Amniopatch: Way Forward for Mid-trimester Premature Rupture of Membranes (PROM)

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Abstract Fetal membranes are essential for the maintenance of sterile intrauterine milieu for proper fetal growth and development. Chronic infection and inflammation may lead to progressive stretching, hardening of the membranes, making them less elastic and more susceptible to premature rupture of membranes (PROM). PROM is associated with fetal morbidity and mortality which is inversely proportional to the period of gestation. Amniopatch even though still in experimental stages to be an established treatment for PROM, is a formidable treatment modality which has shown to seal the chorioamniotic leak and prolonging the pregnancy with improved fetal outcome. With increasing intrauterine fetal interventions both diagnostic (amniocentesis) and therapeutic (fetoscopy), amniopatch is an option for persistent amniotic fluid leakage which has shown to effectively seal the chorioamniotic leak in about two-third of the cases.

Keywords Hardening · Elastic · Rupture · Amniopatch · Fetoscopy

Introduction

Fetal membranes are important for the homeostasis of amniotic fluid. They protect the growing fetus against infection, trauma and provide space for movement and growth. The strength of the fetal membranes is provided by collagen in the amnion, although amnion and chorion together are stronger than either layer [1].

Premature rupture of membranes (PROM) complicates approximately 10–12 % of pregnancies and may happen in 0.8–1 % postamniocentesis. Rate of fetal morbidity and mortality with PROM is very high due to preterm delivery, infection, miscarriage or pulmonary hypoplasia due to chronic oligohydramnios. The clinical approach to the situation lies in waiting for spontaneous closure of the rupture, which is a rare possibility or terminating the pregnancy.

It has been postulated that chronic infection and inflammation increases the production of hormones and cytokines [2] along with repeated stretching of amnio-chorion induces a phenomenon known as strain hardening. This makes the membranes less elastic and more susceptible to preterm PROM. Local alteration in both the amnion and the chorion has been identified adjacent to the rupture site [3].

Little is known regarding the growth and healing capacity of the fetal membrane. As the membranes are not innervated and poorly vascularized, the response of inflammation, scar formation and tissue repair does not happen in the amnion and the chorion. Most cases of post amniocentesis amniorrhexis are self-limiting and resolve spontaneously [4].

Critical point is the detachment of chorion from amnion, which is common in iatrogenic rupture and thus a simple amnio-infusion increases the intra-amniotic pressure and helps in fusing both the membranes together and sealing the amniochoriodal leak.

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Table 1 Description of the cases which underwent amniopatch

No.	Gestational age	PROM	Amniopatch	Delivery	Success
1	18 weeks	Spontaneous	2	32 weeks	Partial success
2	18–19 weeks; c/o bleeding P/V	Spontaneous	2	Miscarriage	Failure
3	18 weeks with DADC twins; c/o bleeding P/V	Spontaneous	2	Miscarriage	Failure
4	24 weeks with c/o leaking >4 weeks	Spontaneous	2	Miscarriage	Failure
5	24 weeks with c/o leaking >4 weeks	Spontaneous	2	31 weeks	Partial success
6	24 weeks with c/o chronic oligohdramnios with PROM >12 weeks	Spontaneous	2	Continuing	Failure
7	18 weeks	Latrogenic (postamniocentesis)	2	Continuing	Success*

* Denotes it is a prospective case—continuing pregnancy at the time

Fig. 1 Ultrasound done after clinical history of PROM with virtually absent AFI in grayscale. What may appear to be amniotic fluid is actually umbilical cord. Postamniopatch-activated platelets look like *shooting stars*

Report of Cases

The authors present a case series of 7 cases (Table 1), with premature rupture of membranes ranging from 17 to 24 weeks. These cases were treated at Fetal and Genetic Medicine unit at Max Super Speciality West. Out of 7 cases, 6 were spontaneous PROM and 1 case was iatrogenic; postamniocentesis.

Diagnosis of PROM was made by clinical history of sudden leakage of amniotic fluid, leaking per vaginam by speculum examination and confirmed by ultrasound examination of amniotic fluid index less than 1 cm (Figs. 1, 2).

All the defined cases were free from clinical signs of overt chorioamnionitis like infection, fever, increased C reactive protein (CRP), white blood cells and uterine tenderness. Detailed informed counseling regarding the potential risks (chronic oligohydramnios, potter facies, club feet and pulmonary hypoplasia with universal moderate pulmonary artery hypertension) and benefits of continuing pregnancy and about the procedure of amniopatch was done.

Autologous platelet apheresis was done (Fig. 2) and an aliquot of 30 mL were made (Fig. 2). Under all aseptic conditions, 20 gauge spinal needle was inserted intra-amniotically; very slowly so as to avoid any fetal or

umbilical cord injury, small quantity of amniotic fluid was aspirated and sent for culture and sensitivity. Through the same needle the autologous platelets were transfused followed by freshly thawed cryoprecipitate via three-way stopcock (Fig. 2). The entire transfusion took around 15–20 min. (Fig. 1).

For the first 7 days, fetus was monitored daily for amniotic fluid index, fetal heart rate and fetal movements.

Discussion

The infusion of platelets followed by cryoprecipitate provides fibrinogen, fibronectin, platelet derived growth factors, TGF-beta, von Willebrand factor, factor VIII and factor XIII in high concentrations, which helps in restoring the amniochorial link.

Other authors have also tried the procedure and have achieved success [5]. Success may be complete which is defined as restoration of amniotic fluid index (AFI) to 50th centile for the gestational age with complete closure of the rent, no leaking per vaginam within a span of 10–14 days and delivery at term (Table 2).

It may be partial with partial closure of the amniotic leak with AFI up to 5th centile for the gestational age and delivered by around 32 weeks.

Fig. 2 Autologous platelet apheresis in process, 30 mL aliquot of autologous platelets and amniopatch in progress

***Table 2** Describing the gradual increase in AFI postamniopatch

PROM	Iatrogenic	Post Amniopatch	AFI (cm)	Leaking P/V
18 weeks AFI—1.4 cm	Postamniocentesis	d 3	6.1	No
		d 6	8.4	No
		d 12	11.3	No

Amniopatch mimics blood patch which is used in cases of spinal headache after iatrogenic cerebrospinal fluid leakage. It is supported by the fact that the activated platelets adhere to the area of leak in amnion and chorion forming a platelet plugs which is subsequently stabilized by cryoprecipitate [6].

Longer lapse after PROM leads to less well defined, torned, rolled-up membranes and thus a larger defect than original. This shows the tissue response to rupture, highlighting the importance of time interval between PROM and amniopatch and the success of the procedure.

Conclusions

There are too few cases to draw a conclusion and formulate a corrective treatment modality. Spontaneous PROM invariably has underlying chorioamnionitis and might explain failure of amniopatches. With increasing fetal interventions both diagnostic and therapeutic, current experience suggests that amniopatch effectively seals the chorioamniotic leak in over two-third of the cases and is an option for persistent amniotic fluid leakage following an invasive fetal procedure [7].

It is still in experimental stages but ample evidence is there to suggest that amniopatch seals the chorioamniotic

leak, is able to significantly prolong the pregnancy and improve the neonatal outcome.

Further research has to be undertaken to delineate the fundamental defect in preterm PROM and to identify the intrinsic repair mechanism. This shall help in optimizing the intervention to repair, heal or seal the amniochorionic repair.

Conflict of Interest Source of funding none.

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