ORIGINAL ARTICLE

Amniopatch – possibility of successful treatment of spontaneous previable rupture of membranes in the second trimester of pregnancy by transabdominal intraamiotic application of platelets and cryoprecipitate

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Abstract

OBJECTIVE: To outline possibility of successful treatment of spontaneous previable rupture of membranes in the second trimester of pregnancy. Spontaneous previable rupture of membranes (SPROM) in the second trimester of pregnancy is one of the most alarming problems in current obstetrics. Perinatal mortality is about 60%, one third of which represents intrauterine fetal demise. Surviving neonates suffer from various complications. There are different clinical approaches regarding treatment of SPROM.

MATERIAL & METHODS: We present a case of a 30 year old secundigravida with a history of SPROM at 19+1 weeks gestation. Ultrasonographic examination revealed anhydramnios. Genital cultures and laboratory studies ruled out infectious etiology of SPROM. Due to expected poor neonatal outcome, decision to attempt amniopatch as an experimental therapeutic alternative was made at 21+1 weeks gestation (two weeks after SPROM had occurred).

Autologous concentrated platelets followed by autologous cryoprecipitate were administered into the amniotic cavity transabdominally under ultrasound guidance. After 3 days sonographic examination showed normal volume of amniotic fluid. On 22 postoperative day, patient notice some leaking of fluid vaginally. Fetal growth was appropriate, amniotic fluid volume was decreased, however, oligohydramnios never progressed to anhydramnios. Pregnancy ended with primary cesarean delivery at 33+1 weeks gestation. Live born male infant with 1 750 g birth weight was delivered. Postnatal development was within normal limits.

CONCLUSION: Intraamniotic application of "amniopatch" may represent a possibly successful treatment of spontaneous previable rupture of membranes. This

case reports the longest stop of the leaking of amniotic fluid and total prolongation of pregnancy with favorable perinatal outcome after „amniopatch" treatment of spontaneous previable rupture of membranes in the second trimester so far published in available literature.

INTRODUCTION

Previable rupture of membranes (PROM) in the second trimester of pregnancy is one of the most alarming problems in current obstetrics. Two types of PROM are distinguished based on its etiology – spontaneous PROM (SPROM), and iatrogenic PROM (IPROM) (Lewi *et al.* 2004). IPROM is mainly encountered as a complication of invasive prenatal diagnostic methods – amniocentesis (incidence: 0.8–1.0%), amniodrainage (4%), fetoscopy in twin-to-twin-transfusion-syndrome (6%), other fetoscopic interventions (30–50%) (Lewi *et al.* 2004). Both types of PROM are accompanied with high fetal morbidity and mortality (intramniotic infection, pregnancy loss, preterm labor, neonatal pulmonary hypoplasia). Perinatal mortality is about 60%, one third of which represents intrauterine fetal demise. Surviving neonates suffer from various ophthalmologic, respiratory, and neurological complications.

Defect in fetal membranes in IPROM is usually located on the anterior wall of the uterus. SPROM typically causes disruption of distal pole of fetal membranes, often times above internal cervical os. SPROM leads into severe oligohydramnios, not infrequently anhydramnios. This phenomenon severely affects fetal development and pregnancy outcome. Most common outcome of IPROM is pregnancy loss few days following surgical intervention (80% of pregnancy losses occur within first 7 days postoperatively). Pregnancy loss is often associated with ascendent intramniotic infection (Contino *et al.* 2004). The likelihood of prolonging pregnancy till fetal lung maturity is achieved is very low. Neonates than suffer from pulmonary immaturity, pulmonary hypoplasia, and intraventricular hemorrhage. There exists whole array of therapeutic approaches to pregnancies complicated by PROM. These range from expectant management combined with antibiotic prophylaxis (high perinatal morbidity and mortality) to aggressive induction of labor being on the other end of the spectrum (Cox *et al.* 1988, Gold *et al.* 1989, Morales & Talley 1993). Amnioinfusion is one of the proactive interventions in this scenario. Repetitive amnioinfusion may successfully be performed to prolong pregnancy after 17 weeks gestation, however, there is high risk of developing intramniotic infection (Fisk *et al.* 1991, Hofmeyer *et al.* 1992). Another proactive management approach of PROM in the second trimester of pregnancy involve procedures leading to resealing fetal membranes. First published studies referring to successful transcervical application of fibrin glue are from 1986 (Baumgarten *et al.* 1986). Quintero in 1996 published his first experience with intracavitary application of cryoprecipitate and platelets (Quintero *et al.* 1996). This American author published multiple studies regarding the procedure (Quintero *et al.* 1996, Quintero *et al.* 1998, Quintero *et al.* 1999, Quintero 2001, Quintero 2003). Promising results of the same therapeutic intervention were also published by Italian authors in 2004 (Contino *et al.* 2004), and case report with positive outcome was also published by Austrian team in 2006 (Sipurzynski-Butraß *et al.* 2006). Most of the above studies only include cases with IPROM. Only the Italian study from 2004 includes 2 cases of spontaneous PPROM out of 5 cases presented (Contino *et al.* 2004).

Spontaneous PPROM remains to be more challenging problem even after application of the above described technique.

CASE REPORT

Course prior to intervention

30 year old secundigravid patient was admitted to local hospital with diagnosis of SPROM at 19+1 weeks gestation. At 21+1 weeks patient was transferred to our institution. Intrauterine pregnancy consistent with given gestational age was confirmed ultrasonographically. Diagnosis of anhydramnios was made. Genital cultures as well as laboratory test ruled out presence of infection. Due to poor prognosis patient was offered intraamniotic application of autologous platelet concentrate along with autologous cryoprecipitate. Patient was appropriately counseled and agreed with the procedure. Plan of care was also approved with hospital ethics committee. Patient's care was coordinated with the department of hematology.

Methods and application of amniopatch

Complete Blood Counts before procedure:	Complete Blood Counts after procedure:
Hb: 120 g/l	Hb: 102 g/l
Le: 10.5×10^9/l	Le: 9.3×10^9/l
Ht: 0.37	Ht: 0.33
Tr: 177×10^9/l	Tr: 119×10^9/l

Blood elements were obtained using cell separator HAEMONETICS MCS+ (protocol card LDP, set number 994 CFE). Products were obtained in two 45-minute cycles. 146 ml of platelets and 248 ml of plasma were separated. Platelet concentration was 1.7×10^{11}. Patient tolerated procedure well. Approximately 30 ml of cryoprecipitate was obtained from 248 ml of autologous plasma. The entire volume of plasma was frozen at –80 °C for 1 hour. While spontaneously thawing, it was centrifuged at 3 000/min for 90 minutes. The volume of the concentrate was then adjusted to 30 ml using plasma. (in compliance with European transfusion guidelines).

Infusion of the blood products into amniotic cavity was performed on the same day. Ultrasound guided amnioinfusion of 90 ml of normal saline was performed prior to administering blood elements. 22 G needle was used. This was done to create adequate pocket of amniotic fluid due to anhydramnios prior to performing procedure. 60 ml of platelet concentrate and 30 ml of cryoprecipitate were then instilled into the amniotic cavity.

Course after intervention

Postoperatively patient remained stable, no signs of intrauterine infection were detected, and no leaking of fluid from vagina was identified. Ultrasound examination confirmed normal volume of amniotic fluid. On the twenty second postoperative day, patient notice some leaking of fluid vaginally. This continued till the end of the pregnancy. Mildly decreased volume of amniotic fluid persisted throughout the remainder of pregnancy (AFI = 4.8–5.4 cm). Fetal growth and development continued to be adequate. No signs and symptoms of infection were present at any point during pregnancy. At 33+1 weeks gestation patient noticed significant increase in vaginal leakage and she also passed pieces of „tissue". This was consistent with „amniopatch" mass. Exactly 12 weeks after the procedure, the pregnancy ended with cesarean delivery. Delivery was uneventful and without any complications. Live born male infant was delivered. Birth weight was 1 750 g, neonate was 42 cm long, Apgar scores at 1 and 5 minutes were 9 and 10, respectively. Minimal compression deformities were present of neonatal face, neck, and extremities. No fetal and maternal infection was detected.

Placenta and fetal membranes were examined by pathologist and findings were then compared with normal pregnancies. Site of disruption of fetal membranes was identified, „amniopatch" material was present in the area. (Figure 1). Microscopic examination of the defect showed that amniopatch was formed by fibrin mesh infiltrated by platelets (Figure 2). Fetal membranes were missing amniotic layer in the area of defect. Chorion layer was intact throughout (Figure 3).

First 36 months of life of the child from this case were within normal limits, all the developmental aspects were normal

DISCUSSION

According to current medical literature, there is not any adequate treatment algorithm of previable rupture of membranes. Management protocols significantly vary in between institutions. They include observation, immediate pregnancy

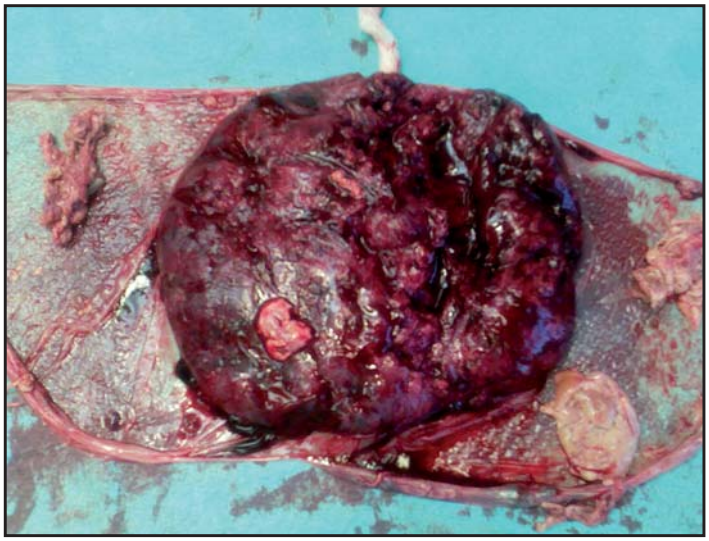

Fig. 1. Placenta with pieces of amniopatch mass.

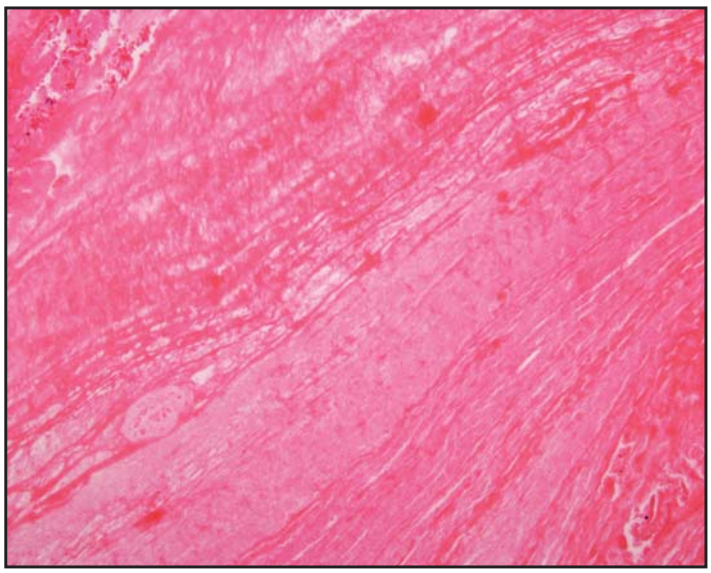

Fig. 2. Detail of amniopatch formed by fibrin mesh infiltrated by platelets.

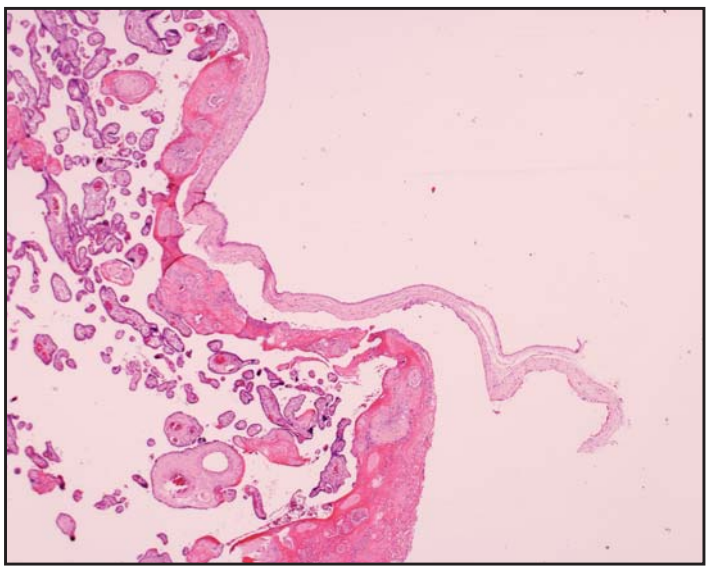

Fig. 3. Fetal membranes are missing amniotic layer in the area of defect. Below amniopatch without amniotic layer can be seen. Chorion layer is intact.

termination, tocolytic therapy, administration of antibiotics and steroids, and various combinations of above described treatment options (Bilic *et al.* 2004). Adequate treatment modality may involve repair of defect in fetal membranes. Original studies first described use of various fibrin based substances transcervically. This was followed by Quintero study presenting use of intraamniotic application autologous maternal blood products – platelets and cryoprecipitate (Quintero *et al.* 1996). He published multiple studies regarding use of blood products in IPROM (Quintero *et al.* 1996, Qunitero *et al.* 1999, Quintero 2003). In 2001 he also reported its unsuccessful use in 12 cases of SPROM between 13 and 24 weeks (Quintero 2001). Contino study from 2004 also included two patients with SPROM in his report of 5 patients treated with amniopatch. First patient was treated at 19 weeks gestation. This case ended with pregnancy loss at 22 weeks gestation. Second patient underwent successful treatment of SPROM with amniopatch at 23 weeks gestation. This pregnancy ended with cesarean delivery of live born infant at 27 weeks (Contino *et al.* 2004). *In vitro* study from 1998 regarding interaction of platelets with fetal membranes was presented by Louis-Sylvestre and confirmed the theory of repair of fetal membranes by application of maternal blood products (Louis-Sylvestre *et al.* 1998). This was followed by another study presenting reparation abilities of fetal amnion (Bilic *et al.* 2004). Most of the reported studies are in favor of amniopatch as a therapeutic option of second trimester IPROM.

Our first experience with this method involves treatment of a patient with **spontaneous** PROM. Despite massive leaking of fluid from vagina, we opted for this treatment option. Prior to attempting amniopatch we exhausted essentially all conservative modalities and the procedure was performed 2 weeks after the initial event. Ultrasound examination of the pregnancy performed on the fourth postoperative day revealing normal volume of amniotic fluid was extremely promising and unexpected. On the twenty second day after the procedure, leaking of fluid was detected. However, this was never so extensive to cause anhydramnios. We explain this by following mechanism which could involve the size of the original defect in fetal membranes. Retrospectively, after examining the membranes and the defect post partum, we postulate that fibrin mesh formed valve-like seal in the defect in fetal membranes and allowed distension of amniotic cavity only to certain extent. When pressure in the amniotic cavity exceeded „tolerated" values, leaking of fluid increased. This mechanism still allowed for adequate fetal growth and development of vital organs.

Our management also targeted infection prevention. This included intermittent antibiotic prophylaxis, laboratory monitoring, strict limitation of vaginal exams.

CONCLUSION

Intraamniotic application of amniopatch may represent a possibly successful treatment of SPROM. This case reports the longest stop of the leaking of amniotic fluid and total prolongation of pregnancy with favorable perinatal outcome after "amniopatch" treatment of spontaneous previable rupture of membranes in the second trimester so far published in available literature.

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