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PROLONGATION OF PREGNANCY TILL TERM AFTER MID-TRIMESTER PRETERM PRELABOUR RUPTURE OF MEMBRANES AT PREVIABLE GESTATION: 2 CASE REPORTS

KEY WORDS: previable, preterm prelabour rupture of pregnancy, amnioinfusion

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ABSTRACT

In early pregnancy at less than 14-24 weeks of gestation i.e. prior to fetal viability , preterm prelabour rupture of membranes poses higher risk for early preterm delivery , thereby leading to poor prognosis of neonatal survival and also there are higher rates of severe , long-term neonatal morbidity in those who survive due to prematurity. In absence of intrauterine infection at the time of diagnosis and if patient wants to continue the pregnancy, expectant management may be offered even in extreme prematurity. But termination of pregnancy is commonly preferred because spontaneous resealing of the membranes rarely occurs.

Case 1: A 26 year old female, G3 P0+2 L0 at 22 weeks of pregnancy had spontaneous preterm prelabour rupture of membranes. Patient was managed expectantly following which she had cessation of amniotic fluid leak and the pregnancy was continued till term with normal feto-maternal outcome at 37weeks. Here the latency period was prolonged for more than 16 weeks without any evidence of infection with normal feto-maternal outcome at term.

Case 2: A 24year old, G2 P1 A0 L0 with previous caesarean section was presented with spontaneous preterm prelabour rupture of membranes at 18 weeks of gestation. Patient was insisted for expectant management. Although off and on slight leaking pervaginum continued but her pregnancy continued till 33 weeks when she had delivered vaginally with normal feto-maternal outcome. Her latency period was 15weeks without any evidence of infection.

INTRODUCTION:

Chorioamniotic membrane makes a seal proof cavity known as amniotic cavity in which the product of conceptus is kept safe. Any breech in the integrity of the membrane is rupture of the membrane and the subsequent closer of the breech is considered resealing of the membrane.[1] Spontaneous resealing of the fetal membrane with rewarding outcomes are rarely seen. To prevent the leakage of amniotic fluid, several techniques have been developed to artificially reseal the fetal membranes which include: intra-amniotic injection of platelets and cryoprecipitate (amniopatch), sealing the cervical canal, and fetoscopic laser coagulation. But these techniques are not safe and even not very effective to reseal the fetal membranes.[2]

Preterm prelabour rupture of membranes (PPROM) before 37 weeks gestation complicates 3% of pregnancies and is involved in 30–40% of preterm births.[3] PPROM accounts for 40% of all spontaneous preterm deliveries, representing significant perinatal morbidity and mortality worldwide.[1,4,5] Rarely when spontaneous rupture of membrane occurs between 13 and 23+6/7 weeks of gestation, which is defined as Previable PPROM complicating 1.37% of twin and 0.52% of singleton pregnancies.[6] Resealing of leaking following amniocentesis occurs in approximately 86% cases but resealing of spontaneous PPROM is rare.[7]

Here we report two cases of PPROM in which membranes ruptures before 23 weeks i.e. previable gestation, managed expectantly with successful outcome.

Case Report 1:

A 26year old, G3 P0 A2 L0, known case of hypothyroidism since 2year, was presented in the emergency department at 22weeks of gestation with leaking per vaginum from last 4 hours. There was history of McDonald stitch which had been applied at 14 weeks of gestation but TVS for cervical length and os diameter had not been advised. She perceived normal fetal movement at the time of presentation. She had history of urinary symptoms since 3rd month of gestation. Urine culture showed Escherichia coli infection sensitive to Cefixime, for which she had been advised Tab. Cifixime 200mg twice a day for 10days. There was no history of fever, abdominal pain, trauma or recent coitus or any history of vaginitis. She had no comorbidities, including hypertension, anaemia, diabetes, blood dyscrasias, connective tissue disorder, immune system and neurological disorders except hypothyroidism.

On per abdominal examination, uterus was 20-22 weeks in size corresponding to the period of amenorrhoea and fetal heart sound was audible with Doppler. Abdomen was non tender. On per speculum examination, pooling of amniotic fluid from the cervical os was visualized which was closed and McDonald stitch was seen. The litmus paper test was used to confirm the diagnosis of premature rupture of membrane. She came with ultrasonography report which was indicative of mild fetoplacental insufficiency with increased S/D ratio in umbilical artery, Maximum Liquor Pocket of 55mm and fetal parameters corresponding to 22 weeks of gestation.

She had history of previous two spontaneous abortions which occurred at one and half months and 2 months gestations, respectively. Dilatation and curettage was done every time. Nothing significant was present in her family and personal history. She was afebrile with no abnormality detected on systemic examination.

She was taking levothyroxine 150mg, Inj. Lonopin 40mg subcutaneous, Tab. Ecosprin 75 mg along with iron and calcium. She was also taking Inj. 17 hydroxyprogesterone caproate 250mg intramuscular weekly which she had received 3 days back.

Mc Donald stitch was removed. The risks and benefits of active and expectant management were explained to her. She insisted on the expectant management and was thereby admitted. Inj. Ampicillin 2 gm and injection Erythromycin 250 mg, intravenously, 6 hourly for 2 days followed by Tab.

Amoxycillin 500 mg and Tab. Erythromycin 250 mg 8 hourly, orally for 5 days was given. Injection lonopin 40mg, ecospirin 75mg and Injection 17α hydroxyprogesterone caproate 250mg intramuscular weekly and iron and calcium were continued as patient was already taking them.

Her laboratory investigations were as follows: Blood group - "AB" Rhesus-Positive, Hb - 9.5 gm/dL, WBC - 11900/μL, Platelet count - 201,000/μL, Prothrombin time - 10.50 sec, INR - 0.8 sec, Fibrinogen was 4.10 g/L, aPTT was 22 sec, serum creatinine - 0.4mg, Random plasma glucose was 112 mg/dl. CRP (C-Reactive Protein), APLA, Hepatitis B surface Antigen, Hepatitis B surface Antibody, Hepatitis B e Antigen, HB e Antibody, HB c Antibody, HCV Antibody and HIV I & II were Negative. VDRL was Non-Reactive. Glucose stress test came out to be 152mg/dl and so was started on diabetic diet.

On urine examination: Routine and microscopy was normal. Urine culture and sensitivity report showed Escherichia coli infection sensitive to Nitrofurantoin, thereby she was also advised Tab. Nitrofurantoin 100mg twice a day for 10days. Plenty of oral fluids along with high protein and iron rich diet was advised. Slight leaking pervaginum continued for one week.

HbA1c and repeat thyroid profile was sent due to raised GST values and hypothyroidism respectively. HbA1c came out to be in normal range i.e. 5.1 but Serum TSH was 3.36, which was slightly raised according to pregnancy values. Therefore, the dose of levothyroxin was increased to 175mcg. Complete blood counts were done weekly; four point blood sugar was done every two weeks.

Repeat USG was done four weeks later which showed normal growth parameters of fetus corresponding to gestational age, AFI – 12.9cm with normal colour Doppler studies.

She had again developed burning during urination and heaviness in lower abdomen after 3 weeks of completion of antibiotic therapy. Urine sent for culture and sensitivity showed Klebsiella species sensitive to Erythromycin. Tab. Erythromycin 250 mg four times a day was started for 10 days. She had taken Tab Nitrofurantoin 100mg at night daily till delivery as she developed recurrent UTI.

Four doses of injection Dexamethasone 6mg 12hourly were given intramuscularly at 28weeks of gestation.

Patient was discharged after 6weeks on injectable lonopin 40mg, injectable progesterone, oral Aspirin 75mg, Tab. Thyroxin 175mcg, Tab. Nitrofurantoin 100mg, oral and powder form of amino acids, along with iron and calcium supplements and diabetic diet. Patient was followed every two weeks and monthly USG with color Doppler was done to monitor the growth of the baby.

At 34 weeks of gestation, patient started developing itching over her palms and soles for which liver function test was done which came out to be deranged and a diagnosis of Intrahepatic Cholestasis of Pregnancy (IHCP) was made. Tab Ursodeoxycholic acid 300mg twice a day was started. After 36weeks weekly cardiotocography was done to monitor fetal well-being. Patient was admitted at 38 weeks of gestation and induction was done in view of IHCP. LSCS was performed in view of fetal distress and full term female baby was delivered abdominally. Neonate cried immediately at birth with APGAR score of 8/10, had a birth weight of 2110gms and was discharged on day 3 of life. Milestones of the baby were normal.

Case Report 2:

A 24years old, G2 P1 A0 L0 with previous caesarean section, was presented in the emergency department at 18 weeks of gestation with leaking per vaginum from last 6 hours. There was no history of fever, abdominal pain, urinary symptoms, trauma or recent coitus or any history of vaginitis. She had no comorbidities, including hypertension, anaemia, diabetes, blood dyscrasias, connective tissue disorder, immune system and neurological disorders. On per abdominal examination, uterus was 16-18 weeks in size corresponding to the period of amenorrhoea. Abdomen was non tender. On per speculum examination, pooling of amniotic fluid from the cervical os was visualized which was closed. The litmus paper test was used to confirm the diagnosis of prelabour rupture of membrane. She had no complaints in previous two antenatal visits: one at first trimester and second at three and half months. She had taken Tab. folvite in first trimester and iron and calcium in second trimester. Her previous antenatal investigations including urine culture and sensitivity were normal.

She had history of previous caesarean section 2 year back for fetal distress, baby had expired 3 days after birth due to sepsis. Her family and personal history was not significant. She was afebrile with no abnormality detected on systemic examination.

Her ultrasound report showed fetal parameters corresponding to 17 weeks 4 days with normal fetal heart rate. AFI was 7.5.

As she was just 18 weeks pregnant, she was advised for termination of pregnancy. Despite all the risks explained to her, she insisted to continue the pregnancy, and was thereby admitted and administered inj. Ampicillin 2 gm and injection Erythromycin 250 mg, intravenously, 6 hourly for 2 days followed by Tab. Amoxycillin 500 mg and Tab. Erythromycin 250 mg 8 hourly, orally for 5 days.

Her laboratory investigations were as follows: Blood group – B positive, Hb - 10.5 gm/dL, WBC - 9500/μL, Platelet count - 191,000/μL, Serum creatinine - 0.4mg. Hepatitis B surface Antigen, HCV Antibody and HIV I & II were Negative. VDRL was Non-Reactive. Glucose stress test 132mg/dl.

On urine examination: Routine and microscopy was normal. Urine culture and sensitivity report was also normal. Plenty of oral fluids along with iron, calcium, high protein and iron rich diet were advised. Complete blood counts were done weekly. On and off leaking per vaginum continued. Repeat USG was done four weeks later which showed normal growth parameters of fetus corresponding to gestational age, AFI – 8 with normal colour Doppler studies.

Four doses of injection Dexamethasone 6mg 12hourly were given intramuscularly at 28weeks of gestation. As slight leaking continued, antibiotic course was repeated at 32 weeks. USG with color Doppler was repeated monthly to monitor the growth of baby and liquor pocket.

At 33 weeks of gestation, patient developed labour pains, rescue dose of Dexamethasone and Group B streptococcus prophylaxis were given. She had delivered a male baby vaginally. Neonate cried immediately at birth with APGAR score 7/10 and had a birth weight of 1680gms. Baby remained normal in postnatal period and both mother and baby was discharged in healthy condition after one week. On follow-up visits, milestones of baby were normal.

DISCUSSION:

Throughout the world, premature birth is a significant health problem. Rupture of membranes before viability occurs in less than 1% of pregnancies.[8] The probability of neonatal death and morbidity associated with preterm PROM decreases with longer latency and advancing gestational age.[9]

In a review of pre-term PROM between 14 weeks and 24 weeks of gestation perinatal deaths were more or less equally

divided between still births and neonatal deaths. Survival rates were much improved with expectant management following membrane rupture with 22 weeks of gestation compared with membrane rupture before 22 weeks of gestation (57.7% vs 14.4% respectively).[10] Significant maternal complications may occur with pre-viable PROM include intra-amniotic infections, endometritis and abruptio placentae and retained placenta. Although it occurs infrequently, life threatening maternal infection may complicate expectant management of pre-viable form in approximately 1% of cases.[10] Latency periods appear to be prolonged with second trimester preterm PROM compared with later gestational age. However 40 to 50% of pre-viable PROM will give birth within the first week and approximately 70-80% will give birth 2-5 weeks after membrane rupture.[10,11]

Extreme prematurity may also represent the main risk factor for all perinatal adverse outcomes, in particular inflammatory diseases such as intraventricular haemorrhages, sepsis, necrotizing enterocolitis or chronic lung disease and pulmonary hypoplasia in 10-20% of cases.[8,12-14] but both nenates observed in the present study were free of all these abnormal symptoms.

Currently, there is no consensus on management with early preterm premature rupture of membranes (EPPROM) occurring between 14 and 24 weeks of gestation before viability of the fetus. A common approach is expectant management hoping to reach a viable period from 23-24WG in order to use corticosteroids, antibiotics and transfer to level III ward.[8,15-17]The administration of antibiotics after PROM is associated with a prolongation of pregnancy and a reduction in maternal and neonatal morbidity.[18,19]

Membrane rupture may occur for a variety of reasons and preterm PROM may result from a wide array of pathological mechanisms that act individually or in concert.[20,21] Intra amniotic infection has been shown to be commonly associated with preterm PROM especially at earlier gestational ages.[22]Additional risk factors associated with preterm PROM included previous history of preterm PROM, short cervical length, second and third trimester bleeding, low BMI, low socio-economic status, smoking and illicit drug use.

A study published by Byonanuwe S. et al 2020, were found more than 13-fold increase risk of PROM in pregnant women with history of three or more abortions (a**OR**=13.1,, 95% CI: 1.12-153.62, p = 0.05) and history of urinary tract infections (UTIs) in the previous one month was also a significant predictor of a higher likelihood of PROM.[23]

Treadwell et al, published the largest retrospective review of 482 patients receiving cerclage (364 elective and 118 emergent). They found premature rupture of membranes (PROM) in 38% of the subjects with 9% delivering <27 weeks.[24]

Although the first case was free of any potential risk factors for PROM, the second case had history of two abortions, recurrent UTI and McDonald's stitch was also applied.

Additional treatment with amnioinfusion (AI) has recently emerged as an option to prolong the latency period after the PPROM. But repetitive puncture in the Amnioinfusion method increases the risk of separation of amniotic membrane from the uterus, abruption of the placenta, and can also injure umbilical cord causing a trauma to the fetus.[25] Irreversible change in the fetal programming and/or damage to some fetal organs especially fetal kidney, skin, eyes, gut and bronchopulmonary systemcan occur due to repetitive or continuous amnioinfusion of saline solutions different from physiologic amniotic fluid. Due to these complications of amnioinfusion, more studies are required to recommend amnioinfusion in the management of PPROM.[26] As maximum liquor pocket was normal in the USG done just after leaking in the cases presented here, amnioinfusion was not considered as a treatment modality.

CONCLUSION:

Previable preterm prelabour rupture of membranes can be managed with proper and meticulous expectant management. Thus, not all pregnancies with previable rupture of membranes need to be terminated. Patient needs to be followed regularly to rule out any infections and for growth of fetus with repeated Ultrasonography. Women with PPROM and their partners should also be offered additional emotional support, both during pregnancy and postnatally.

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