Delayed interval delivery in twin pregnancy – case reports

CONSTANTIN-CRISTIAN VĂDUVA1, CARMEN CONSTANTINESCU2, MIHAELA ȚENOVICI3, ALICE ROXANA VĂDUVA4, MIHAELA NICULESCU5, DAMIAN DIȚESCU6, CRISTINA CRENGIȚA ALBU7, DINU FLORIN ALBU8

1) Department of Obstetrics and Gynecology, University of Medicine and Pharmacy of Craiova, Romania
2) Department of Obstetrics and Gynecology, Railroads Clinical Hospital, Craiova, Romania
3) Department of Pathology, Railroads Clinical Hospital, Craiova, Romania
4) Department of Endocrinology, HitMed Medical Center, Craiova, Romania
5) Department of Anatomy, University of Medicine and Pharmacy of Craiova, Romania
6) Department of Obstetrics and Gynecology, "Constantin Brâncuși" University, Târgu Jiu, Romania
7) Department of Genetics, "Carol Davila" University of Medicine and Pharmacy, Bucharest, Romania
8) Department of Obstetrics and Gynecology, "Carol Davila" University of Medicine and Pharmacy, Bucharest, Romania

Abstract
The implementation of assisted reproduction has increased the incidence of multiple pregnancies. Prenatal death of one fetus in the second trimester of twin pregnancy confronts the obstetrician with a difficult problem with regard to the management of pregnancy. The scarcity of the condition and the absence of the large-scale studies make it difficult to advise the parents on the prognosis and optimal management. The unavoidable birth or death of one premature neonate has led to the aim of delayed interval delivery for the other twin. We present in this report two cases of twin pregnancies with delayed-interval delivery and favorable outcomes for the surviving twins. The twin pregnancies conceived by in vitro fertilization (IVF) in HitMed Medical Center, Craiova, Romania. In the first case, one fetus dismisses in utero at 20 weeks of gestation. The second fetus was successfully delivered by Caesarean section, at 36 weeks. In the second case, the first fetus was delivered at 22 weeks. To save the surviving fetus, ligation of the umbilical cord at the cervical level was performed. The second fetus was delivered at 31 weeks by Caesarean section, in good conditions. We describe our management of the cases and the deliveries and the neonatal outcomes. In multiple gestation, prolongation of pregnancy after preterm dismiss in utero or even after delivery of one fetus is feasible in a closely monitored environment.

Keywords: delayed delivery, fetus papyraceous, twin pregnancy, in vitro fertilization.

Introduction
In the last years, the number of multiple pregnancies has increased. This is due to an increase in assisted reproductive technology and the higher age at which women get pregnant [1]. In twin pregnancies, there is a high risk of preterm delivery, that is about 4%, 8%, 16% for delivery before the 30th, 32nd, and 34th weeks, respectively. Multiple pregnancies are often impacted by conditions that can lead to preterm delivery and thus high morbidity and mortality of the neonates involved [2]. Morbidities associated with prematurity include respiratory failure, pneumonia, congenital malformations, necrotizing enterocolitis, intraventricular hemorrhage and retinopathy of prematurity, as well as long term deficits such as cerebral palsy and neurological and motor dysfunction. Multifetal pregnancy also exposes the mother to increased risk of preeclampsia, placental abruption, post partum hemorrhage, gestational hypertension and operative delivery among other obstetrical complications. With more twin pregnancy have come more variations on the twin birth experience, sometimes including very prolonged intervals between deliveries of the twin themselves. The delayed interval delivery technique may be applied in the case of multiple, multi amniotic pregnancy if the first premature labor occurs before 20 weeks of pregnancy, which gives little chance of survival of the fetus after delivery. This procedure is justified in women treated for infertility, for which it may provide the last chance to have a baby. The delayed interval delivery should be performed in a highly specialized center, with appropriate equipment and a neonatal intensive care unit. In the published literature, intervals between described deliveries of between 5 and 143 days have been reported and the gestational age of the fetus delivered first varied between 16 and 32 weeks [3].

The chance of neonatal survival has increased during the last decade; however, there are still conflicting results whether this is combined with a decreased long-term handicap. There is not much experience with and therefore little consensus on the procedure to delay delivery. The following three methods are most commonly used: (1) only tocolytics, (2) tocolytics and antibiotics together, and (3) tocolytics and antibiotics plus cerclage. According to the literature, mean term at delivery of the second twin is 27.7 weeks, and delay of delivery beyond 35 weeks is rare [4, 5].

The study aim was represented by the identification of placental lesions that may explain the pregnancy progress and death of fetuses, in order to improve the monitoring and management of twin pregnancies.
A 40-year-old woman had conceived by in vitro fertilization (IVF) with short stimulation protocol. The down-regulation protocol and the dose of gonadotropin used were determined by patient’s age, ovarian reserve tests and prior response to ovarian stimulation. Oocytes were inseminated by intracytoplasmatic sperm injection (ICSI), as appropriate. She had her earlier obstetric ultrasound examination (USG) on four weeks. First trimester gestational ultrasound showed dichorionic diamniotic discordant twins, crown-rump lengths (CRLs) were different between twins.

Routine investigations were normal. At 20 weeks, USG showed a viable twin (A)-female with biparietal diameter of 45 mm, femur length of 31 mm and fundal posterior placenta and a non-viable twin (B)-male with biparietal diameter 38 mm, femur length 27 mm and anterior fundal placenta. Her coagulation profile was as under: platelet count 220 000/mm³, prothrombin time index 90%, bleeding time 1 min 30 s and clotting time 2 min 20 s. Doppler flow study showed a normal flow in umbilical artery of twin A. The patient remained in the hospital until the end of her pregnancy. Serial scans at 22, 24, 26, 28 weeks of gestation showed a persistence of dead fetus. Throughout the antenatal period, the patient followed-up regularly for infections, consumptive coagulopathy and also for wellbeing of live twin. Fetal monitoring was done with daily fetal movements counts, non-stress test repeated every alternate day. Patient was managed with coagulation profile, hemogram and renal tests weekly. Every second every alternate day. Patient was managed with coagulation regularly for infections, consumptive coagulopathy and

The interval between delivery of the first and dismiss of the second fetus was 16 weeks. A piece of placenta of the papyraceous fetus was investigated for histological changes. Harvested tissue was fixed in 10% buffered formalin solution and embedded in paraffin. Serial sections were made with a thickness of 3 μm. These were stained with Hematoxylin–Eosin (HE), green light trichrome, Goldner–Szeckely (GS) technique, Periodic Acid–Schiff (PAS)–Hematoxylin followed by optical microscope examination ×100 magnification.

For the immunohistochemical study, we used the following antibodies: anti-CD34 (clone EP373Y/ab81289, Abcam, 1:100 dilution), anti-CD68 (clone KP1, Dako, 1:200 dilution), anti-estrogen receptor (ER) (clone 1D5, Dako, 1:50 dilution), anti-progesterone receptor (PR) (clone PgR636, Dako, 1:50 dilution).

The placental histopathological lesions identified on the serial sections commonly and immunohistochemically stained were polymorph. They were identified both in the placental base plaque (basal decidua) and in the villositary tree. The differentiation of the villositary tree was made only until the stem villosities. At decidual level, by common staining (HE), there were observed phenomena of decidual involution, necrobiosis, a rich inflammatory infiltrate with polymorphonuclear neutrophils and hematic suffusions, present mainly in the peridecidual area (Figure 2A).

In the differentiated villositary tree, the lesions were present especially in the stem villosities, which presented total or partial fibrinoid necrosis, with syncytial polar proliferation, rich acute perivillous inflammatory infiltrate. Also, there were identified polymorphonuclear neutrophils intravillositary degenerations, associated with trophoblast pseudo stratifications, dystrophic lesions in various stages of involution, and the acute inflammatory infiltrate was grouped as a microabscess (Figure 2B). On other sections, there was observed the formation of fibrinoid intervillous bridges with sclerohyaline stem villosities. In other areas, together with the stem villosities with circumfering, extravillous fibrinoid necrosis, there were observed extended foci of intense basophil material (stony impregnations).

The examination of GS-stained sections highlighted decidual fibrinoid necrosis, stony impregnations, and hyaline dystrophy in the stem villosities (Figure 3A). In comparison to the immature intermediary villosities that presented numerous angiogenesis foci and fibrocyte stroma, the stem villosities presented a fibrous stroma or with hyaline dystrophy (Figure 3B).

In the PAS staining, there was observed a perivillous fibrinoid necrosis with hyaline dystrophy of the stem intermediary villosities, while the immature intermediary villosities were normally differentiated (Figure 4A). The same aspect of fibrinoid necrosis was also observed at decidual level (Figure 4B).

The evaluation of microvascularization by using the anti-CD34 antibody showed the presence of some areas with intense angiogenesis in the immature intermediary villosities (Figure 5A), but the immunohistochemical reaction was low or absent in villosities with fibrinoid necrosis or hyaline dystrophy. Also, the reaction was negative on the extended decidual areas with signs of hyaline involution (Figure 5B).

Figure 1 – Fetus papyraceous in a twin pregnancy. Placentas of the twins: normal one and atrophic placenta near the papyraceous fetus.

The post-operative recovery of the mother was uneventful. The neonate stayed in the hospital for seven days and was dismissed weighing 3050 g, in excellent condition. The interval between delivery of the first and
The use of the anti-CD68 antibody highlighted an intense reactivity in the immature intermediary villosities and a poor reactivity in the stem villosities (Figure 6A), namely at decidual level (Figure 6B).

The evaluation of the immunoreactivity of estrogen receptors (ERs) showed a poorly positive reaction both at decidual level and in the differentiated villositary tree (Figure 7A), while for the progesterone receptors (PRs), the reaction was negative both in the villosities and in the basal plaque (Figure 7B).

Figure 2 – (A) Acute decidual inflammatory infiltrate; (B) Hematic and inflammatory extra-villositary infiltrate as microabscess. HE staining: (A) ×100; (B) ×200.

Figure 3 – (A) Decidual involution, sclerohyaline villosity, stony impregnation; (B) Normal intermediary immature villosities together with hyaline stem villosities. GS trichromic staining: (A) ×200; (B) ×100.

Figure 4 – (A) Perivillositary fibrinoid necrosis, sclerohyaline stem villosities; (B) The same aspect with acute diffuse and marginal inflammatory aspect. PAS staining: (A) ×200; (B) ×100.
Figure 5 – (A) Intensely positive vascular immunoreactivity in the immature intermediary villosities, negative in stem villosities with fibrinoid necrosis, or with hyaline dystrophy; (B) Decidual negative immunoreactivity with hyalinosis, positive in the mesenchymal villosity. Immunostaining with anti-CD34 antibody: (A) ×100; (B) ×200.

Figure 6 – (A) Intense macrophage reactivity in the immature intermediary villosities, negative in the stem villosities with fibrinoid necrosis; (B) Poor decidual macrophage reaction with involution. Immunostaining with anti-CD68 antibody, ×100.

Figure 7 – (A) Poor intracytoplasmic estrogenic positivity in the villosities (Immunostaining with anti-ER antibody, ×100); (B) Negative progesterone reactivity in the villosities (Immunostaining with anti-PR antibody, ×100).
Case No. 2

A 35-year-old woman had conceived by IVF and ICSI and had begun prenatal care at 12 weeks in our IVF Department, with no specific complaints. During the present pregnancy, first trimester obstetric ultrasound examination showed dichorionic diamniotic twins. In second trimester, the patient was treated with bed rest, tocolytics and progestagens because showed some bleeding and increased uterine tone. At 17 weeks was placed a cervical cerclage because the cervix is shortened (~2 cm). The value of α-fetoprotein, beta-human chorionic gonadotropin (β-HCG) and estriol were normal. Then, a follow-up ultrasound examination was done at 20 weeks, which showed a viable twin (A)-female with biparietal diameter of 47 mm, femur length of 32 mm and weighing 446 g and a viable co-twin (B)-male with biparietal diameter of 44 mm, femur length of 31 mm and weighing 410 g.

The patient was admitted to the hospital at 22nd week because of uterine contractions. USG reveal cervical shortening the cervix <0.5 cm.

With all established treatment occurred premature rupture of the membranes of the first amniotic sac. The second sac had normal amniotic fluid index and two independent placentae were visualized. Both parents and obstetrical team decided to retain the second fetus in utero. Informed consent was obtained from both the patient and her husband regarding the risks of delaying delivery. It was removed cerclage wire because the patient had frequent uterine contractions. The first, female, infant was born with a weight of 410 g. She died within the hour. The umbilical cord was tied up as high in the cervix as possible, in aseptic condition, and placenta was left inside the uterus. The fetal heart rate of the second twin was normal, and membranes remained intact. After the exit of first twin, the uterine contractions was ceased. A cervical dilatation of 3 cm was noted after delivery of the first twin. USG reveal a fetus in good condition of health.

Also, patient remained in the hospital until the end of her pregnancy. The patient was treated with bed rest, tocolytics, antibiotics, corticosteroids and vaginal antiseptic suppositories. Routine investigations and coagulation profile were normal. She was followed-up regularly for infections: complete blood cell count, C-reactive protein and vaginal cultures. The cervix was closed with the minim prolabation of the withered umbilical cord. At 27 weeks of gestation, she was give her first dose of steroid (Dexamethasone 2 g ×3). The same dose was repeated after eight days. At 31 weeks + two days, she started to have contractions and on vaginal examination, the dilatation of cervix progressed. Pregnancy was terminated by Caesarean section. A male infant was born weighing 1660 g. Post-operative patient was stable. Baby was admitted to the neonatal care unit. There was no need for surfactant. The newborn discharged form intensive care 14 days later and from neonatal care unit one month later. The interval between delivery of the first and the second fetus was nine weeks!

The histopathological examination of the aborted fetus placenta highlighted frequent immature intermediary villosities and stem villosities, some with polar or total fibrinoid necrosis, dilated vessels with stasis, numerous syncytial buds and a discrete hematic infiltrate (Figure 8A). On other sections, there were observed immature intermediary villosities and stem villosities with stromal vacuolar degenerescence (hydropic), trophoblast lesions with intranuclear vacuolizations or apoptotic phenomena, including the syncytial buds (Figure 8B). In the GS trichrome staining, besides the above-mentioned lesions, there were highlighted perivascular hyaline fascicles in the stem villosities with stromal vacuolar degenerescence (Figure 9A), dilated vessels with stasis and perivillous hematic infiltrate (Figure 9B).

The sections stained with PAS–Hematoxylin highlighted fibrinoid necrosis and stonic impregnations, as well as syncytial buds (Figure 10, A and B).

Immunomarking with anti-CD34 antibody showed the presence of a well-developed vasculary network, with an intense positive reaction in the immature intermediary villosities; still, in the stem villosities with fibrinoid necrosis, blood vessels were reduced or absent, and the reaction to CD34 was negative (Figure 11A). The antagonist, proliferation and involution phenomena were observed on the areas where there were foci of fibroblast proliferation with relatively frequent vessels, namely areas with stromal vacuolar degenerescence, dilated vessels, others with perivascular hyaline degenerescence (Figure 11B).
Figure 9 – (A) Stem villosity with perivascular fascicles (GS trichromic staining, ×100); (B) Stem villosity marked with GS trichromic staining, ×200.

Figure 10 – (A) Frequent stem villosities with variable degenerative lesions, stony impregnations; (B) Villositary vacuolar degenerescence with fibrinoid necrosis foci. PAS staining: (A) ×100; (B) ×200.

Figure 11 – (A) Intensely positive vascular immunoreactivity in the immature intermediary villosities, negative in the stem villosities with fibrinoid necrosis; (B) Stem villosity with foci of vascular positive immunoreactivity. Immunostaining with anti-CD34 antibody: (A) ×100; (B) ×200.

Immunoreactivity to CD68 was negative in the stem villosities with fibrinoid necrosis, and positive in those with stromal vacuolar degenerescence (Figure 12, A and B). Immunoreactivity for hormonal estrogen-progesterone receptors was poorly positive intracytoplasmatic for estrogens, both decidually and villositary (Figure 13A), but negative for progesterone in both localizations (Figure 13B).
Figure 12 – (A) Macrophage reactivity in the stem villosities, negative in those with fibrinoid necrosis; (B) Positive macrophage reactivity in villosities with vacuolar degenerescence. Immunostaining with anti-CD68 antibody: (A) ×100; (B) ×200.

Figure 13 – (A) Villositary estrogen intracytoplasmic poor positivity (Immunostaining with anti-ER antibody, ×100); (B) Villositary progesterone negative reactivity (Immunostaining with anti-PR antibody, ×100).

Discussion

Delayed interval delivery is becoming more and more common, especially because of the increase in multiple pregnancies for the use of assisted reproductive technologies; given that between 10 and 15% of couples in the general population have problems with sterility [5].

Intrauterine fetal death of a one twin in second trimester is a rare obstetric complication. This situation confronts the obstetrician with a difficult problem with regard to the management of pregnancy [6]. The choice of management of the mother and viable twins is very complex and difficult [7]. In this case is important the balance between the risks of leaving the surviving fetus in an intrauterine environment that may have caused the death of its co-twin or exposing the pregnant women to an associated risk of coagulopathy and prematurity [8]. In general, conservative management is advocated. Post mortem examination should be arranged, but in most cases, it does not reveal any cause, because the fetus is macerated and the tissues are autolysed [9]. Fetus papyraceous or compress is the compressed, mummified, parchment-like remains of a dead twin, which is retained in utero after intrauterine death in the second trimester and the other fetus(es) continue to grow [10]. When the fetus dies in early pregnancy (15–20 weeks) the amniotic fluid and the dead placental tissue are gradually absorbed and the fetus is compressed and becomes incorporated into the membranes. The co-living twins continue to grow [8]. The incidence of fetus papyraceous has been reported at one in 17 000 to 20 000 pregnancies and one in 184 to one in 200 twin pregnancies [11, 12].

Although there are no consensus guidelines on this approach, many case reports have suggested options that have provided positive outcomes that reduce neonatal morbidity and mortality. We recommend evaluating each situation on a case-by-case basis, depending on the possible risks and contraindications. The cause of intrauterine death of the fetus could not be ascertained. Twin pregnancy or multiple gestations is a common finding in today’s era especially due to artificial reproductive technology and in vitro fertilization [13]. Maternal complications include preterm labor, infection from a retained fetus, severe puerperal hemorrhage, consumptive coagulopathy, and obstruction of labor by a low-lying fetus papyraceous causing dystocia leading to Caesarean delivery. Laboratory
tests to rule out infection and coagulation disorders were performed at regular intervals. Fetal monitoring consisted of frequent biophysical assessment, including cardiotocography, Doppler flow velocimetry, and real-time ultrasound. Fetal biometry and the amount of amniotic fluid were examined by ultrasound at regular intervals [14]. In our first case, reported routine ultrasounds allowed the diagnosis of fetus papyraceous early in pregnancy (20 weeks). Close monitoring of the evolution of gestation period confirmed no adverse effect on the mother or on surviving twin.

In twin pregnancies, delivery of the second twin usually results from persistent uterine activity after the first expulsion. Even when this activity stops, concern about chorioamnionitis generally prevents obstetricians from prolonging the pregnancy after the first delivery.

For the second case, delayed interval delivery was necessary for aging baby remained in the womb. Intervention with tocolysis, antibiotics, and cervical cerclage after delivery of the first fetus is a reasonable option. In cases where the membranes of the second twin remained intact with no evidence of ongoing labor or other obstetric risk factors, a conservative approach could be adopted [15]. Asynchronous delivery is a flexible procedure because no accepted protocol for the treatment of this condition currently exists. Cervical cerclage has been used with a reasonable success rate, even in widely dilated cervixes. In our case, cervical cerclage was not necessary due to progressive closing of cervix. It is recommended that women should stay in bed, for the rest of their pregnancy, although there are rare reports where patients were permitted to leave hospital under medical supervision. Suppression of premature contractions can be achieved with tocolytics like beta-mimetic, magnesium sulfate, oxytocin-receptors inhibitor or non-steroid anti-inflammatory drugs. Tocolysis may be used precautionarily after first twin’s birth, or only later during uterus contractions, but never in the presence of a well-established chorioamnionitis. There was no evidence that retention of placenta caused disseminated intravascular coagulation (DIC) [16]. The underlying mechanism of DIC is not known; there may be a breach between the maternal and fetal circulations, which allows the passage of tissue thromboplastins from the dead fetus and its placenta into the maternal circulation. The transferred thromboplastins activate the extrinsic coagulation pathway and thereby consume platelets and coagulation factors. Conservative management remains the mainstay but the risk of keeping the live fetus in the hostile intrauterine environment has to be weighed against the risk of preterm delivery. According to the literature, mean term at delivery of the second twin is 27.7 weeks, and delay of delivery necessary for aging baby remained in the womb. Intervention with tocolysis, antibiotics, and cervical cerclage after delivery of the first fetus is a reasonable option. In cases where the membranes of the second twin remained intact with no evidence of ongoing labor or other obstetric risk factors, a conservative approach could be adopted [15]. Asynchronous delivery is a flexible procedure because no accepted protocol for the treatment of this condition currently exists. Cervical cerclage has been used with a reasonable success rate, even in widely dilated cervixes. In our case, cervical cerclage was not necessary due to progressive closing of cervix. It is recommended that women should stay in bed, for the rest of their pregnancy, although there are rare reports where patients were permitted to leave hospital under medical supervision. Suppression of premature contractions can be achieved with tocolytics like beta-mimetic, magnesium sulfate, oxytocin-receptors inhibitor or non-steroid anti-inflammatory drugs. Tocolysis may be used precautionarily after first twin’s birth, or only later during uterus contractions, but never in the presence of a well-established chorioamnionitis. There was no evidence that retention of placenta caused disseminated intravascular coagulation (DIC) [16]. The underlying mechanism of DIC is not known; there may be a breach between the maternal and fetal circulations, which allows the passage of tissue thromboplastins from the dead fetus and its placenta into the maternal circulation. The transferred thromboplastins activate the extrinsic coagulation pathway and thereby consume platelets and coagulation factors. Conservative management remains the mainstay but the risk of keeping the live fetus in the hostile intrauterine environment has to be weighed against the risk of preterm delivery. According to the literature, mean term at delivery of the second twin is 27.7 weeks, and delay of delivery beyond 35 weeks is rare. Of 54 pregnancies from the four principal series with available information, only four involved delivery after 35 weeks [4, 17–19]. Prolongation appears longest when the first birth was earliest (before 24–25 weeks) [20]. In contrast, Livingston et al. found a high perinatal mortality of 61% associated with delayed interval delivery [20]. In the same study, only one of 19 retained fetuses survived without major sequels. Another study concluded that delayed interval appears to be associated with improved outcomes for the twin whose delivery is delayed when the first twin is delivered at 22 to 23 weeks and the delivery interval is ≤3 weeks [21].

Our report favors conservative management until 30–34 weeks gestation, if fetal movements, cardiotocography, and ultrasonography show no abnormalities. Our cases were not complicated by signs of infection or DIC.

A thorough neonatal evaluation is indicated for the surviving twin to detect central nervous system, renal, circulatory, and cutaneous defects. Investigations may include high-resolution ultrasonography of the brain, computed tomography, renal function studies, and magnetic resonance imaging. Long-term follow-up is mandatory [22].

Generally, from the histopathological point of view, there was identified a placental chronic inflammation in twin pregnancies that may be present in the villous tree, and also in the placental base plaque, named chronic villitis or chronic deciduites, respectively. [23]. In these cases, the villites are of unknown etiology (VUE), being defined by the infiltration of lymphocytes and macrophages in the chorionic villitis [24]. Generally, chronic inflammation may be caused by infectious agents, like viruses, bacteria, parasites [25, 26]. The maternal anti-fetal rejection is suggested to play a role in the pathogenesis of these conditions [23]. Anyway, the etiology of these infections is not identified in most cases of placental chronic inflammation. [23]. In the first case, there was identified an abundant extravillosity acute inflammation, although in the immature intermediary villitis there appeared macrophages, which suggests the presence of a chronic infection that became acute under unknown conditions. The presence of the inflammatory infiltrate with polymorphonuclear neutrophils was most often grouped as a microabscess, being also accompanied by an extravillosity hematic infiltrate.

The study of literature showed that a chronic placental inflammation especially with VUE (villitis with unknown etiology) is found more frequently in twin pregnancies than in singular ones. The absence of the association with intrauterine growth restriction (IUGR) with VUE in twin pregnancies may be influenced by other factors specific to twin pregnancies that have an IUGR effect, limitation of uterine space, utero-placental functional failure, twin-to-twin transfusional syndrome [27]. In our case, there were associated and dystrophic lesions of hyaline degenerescence, fibrinoid necrosis that were predominant in stem villitis, but also in the placental base plaque. For the fetal evolution, the acute inflammation was possibly determined for the involution of villous tree, namely decidual. The association with degenerative lesions led to fetal death.

In the second case, the morphological aspects were represented by degenerative stromal lesions of vacuolar and trophoblastic type and syncytiatal buds. The lesions were not of typical vascular anastomotic or placental infarction, but the apoptotic changes of trophoblast level and of syncytiatal buds were observed as an effect of oxidative stress. This phenomenon of trophoblast apoptosis is high in cases of preeclampsia and abortion, in accordance with the oxidative stress [28, 29]. An excess placental apoptosis and changes in the synthesis of varied trophoblast proteins
were found in dichorionic twin pregnancies, thus confirming the role of oxygenation, apoptosis and oxidative stress in fetal development abnormalities [30, 31]. This phenomenon of trophoblast apoptosis and especially in the syncytial buds was also observed in our case. There are authors that consider oxygenation fluctuation as an inducing factor for oxidative stress with placental apoptosis [29, 32]. The molar transformation of an ovule from a twin pregnancy is a rare complication that may co-exist with a normal fetus [33]. The twin pregnancy that involves a complete molar development has a high risk of developing a severe complication, such as preeclampsia or fetal loss [17]. In our case, a stromal vacuolar degenerescence, with no atypical trophoblast proliferation, suggests a mesenchymal dysplasia associated with fibrinoid degenerescence. These lesional associations, such as trophoblast apoptosis and mesenchymal vacuolar degenerescence, were not described in the literature until now.

Conclusions

It is recommended that all twin pregnancies with one dead fetus should be managed in tertiary referral centers with sufficient neonatal support and a multidisciplinary approach should be employed. A management plan should be individualized. Successful outcome is related to careful monitoring during pregnancy. In our experience, delayed-interval delivery can prolong pregnancy for a sufficient amount of time to achieve good prognosis for the second baby. We believe that delayed-interval delivery can be effective in prolonging gestation until a gestational age at which the chance of survival for the second fetus is higher. The delayed delivery of the second twins, which occurred in the third trimester, is associated with favorable outcome; however, the risks should not be ignored. Placental lesions in dichorionic twin pregnancies may be polymorphic, associating various placental lesions of inflammatory, hemorrhagic type, hyaline dystrophy, fibrinoid necrosis, vacuolar mesenchymal dysplasia up to trophoblast apoptosis.

Consent

Written informed consent was obtained from the couple of patients for publication of this Case report and any accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this Journal.

Conflict of interests

The authors declare that they have no conflict of interests.

References


**Corresponding author**

Mihaela Niculescu, Lecturer, MD, PhD, Department of Anatomy, University of Medicine and Pharmacy of Craiova, 2 Petru Rareş Street, 200349 Craiova, Dolj County, Romania; Phone +40722–463 595, e-mail: ela07071@yahoo.com

Received: January 8, 2016

Accepted: December 11, 2016