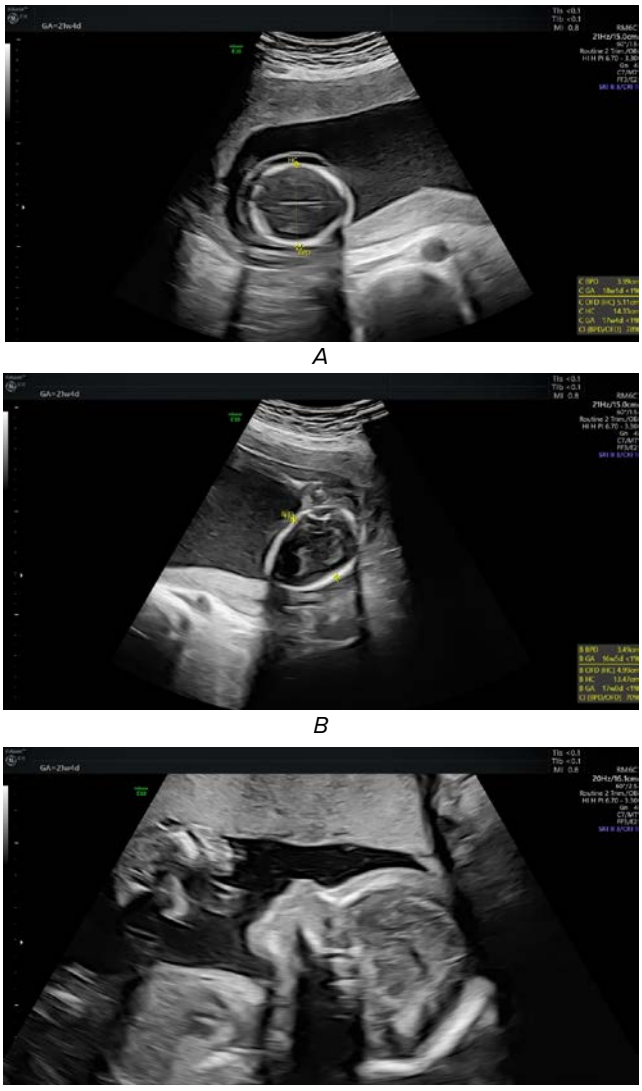
• constant ultrasound and laboratory monitoring of the condition of the fetus and the woman.

At 37–38 weeks, a healthy boy weighing 3400 g and measuring 50 cm was born by cesarean section at the Lviv Regional Perinatal Center. Follow-up: at 4 years of age, the child is healthy.

Discussion

Dichorionic Triamniotic (DCTA) pregnancies are rare and significantly riskier than trichorial pregnancies [7]. Dichorionic triamniotic triplet pregnancies are estimated to have an incidence of approximately 1 in 25,000–30,000 pregnancies, and they carry substantially higher maternal and perinatal risks compared to trichorionic triplets [12]. The presence of a monochorionic component predisposes to unique complications such as TTTS, selective intrauterine growth restriction, and acute hemodynamic shifts following the demise of one co-twin. Detection of TTTS in the monochorionic part of triplets complicates diagnosis and management tactics, leading to the loss of one or more fetuses [7,15]. The management of TTTS in triplet pregnancies is more complex than in twins due to the coexistence of an unaffected fetus in a separate chorionic sac.

Several large cohort studies [9] have shown that monochorionic triplets are at increased risk of perinatal loss, neurological morbidity, and maternal



A

B

C

Fig. Ultrasound results at 21+4 weeks of pregnancy: A – Fetus 1 (biparietal diameter (BPD) – 39,9 mm. The fetus died at 16–17 weeks); B – Fetus 2 (BPD – 34,9 mm. The fetus died at 16–17 weeks); C – Fetus 3 (alive, normal fetal profile)

complications. In TTTS, vascular anastomoses between monochorionic fetuses result in chronic inter-twin transfusion, leading to hypovolemia and oligohydramnios in the donor and hypervolemia with polyhydramnios in the recipient. When one or both monochorionic fetuses die, the surviving fetus in the same placenta is at risk of sudden cardiovascular collapse due to acute transfusion events. In DCTA configurations, the fetus in the separate chorion is spared direct vascular connections but remains at risk of maternal complications from retained demised fetuses, including sepsis and disseminated intravascular coagulation (DIC).

The case described in this article is unique because of the successful preservation of one fetus after the death of two others in the second trimester, without the development of septic complications in the mother. The critical situation in which the patient and the attending physician found themselves, with two dead fetuses at 19 weeks and a living child at 20 weeks, prompted us to seek answers in the literature and seek help from colleagues. On the one hand, against the background of rising D-dimer, C-reactive protein, and blood indicators characteristic of the inflammatory process, there was an opinion to terminate the pregnancy to avoid the risk of sepsis and loss of the woman. On the other hand, there are literary data on cases of pregnancy termination. However, in the publications of our colleagues, we did not find a similar case where one fetus was alive, and the other two died at 19 weeks. The literature contains reports favoring early selective reduction or fetoscopic laser coagulation when TTTS is diagnosed in the first or early second trimester [17,20], but in our case, intervention was no longer feasible once both monochorionic fetuses had died.

Key management options in similar scenarios include expectant management with intensive surveillance, multifetal pregnancy reduction (MFPR), or fetoscopic laser coagulation of placental vascular anastomoses. Data from case series and systematic reviews indicate that in triplet pregnancies complicated by TTTS, laparoscopic/fetoscopic laser ablation can improve the survival of some fetuses and prolong gestation – often toward the late second or early third trimester – although outcomes depend heavily on chorionicity type and vascular anatomy [3]. In triplets, both successful outcomes after laser ablation and cases with minimal prognostic improvement have been reported, largely due to the complexity of the placental vascular network.

An alternative approach is planned selective reduction. Recent retrospective series [14] show that reducing DCTA triplets to dichorionic diamniotic (DCDA) early in gestation is associated with better obstetric and neonatal outcomes compared with reduction to MCDA pairs – lower rates of early miscarriage, late preterm delivery, and adverse neonatal outcomes, with higher rates of term delivery and infant survival. These findings provide a rationale for offering early MFPR to patients who wish to reduce risks.

Conversely, a conservative approach – intensive surveillance, anticoagulant therapy when indicated, inflammatory status monitoring, and careful infection screening – can also lead to favorable outcomes, although it carries risks of maternal infectious complications and coagulopathy when dead fetuses are retained for a prolonged period. The literature contains isolated cases in which maternal septic complications or DIC did not occur after intrauterine demise of one or more fetuses, but these are not representative, and risks remain clinically significant. This dilemma – continuing the pregnancy with potential septic/hemostatic risk versus the possibility of losing a viable fetus if pregnancy is terminated immediately – was central to our decision-making [15].

Our case underscores several clinically important points. First, a double reinterpretation of chorionicity/amnionicity (initially as biamniotic, later as triamniotic) complicated early diagnosis and counseling – emphasizing the critical importance of accurate first-trimester determination of chorionicity for planning DCTA pregnancy management [5]. Second, the decision to forgo invasive interventions (neither MFPR nor fetoscopic laser ablation) despite laboratory signs of inflammation (elevated D-dimer, CRP) and instead implement a comprehensive monitoring protocol (frequent ultrasound, laboratory monitoring, anticoagulation as indicated) resulted in a term delivery without maternal septic morbidity – illustrating that in selected cases, individualized conservative management in a high-expertise center can be a viable option. This aligns with some series showing survival with expectant management under strict monitoring, although it does not justify recommending this strategy universally.

Conservative management in similar scenarios has been described [1], but always with recognition of the maternal risk for coagulopathy and infection. The risk of maternal DIC after retention of a dead fetus for more than 4 weeks has been estimated at

10–25% [8]. In our case, careful serial monitoring of coagulation parameters, inflammatory markers, and ultrasound findings allowed us to proceed without complications until delivery at term.

A recent systematic review [4] emphasizes that individualized care in high-risk triplet pregnancies should involve maternal-fetal medicine specialists, neonatologists, and hematologists, especially when balancing maternal risks against the potential survival of the remaining fetus.

Practice implications based on available evidence:

1. Early, accurate assessment of chorionicity/amnionicity in the first trimester is essential for forming a management plan for DCTA pregnancies.
2. For TTTS in triplets, multidisciplinary consultation should consider fetoscopic laser ablation and MFPR; the choice depends on gestational age, placental anatomy, and patient priorities.
3. In selected clinical contexts, carefully monitored expectant management can result in favorable outcomes but requires intensive follow-up and readiness for prompt intervention if threatening complications develop.

Conclusion

Our case adds to the knowledge base on DCTA triplets with TTTS as an example of successful conservative management under unique circumstances. However, because the data remain limited and heterogeneous, larger multicenter registries and standardized outcome sets are needed to develop reliable clinical guidelines.

This clinical case highlights the importance of:

- an individualized approach to managing multiple pregnancies after ART;
- continuous multidisciplinary monitoring in high-risk situations;
- careful study of TTTS cases in the context of triplet pregnancies.

Our experience may be useful for clinicians managing similar cases, as well as for the development of updated protocols for the management of high-risk multiple pregnancies. Timely diagnosis, dynamic and intensive monitoring, and a personalized approach to individualized treatment made it possible to avoid septic complications and ensure the birth of a healthy full-term baby.

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