Brief Report

Premature Rupture of Membranes in the Second Trimester

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Spontaneous rupture of membranes during the second trimester presents difficult medical and ethical questions for the patient and physician. Such pregnancies are at high risk for preterm birth, chorioamnionitis, and neonatal complications. Treatment can range from expectant management to pregnancy termination. This case presentation describes a patient with premature rupture of membranes at 21 weeks' gestation who gave birth at 35 weeks.

Key words. Fetal membranes, premature rupture; labor, premature; pregnancy complications; gestational age.
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Premature rupture of membranes (PROM) in the second trimester results in a high incidence of pregnancy loss, premature birth, and chorioamnionitis. The family physician involved in maternity care should be aware of the relative risks and benefits of both expectant management and pregnancy termination. The family physician should counsel the patient during the stressful time, and consultation with a perinatologist is usually beneficial. Optimal care may be ensured by having the family physician either continue as primary care provider or develop a plan of co-management. Recent developments in the management of second trimester PROM have led to the consensus that expectant management should be offered, including the use of corticosteroids to promote pulmonary maturity and home management in selected cases.

Case Presentation

A 32-year-old woman, G4P1SAB2, was receiving prenatal care at the university family practice clinic in a moderate-sized southwestern city. Her pregnancy was unplanned but mutually desired by the patient and her fiancé, who was in the armed services and stationed across the country. Her past medical history was notable for cryotherapy for cervical intraepithelial neoplasia (CIN 1) 3 years earlier, followed by negative Papanicolaou smears. She denied use of alcohol, tobacco, or illicit drugs. Her previous childbirth 5 years earlier was a spontaneous vaginal delivery of a term 3850-g female infant with Apgar scores of 5 and 7, complicated by preeclampsia and a postpartum hemorrhage. Her first spontaneous abortion occurred at 4 to 6 weeks estimated gestational age (EGA) and did not require dilation and curettage. Her second spontaneous abortion occurred at 4 to 5 months EGA and required a dilation and curettage.

At the initial visit, fundal height measured 18 cm; fetal heartbeat was auscultated by Doppler but not by fetoscope. The date of her last menstrual period was unknown. An ultrasound examination performed 4 days later demonstrated an intrauterine pregnancy of 17.9 weeks EGA. Amniotic fluid volume was normal, and no fetal or placental anomalies were noted. Routine prenatal laboratory test results were unremarkable. Three weeks later, the patient called her family physician to report that she had a "gush" of clear fluid from her vagina. She was instructed to come to the antepartum evaluation clinic at the university hospital (Table 1).

A diagnosis of premature rupture of membranes was made by means of a sterile speculum examination, which revealed a pool of fluid in the vagina. The fluid was identified as amniotic fluid based on a ferning pattern revealed by microscopic examination and nitrazine pH paper. An ultrasonogram obtained by a perinatologist demonstrated a 474-g fetus at 21 5/7 weeks EGA with decreased amniotic fluid volume and without apparent fetal or placental anomalies. The patient did not have a fever, abdominal

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Table 1. Evaluation of Possible Midtrimester Premature Rupture of Membranes

- Diagnose preterm premature rupture of membranes with criteria of pooling, nitrazine positivity, and ferning pattern. Do not perform digital cervical examination unless active labor has begun.
- Obtain cervical, vaginal, and urine cultures.
- Perform ultrasound examination to estimate gestational age and assess fetal weight, amniotic fluid volume, presentation, and fetal or placental anomalies.
- Perform maternal examination to include assessment for fever, blood pressure, and abdominal tenderness.
- Monitor for fetal tachycardia or bradycardia, heart rate variability, and decelerations.
- Use tocodynamometry to detect uterine contractions.

tenderness, or clinical signs or symptoms of infection. All routine cervical cultures were negative. The family practice service obtained a consultation from the maternal-fetal medicine service, and the patient was admitted to the university hospital.

The potential risks of premature birth, intrauterine infection, and neonatal complications were discussed and the options of termination or expectant management were reviewed. The patient was given a tour of the newborn intensive care unit to observe the realities of premature birth and the potential complications. During this process, she became increasingly confused about what she should do, and explained to one of the nurses that she felt the physicians wanted her to terminate her pregnancy. She reported that she had been counseled that this would not be viewed as an abortion because the baby would not be able to live on its own and was unlikely to reach a viable age without serious complications.

The patient stated that she could not end the pregnancy despite all the risks because she could feel the baby move. In response to discussions about the inability of a baby to live when born before 25 weeks' gestation, she said that she felt the baby was "strong" because of her perception that it kicked hard. She explained that although in her Pueblo Indian culture the baby is not truly considered an individual or given a name until taken to the village and held up to the light of the morning sun, her religious and cultural beliefs prohibited terminating a pregnancy that felt "strong."

She agreed to a discharge plan for bedrest at home with frequent visits by a home health aide and the involvement of a social worker. She was to monitor her temperature at home and come to the hospital for immediate evaluation if she developed a fever, abdominal pain, contractions, or a change in color or smell of the leaking amniotic fluid.

At 26 weeks into the pregnancy, she began daily clinic visits for antepartum testing, which included nonstress tests and biophysical profiles. She continued to leak clear amniotic fluid throughout the pregnancy, and ultrasonography continued to show decreased amniotic fluid volume. Her nonstress tests were all reactive with no evidence of fetal tachycardia or abnormal decelerations. Her biophysical profile scores were all 8/10 or higher, the only deficit being low amniotic fluid volume. (Corticosteroids to promote lung maturity and decrease the rate of intraventricular hemorrhage were not given because at that time rupture of membranes was a contraindication for corticosteroid use. Current National Institutes of Health [NIH] recommendations would favor corticosteroid use in this scenario.)

The patient presented to labor and delivery at 35 weeks EGA with signs and symptoms of an upper respiratory tract infection, a 38°C oral temperature, abdominal tenderness, and uterine contractions occurring 3 to 5 minutes apart. A cervical examination revealed 1-cm dilation with a breech presentation. She declined a trial of labor for a vaginal breech delivery, and a cesarean section was performed. A 2600-g male infant of 37 weeks EGA was born, with Apgar scores of 5 and 8. The amniotic fluid was foul-smelling, and uterine atony was noted. Umbilical cord blood gases revealed an arterial pH of 7.23 and venous pH of 7.33.

The baby was brought to the newborn intensive care unit because of decreased neuromuscular tone and poor respiratory efforts. He required endotracheal intubation for less than 48 hours and his condition was diagnosed as neonatal pneumonia, for which he received a 10-day course of antibiotics. He was discharged home after a 16-day hospital stay. At a 6-week developmental assessment, he was felt to have age-appropriate motor skills, and at his 4-month well-child visit, he was growing well and had no medical problems. The family subsequently moved out of state, and when the infant was approximately 9 months old, they mailed photos and a letter describing a healthy boy and mother.

Discussion

Premature rupture of membranes is not an uncommon problem. A retrospective study at one hospital reported a rate of 1.75% before 34 weeks.[1] Management issues are very different in women with second-trimester PROM, as their fetuses may not be of viable age (Table 2). To counsel patients with PROM, family physicians should be familiar with the risks for neonatal morbidity and mortality. Although there are no large studies of second-trimester PROM, the small studies demonstrate a high rate of neo-

Table 2. Management of Premature Rupture of Membranes During the Second Trimester

Therapeutic decisions
- Discuss options for expectant and interventive management with patient and family. If the fetus is not yet viable, pregnancy termination can be presented as an option.
- Initiate course of corticosteroids (intramuscular betamethasone or dexamethasone) if less than 30 to 32 weeks' gestation and without evidence of chorioamnionitis; consider corticosteroids if the patient is between 32 and 34 weeks' gestation and discuss with perinatal consultant.
- Consider using prophylactic antibiotics or tocolytics.

Site of medical care
- If preterm labor has begun or the patient is at a site remote from a tertiary care center, consider immediate transfer to institution with neonatal intensive care unit if the fetus is viable and delivery not imminent.
- All patients with premature rupture of membranes during the second trimester should be monitored in a hospital for at least 48 hours because of high frequency of onset of preterm labor. If labor does not begin within 48 hours, home management can be considered for certain patients. Once the fetus reaches a viable age, it is essential that patients be in a home or hospital in close proximity to a neonatal intensive care unit.

Antenatal surveillance
- If expectant management has been chosen, a plan for fetal surveillance after viability should be developed. Minimum biweekly nonstress tests with biophysical profile as backup for nonreactive tests. The plan should be developed in consultation with a perinatologist.
- Consider amniocentesis to ascertain pulmonary maturity after 32 weeks' gestation. Consider induction at 36 weeks or when pulmonary maturity has been documented. Alternatively, may continue expectant management and await spontaneous labor.

Other
- Consult perinatologist because of high morbidity of midtrimester premature rupture of membranes.
- Provide emotional support and counseling.

natal mortality and morbidity from this condition. The primary neonatal complications of PROM are due to prematurity, intrauterine infection, pulmonary hypoplasia, and orthopedic deformities secondary to the prolonged period of oligohydramnios. Prematurity is the primary source of morbidity because the mean latency period between PROM and delivery is between 10 and 21 days.[2–5]

In three small studies of PROM managed expectantly, perinatal survival ranged from 25% to 63%, and normal neurologic and physical development occurred in 55% to 68% of survivors. Chorioamnionitis occurred in 41% to 77% of the patients in these studies.[2,5,6] In 1993, Morales and Talley[4] summarized six studies of expectant management of midtrimester PROM that demonstrated neonatal survival ranging from 22% to 63%, with approximately 60% of survivors having normal development at 1 year. Mercer's analysis[3] of four midtrimester PROM studies using age-specific survival rates revealed a 23% rate of survival for PROM at 22 weeks EGA or earlier, compared with 53.9% at 23 weeks or more. Thus, most patients with PROM before 23 weeks will not give birth to a viable fetus.

The above studies of the natural history of the expectant management of PROM all understate the morbidity and mortality of this condition. Each study is an analysis of the expectant management of PROM in which the entrance criterion was the decision for expectant management. Patients with imminent delivery, signs of infection, or delivery before evaluation at the tertiary care center are generally not included in the statistics for expectant management. Therefore, the resulting data most accurately represent the patient who has had PROM for 24 hours without labor rather than all patients with PROM initially presenting to a primary care setting.

The use of corticosteroids to promote lung maturity, prophylactic antibiotics to reduce chorioamnionitis, and tocolysis to prevent prematurity remain active areas of research. These interventions are controversial with respect to both effectiveness and the potential for complications secondary to the interventions. Concerns about complications include the potential of steroids to increase the rate of neonatal sepsis, tocolysis to delay the delivery of infected or distressed neonates, and prophylactic antibiotics to result in infection with resistant organisms. The conflict about the use of these interventions in preterm PROM is accentuated in cases of second-trimester PROM by a relative paucity of data. The evidence from studies of PROM at 26 to 34 weeks is used to guide clinical decisions in women with second-trimester PROM.

Corticosteroids

Because of questions regarding safety and efficacy, the use of corticosteroids to prevent or decrease the severity of respiratory distress syndrome (RDS) and intraventricular hemorrhage (IVH) in premature infants has been controversial since it was first introduced in 1972. Recent studies and a meta-analysis have conclusively demonstrated beneficial effects in decreasing the incidence of RDS. The 1990 meta-analysis by Crowley and colleagues[7] showed that the use of corticosteroids in PROM was associated with a 50% reduction in neonatal RDS. There are no studies specifically analyzing steroids in midtrimester PROM; however, the seven studies in the meta-analysis in which available data permitted subgroup analysis demonstrated a 0.38 relative risk of RDS in women giving birth before 31 weeks' gestation. The analysis by Maher and co-workers[8] of 432 cases showed a 0.20 relative risk of RDS due to the use of corticosteroids, which agrees with the findings of the meta-analysis. Kari and associates[9]

demonstrated that the availability of human surfactant does not reduce the benefit of corticosteroids.

Corticosteroids have now been shown to decrease the likelihood of IVH in preterm infants. The meta-analysis by Crowley et al[7] showed an odds ratio of 0.5 in all preterm births. Of particular relevance to midtrimester PROM is the study by Maher and co-workers,[8] which demonstrated an odds ratio of 0.26 for incidence of IVH in neonates who had received corticosteroids and were born at 26 to 31 weeks' gestation. Although the mechanism by which corticosteroids reduce the incidence of IVH is unknown, three studies have shown that the reduction is not simply due to increased pulmonary maturation.[9–11] The corticosteroids may prevent IVH by decreasing the risk for hypotension or by causing accelerated maturation of blood vessels in the germinal matrix.

The increasing evidence for the benefit of corticosteroids led to a 1994 NIH consensus conference, which concluded: "Antenatal corticosteroid therapy is indicated for women at risk of premature delivery with few exceptions and will result in a substantial decrease in neonatal morbidity and mortality, as well as substantial savings in health care costs."[12] The statement, which specifically called for the routine use of steroids in cases of PROM occurring before 30 to 32 weeks' gestation, is expected to become the standard of care. The NIH statement acknowledges that the evidence does not show as strong an effect in reducing RDS in PROM as in cases of anticipated prematurity with intact membranes, and that it is still unclear whether steroids increase the risk of maternal or neonatal infection. The decision to recommend steroids is based on the observation that the risks of prematurity are much greater than the theoretical risks of infection. The decreased incidence of IVH was felt to be of particular importance in deliveries occurring at 24 to 28 weeks' gestational age, which is a frequent outcome of midtrimester PROM.

The conclusions of the NIH panel on corticosteroid use are important for family physicians. The panel estimated that only 12% to 18% of women giving birth to 501-g to 1500-g preterm infants receive corticosteroids.[12] Evidence indicates benefit even if the corticosteroids are given less than 24 hours before delivery. To ensure maximum therapeutic benefit, corticosteroids should be given as soon as possible to women who are at risk for preterm delivery between 24 and 34 weeks' gestational age. The family physician managing or transferring such a patient to a tertiary care center has the option of initiating the corticosteroid treatment in the primary care setting, with perinatal consultation as indicated.

Tocolysis and Antibiotic Therapy

Because the evidence supporting the use of prophylactic antibiotics and tocolysis in PROM is much less persuasive than the support for corticosteroid use, further research is needed before these interventions are recommended. It has been theorized that antibiotics are beneficial because of the high rate of chorioamnionitis in PROM and the role of infection with bacterial vaginosis, chlamydia, and group B streptococci in the initiation of rupture of membranes and preterm labor. The prospective studies to date have shown a small effect in prolonging the latency period until delivery but with no statistically significant effect on neonatal morbidity and mortality.[13–17] The failure to detect improvement in neonatal outcomes may reflect the small size of the studies, and a large prospective trial is clearly needed. If the routine use of corticosteroids increases the incidence of infection, the prophylactic use of antibiotics may potentially result in a beneficial effect on neonatal morbidity and mortality. Although the use of prophylactic antibiotics in the expectant management of midtrimester PROM is controversial, the detection and treatment of chorioamnionitis is considered essential to reduce maternal and neonatal infectious complications.

Tocolysis for patients with PROM has been attempted only in a few small studies. The major concern is the risk of prolonging a pregnancy that has occult infection related to PROM. Only two randomized studies have included an analysis of the utility of tocolysis in cases of second-trimester PROM. The study by Garite and colleagues[18] of the use of ritodrine tocolysis in cases of PROM at 25 to 30 weeks' gestation showed no evidence of increased gestational age at delivery, increased time from PROM to delivery, or decreased neonatal morbidity or mortality. A study of tocolysis in PROM by Weiner and co-workers[19] showed no benefit when analysis was based on all cases occurring sooner than 34 weeks' gestation; however, a subgroup analysis of women before 28 weeks' gestation showed an effect of prolonging the interval from onset of contractions to delivery from 53 to 233 hours. Unfortunately, this increased interval did not improve neonatal morbidity. A literature review of the use of tocolytics in all cases of PROM (ie, up to 36 weeks' gestation) has not shown any consistent benefit in this group.[20] There are no studies of tocolysis in PROM that consistently utilize corticosteroids, and the studies of Weiner and Garite and their associates specifically excluded women receiving corticosteroids. It is possible that tocolytic agents may sufficiently prolong the interval before delivery so that the full benefit of corticosteroids can occur. At the present time, tocolysis can be clearly recommended only for use in forestalling delivery until a woman

with PROM can be transported to a facility with a neonatal intensive care unit.

Pulmonary and Orthopedic Complications

Pulmonary hypoplasia and skeletal deformations are distressing areas of morbidity; they can fatally complicate what had apparently been a successful case of expectant management of PROM. The combination of oligohydramnios, pulmonary hypoplasia, and skeletal deformations was initially described in the setting of renal agenesis as Potter's syndrome. The syndrome was renamed *oligohydramnios tetrad* when it was demonstrated that the precipitating factor was severe oligohydramnios and that the syndrome was not specific to renal agenesis.[21] Pulmonary hypoplasia, which is the lack of development of adequate pulmonary tissue, can result in mortality rates ranging from 50% to 80%.[22–24] Normal lung development depends on the presence of intrapulmonary fluid, a deficiency of which can cause hypoplasia. The likelihood of pulmonary hypoplasia is more directly related to the occurrence of oligohydramnios at a critical period of lung development than to the duration or severity of oligohydramnios.

Rotschild and colleagues, with their logistic equation relating gestational age of rupture to probability of pulmonary hypoplasia, revealed a 50% risk with PROM at 18 weeks' gestation, which decreased to 10% at 26 weeks and to minimal risk after 28 weeks.[24] A recent retrospective study of the cause of postnatal death in infants born after PROM showed that pulmonary hypoplasia was responsible for 92% of infant deaths when maternal PROM occurred before 20 weeks' gestation, and for no deaths if PROM occurred after 23 weeks.[25]

The skeletal deformities attributable to PROM consist primarily of flattened facial features and limb contractures that usually but do not universally resolve during infancy. The deformities are a consequence of the lack of fluid, and thus correlate with severity and duration of oligohydramnios rather than with the gestational age at which PROM occurs. Morales and Talley's review of 453 cases described above showed that the incidence of orthopedic deformities was less than 1%.[4]

Management Site

Midtrimester PROM is extremely stressful to patients and their families. Costs of prolonged inpatient hospitalization are substantial. These factors have led to the suggestion that outpatient management may be appropriate for certain patients. In the only randomized study of home vs hospital management of patients with PROM (before 37 weeks' gestation), only 18% of patients were eligible for randomization at 72 hours after PROM.[26] Most patients either went into labor, had breech presentation, had oligohydramnios, lived far from the hospital, or had other exclusion factors. Of the 67 patients randomized, no differences were found in maternal and neonatal outcomes, and the expense for patients in the home group was $5000 less than the expense for the inpatient group. The authors cautioned that their conclusions apply only to the small selected group eligible in their study. This study did not focus on midtrimester PROM, for which both the neonatal risk due to prematurity and the potential cost savings due to prolonged hospitalization are greater.

The 1988 technical bulletin of the American College of Obstetricians and Gynecologists (ACOG) on premature rupture of membranes states that inpatient management is the norm in preterm PROM after the time of viability but adds that "Discharge of a [viable preterm] patient who continues leakage may be considered in some circumstances, ie, if the patient is reliable and has an acceptable home environment, maternal and fetal assessment can be done as well at home, and there is a vertex presenting."[27] Based on the above evidence, it is reasonable to consider selective home management of patients with preterm PROM after at least a 48-hour period of observation in the hospital.

Antepartum Fetal Surveillance

The type and frequency of antepartum testing in cases of expectant management of midtrimester PROM vary substantially from study to study. Protocols vary from fetal heart rate monitoring every 6 hours to weekly nonstress testing; however, most studies use daily or biweekly nonstress tests upon reaching the age of fetal viability. Although many study protocols use amniotic fluid volume index along with the nonstress test, a small study by Harding and associates[28] found that amniotic fluid volume has relatively large daily fluctuations in cases of PROM and does not contribute to the identification of fetal distress and early infection. A prospective study by Gonik et al[29] demonstrated an association between reduced amniotic fluid and clinical chorioamnionitis and postpartum endometritis, but no statistically significant association with neonatal sepsis. Vintzileos and co-workers[30] studied oligohydramnios in cases of PROM and found an increased incidence of fetal distress and perinatal mortality with oligohydramnios.

A study of the biophysical profile (BPP) in PROM showed that a healthy fetus will have a normal BPP despite PROM, and that a decreased score on a BPP is associated with increased likelihood of impending amnionitis.[31] In this study, the presence of a nonreactive stress

test and loss of fetal breathing were the most common abnormal variables in the BPP, and no evidence was offered that using a BPP as a first-line antepartum test is preferable to using the BPP as a secondary test in the setting of a nonreactive stress test. The 1988 ACOG technical bulletin on premature rupture of membranes states only that "frequent clinical examination and fetal heart rate testing" is indicated.[27] The role of amniocentesis to detect chorioamnionitis or determine pulmonary maturity is not well established among patients with PROM. No definite benefit has been shown with amniocentesis at presentation as compared with clinical detection of chorioamnionitis. Amniocentesis may be appropriate at 34 to 36 weeks' gestation to determine pulmonary maturity if induction is being considered.

Prevention of PROM

Because of the high morbidity and mortality of PROM regardless of management plan, it is important to consider strategies to decrease the rate of PROM. The strongest association is between PROM and infection, with *Chlamydia*, group B streptococcus, and bacterial vaginosis.[32,33] Tobacco smoking, vaginal bleeding, and incompetent cervix are other known causes of PROM.[33] Numerous nutritional factors have been associated with PROM, but none is definitively linked at this time. Sexual activity and exercise have not been shown to cause PROM. A previous history of PROM is associated with a 21% recurrence rate, which requires vigilant avoidance of preventable risk factors, such as infection, smoking, and nutritional inadequacy.[34]

Conclusions

New developments in the management of second trimester PROM include the consensus that expectant management should be offered, the increasing use of corticosteroids, and the use of home management in selected cases. As premature labor and preterm rupture of membranes are common obstetrical problems, the NIH Consensus statement strongly promoting corticosteroid use will affect all family physicians practicing obstetrics. The decision to terminate a pregnancy or attempt expectant management is a complex decision in which the support of the family physician can be invaluable. The patient's religious, cultural, and philosophical beliefs regarding pregnancy termination and medical intervention are likely to be at least as important as a detailed understanding of the medical risks of expectant management.

In the case described in this report, a key factor in how the pregnancy was managed was the mother's conviction that abortion conflicts with the Pueblo Indian culture's views regarding the sanctity of life. Biomedical information concerning the risks of expectant management were outweighed by her perception of active fetal movement, and biomedical assessments of viabilty were outweighed by her cultural and religious beliefs. The counseling family physician in cases of second trimester PROM must set aside personal views regarding pregnancy termination to assist the pregnant woman during this stressful period in making a decision with which she will remain comfortable.

The family physician should stay involved with the care of the patient with PROM to help interpret the biomedical information being presented and to offer social support. Although it may be preferable to maintain the family physician's role as primary caregiver, this may not be feasible if a neonatal intensive care unit is not readily accessible to the clinical setting. The continued involvement of the family physician can facilitate appropriate use of home management to maintain the integrity of the pregnant woman's social support system. Since the most likely scenario is a preterm delivery within 2 weeks of PROM, it is essential to involve a perinatal consultant, who can help guide therapeutic decisions regarding the use of antibiotics, tocolytics, and antepartum testing.

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