Asynchronous delivery in a twin pregnancy. First case report in Peru
Parto asincrónico en un embarazo gemelar. Primer reporte de caso en el Perú

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ABSTRACT
Asynchronous delivery (AD) or delayed interval delivery (DID) is a rare presentation of multiple gestation. This occurs when one fetus is delivered vaginally and the remaining fetus or fetuses are kept in utero and are born with a difference of days or weeks. This is the first report in Peru of a pregnant woman whose first delivery was at 20.1 weeks and the second at 24.4 weeks, and the management and perinatal results of the case are detailed. The evidence suggests that a DID improves survival and reduces morbidity and mortality of the second fetus. Further research on this topic is essential to describe its real prevalence, identify ideal candidates, standardize obstetric management and thus optimize maternal and fetal outcomes.

Key words. Multiple pregnancy, Twins, Complications of labor, Premature birth, Delayed birth.

ABSTRACT
El parto asincrónico (PA) o parto diferido (PD) es una presentación poco prevalente de la gestación múltiple. Este ocurre cuando un feto nace por vía vaginal y el -o- los- fetos restantes se mantienen intraútero y nacen con una diferencia de días o semanas. Se realiza el primer reporte en el Perú de una gestante cuyo primer parto fue a las 20,1 semanas y el segundo a las 24,4 semanas, y se detalla el manejo y los resultados perinatales del caso. La evidencia sugiere que un PD mejora la supervivencia y reduce la morbimortalidad del segundo feto. Es imprescindible continuar la investigación en este tema para describir su prevalencia real, identificar candidatas ideales, estandarizar el manejo obstétrico y así optimizar resultados maternos y fetales.

Palabras clave. Embarazo múltiple, Gemelos, Complicaciones del parto, Nacimiento prematuro, diferido.

CASE REPORT

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INTRODUCTION
Multiple pregnancy, the incidence of which has increased in recent years, is associated with various obstetric and neonatal complications(1). Gestational age is the main factor in the survival of preterm neonates, so it is necessary to prolong pregnancy as long as possible in twin gestations that present a threat of preterm delivery(2).

Usually, delivery of all fetuses in a multiple gestation occurs within a short interval of time; however, the premature birth of one fetus may not necessarily result in the birth of the other fetuses. Asynchronous delivery (AD) or delayed delivery occurs when one fetus of a multiple pregnancy is delivered vaginally and the remaining fetus or fetuses remain intrauterine and are delivered days or weeks apart(3). We report the case of a pregnant woman with a diagnosis of twin AD, of rare occurrence, being the first case reported in Peru.

CASE REPORT

30-year-old patient with a history of mild COVID-19, G3P0020 (spontaneous abortions at 16 and 20 weeks). During the first trimester she presented urinary tract infection treated with antibiotic therapy and vulvovaginitis with local treatment. She was admitted as an emergency patient with a double biamniotic and bicornuate gestation of 20.1...
weeks, referring fluid loss and mucous plug loss. Vital functions were stable and there was no uterine dynamics. Speculoscopy revealed the loss of fluid. The cervix was dehiscent, incorporated and the membranes were ruptured.

Laboratory tests showed leukocytes at 11,000, without left deviation. The rest of the tests were normal. Obstetric ultrasound showed both fetuses with normal cardiac activity, anhydramnios in the first fetus (EFW1: 318 g) and normal amniotic fluid in the second (EFW2: 278 g); with no other abnormal findings. It was decided to hospitalize the pregnant woman with the diagnoses: 1) 20.1 weeks nulliparous tercigesta; and, 2) Inevitable abortion.

During hospitalization, the first fetus, female, weighing 380 g and with no apparent congenital malformations, was expelled. The umbilical cord was clamped and cut, after which the uterine dynamics ceased. In re-evaluation obstetrical ultrasonography, the viability of the second fetus was evidenced, with no signs of labor. A medical meeting was held and the possible fetal and maternal risks and complications were explained to the patient in a clear and understandable manner. In a shared manner, expectant management was decided. Absolute rest and vigilance for signs of chorioamnionitis was indicated. The cord was cut at the level of the cervical os.

On admission, clindamycin and gentamicin were administered intravenously. On the tenth day of hospitalization, the antibiotic regimen was changed to cefuroxime and metronidazole, orally, and micronized progesterone 200 mg vaginally at night was added. After two weeks of hospitalization, with normal laboratory tests and asymptomatic, she was discharged from the hospital, with indication of micronized progesterone, ferrous sulfate, calcium citrate, vitamin D and weekly control.

In the first weekly control, adequate fetal growth was found (EFW in the 49th percentile) and cervical length of 20.8 mm, so it was classified as a short cervix with indication of absolute rest.

Fifteen days after discharge, the patient came to the emergency room for loss of the mucus plug, pain and contractions. Vital functions were normal and uterine dynamics were evident. No fluid leakage was visualized. On vaginal examination the cervix was found to be dehiscent, with 30% of incorporation and intact membranes.

The fern test was negative. Ancillary tests revealed leukocytes at 12,470, no left shift, and no other abnormalities. Obstetric ultrasound showed the fetus with normal fetal heartbeat and amniotic fluid, estimated fetal weight 979 grams, and cervical length of 8.6 mm. The pregnant woman was hospitalized with the following diagnoses: 1) 24.3 weeks’ tercigesta; 2) Threatened preterm labor; 3) Asynchronous delivery; 4) Short cervix; and, 5) Subclinical chorioamnionitis.

It was decided to perform a first cycle of tocolysis with 3 doses of nifedipine, 20 mg every 20 minutes orally, with which the uterine dynamics subsided. Pulmonary maturation was also indicated with two doses of betamethasone, as well as vaginal progesterone and ampicillin with erythromycin.

On the second day of hospitalization, uterine dynamics appeared again, so a new cycle of tocolysis associated with 20% magnesium sulfate was started intravenously for fetal neuroprotection. The uterine dynamics did not improve after two cycles of tocolysis, and on vaginal examination the cervix was 3 cm dilated, with 80% incorporation and intact membranes. It was decided to terminate the pregnancy via the abdominal route.

A corporal low transverse cesarean section and B-Lynch compression suture due to uterine hypotonia were performed. The newborn was female, 25 weeks by Capurro method, Apgar 7-8, weight 740 grams, amniotic fluid with slight yellowish tinge, who was transferred to the neonatal intensive care unit (NICU) for management. Likewise, a 150 g placenta without umbilical cord and another 300 g placenta with cord containing 2 arteries and 1 vein were found (Figure 1).

During the immediate postoperative period, the patient presented desaturation, managed with oxygen therapy. Complementary tests showed hemoglobin 8.2, leukocytes of 17,000, pO2(a)/ FO2(I) of 205, and was therefore classified as gynecologic sepsis, associated with respiratory failure and moderate anemia. Treatment was started with intravenous meropenem and transfusion of a globular pack.
The patient showed clinical and laboratory improvement, so the oxygen supply was progressively decreased, until its total withdrawal at 5 days of puerperium.

Pathological anatomy revealed the first placenta with signs of funisitis and chorioamnionitis, and the second with areas of old and recent infarction, which confirmed the starting point of sepsis. Antibiotic therapy was continued for 10 days, with favorable evolution, after which the patient was discharged and made a complete recovery.

The newborn required respiratory support with Neopuff immediately after delivery. In the NICU, endotracheal intubation and surfactant administration were decided. Hyaline membrane disease associated with bronchopulmonary dysplasia was diagnosed. During his hospitalization he developed late sepsis, bilateral intraventricular hemorrhage and septic ileus. He was discharged after 3 months. In his medium-term evolution, periventricular leukomalacia, retinopathy of prematurity and global developmental delay were evidenced. At the time of the case report, he is stable, receiving treatment and periodic pediatric controls.

**DISCUSSION**

In 1879, Carson JCL reported the first case of AD, with a time interval between both deliveries of 44 days\(^4\). The AD with the longest interval has been 154 days\(^5\). Unfortunately, the actual incidence is not known, since the literature is limited to case reports and series subject to the bias of reporting only positive results. In our case the duration of the interval was 33 days.

A prolonged time interval between births of critical gestational age fetuses significantly improves the perinatal survival of the remaining fetuses\(^2,6\), while one week’s delay in delivery is associated with an increase in birth weight of up to 147 g\(^7\). After explaining to the patient the chances of survival of the second fetus with respect to her gestational age, it was decided to continue with an AD.

Despite attempts to establish guidelines, no validated obstetric management protocol is available. In most studies, the algorithm includes cleaning of the vaginal and cervical canal with an antiseptic solution, leaving the placenta of the firstborn in situ with high umbilical cord ligation performed with absorbable suture, hospitalization with rest, preventive anticoagulation, tocolysis, prenatal glucocorticoids and prophylactic broad-spectrum antibiotics\(^2,8\). In this case, the cord was ligated with resorbable suture at the external cervical os, without removing the placenta. To prevent infection, antibiotic coverage was initiated against possible pathogens of the vaginal canal. The patient remained hospitalized with absolute rest until the intravenous treatment was completed. Pulmonary maturation was performed in the second hospitalization. Three cycles of tocolysis were performed to delay the second delivery, all of which were unsuccessful.
Cervical cerclage is a frequently used treatment, although its effectiveness is still under debate. Some studies report a benefit in postponing the delivery interval in twin pregnancies, while other authors consider it contraindicated due to the risk of chorioamnionitis\cite{6,10}. In this case it was decided not to perform cervical cerclage.

In a meta-analysis by Cheung, the mean gestational age at delivery of the first fetus was 21.6 weeks gestation (range 13 to 31 weeks), with a mean delay interval of 29 days (range 1 to 153 days). In this same study, it was described that the perinatal survival rate with respect to the gestational age at delivery of the firstborn can range from 29% before 20 weeks to 72% after 24 weeks. On the other hand, the gestational age of the second fetus at birth was a determining factor, its survival rate being 0% before 21 weeks, 17% to 33% between 21 and 24.6 weeks, 21% to 78% between 25 and 27.6 weeks, and 100% after 28 weeks\cite{2}. In our case, the first delivery was at 20.1 weeks, so the survival rate of the second fetus with respect to the first could be as high as 29%. On the other hand, since the second delivery was after 32 days, at 24.4 weeks, its survival rate would be up to 33%.

The risk of maternal complications can be up to 38%, with local infections and sepsis being the most frequent, followed by postpartum hemorrhage, placental abruption, postpartum hysterectomy and uterovaginal fistulas. No cases of maternal death have been reported\cite{2,5}. Likewise, a retrospective study in patients with severe complications described negative amniocentesis when evaluating subclinical chorioamnionitis, so it is important to highlight that the risk could be difficult to predict\cite{11}. Although uterine hypotonia requiring a surgical compression technique was described, it did not lead to postpartum hemorrhage. Likewise, the gynecological sepsis evolved favorably until the patient recovered completely.

Finally, neonatal outcomes have also been the subject of study. Gestational age is a critical factor in neonatal morbidity and mortality, and directly influences the development of neonatal sepsis, retinopathy of prematurity, patent ductus arteriosus, necrotizing enterocolitis and bronchopulmonary dysplasia\cite{21}. According to Rosbergen, a significant increase in birth weight and neonatal survival was evidenced, as well as a decrease in diseases in the second fetus of an AD\cite{12}. In this case, the first newborn died immediately after the first delivery and the second newborn presented expected complications due to extreme prematurity. Long-term outcomes were not evaluated.

Due to the maternal and neonatal risks, it is necessary to follow guidelines for shared decision making in cases such as this, which may represent ethical dilemmas. Following the evidence-based medicine approach, we collected available data on the pathology and identified appropriate medical options. Being in an obstetric setting, we recognized that the pregnant patient could be the decision-maker, so we provided clear and understandable information about the options and possible outcomes. Considering the data and ethical principles, a joint decision was made to proceed with the pregnancy. This approach is the most appropriate in situations where the scientific evidence does not clearly support a single management option for all patients\cite{13,14}.

In conclusion, AD is a presentation of very low prevalence, so there are still no clear guidelines for its obstetric management. However, evidence strongly suggests that a prolonged time interval between births of fetuses at a critical gestational age may improve survival and reduce morbidity of the second fetus. In scenarios such as this, shared, evidence-based decision making, considering the ethical principles of medicine, is important. We have not found any reports on this pathology in our environment, so we believe it is important to report this first experience in our hospital. It is essential to continue research on this subject in order to describe its real prevalence, identify ideal candidates, standardize in-hospital and out-of-hospital management and thus optimize maternal and fetal outcomes.

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