First-Trimester Placenta Percreta Causing Massive Vaginal Bleeding Following the use of Misoprostol: A Case Report

M.K. Ramadan1,2,3, J. Darido1,2, Z. Bazzi1,2, G. Wehbe1, J. Khaza' al1,2, R. Chahine1
1Department of Obstetrics and Gynecology, Rafik Hariri University Hospital, Beirut-Lebanon
2Department of Obstetrics and Gynecology, Lebanese University, Faculty of Medicine and Public Health, Beirut-Lebanon
3Department of Obstetrics and Gynecology, Makassed General Hospital, Beirut-Lebanon

Abstract
Medical termination of late 1st trimester pregnancy complicated with lethal fetal anomaly or with failed pregnancy is common in clinical practice worldwide. Misoprostol alone or in combination with Mifepristone, has been the most widely deployed agent. The presence of placenta previa or previous cesarean scar has not been considered frank contraindication for such a practice. Nevertheless, its use in the presence of unidentified PAS could trigger uterine rupture, massive intraperitoneal hemorrhage and hemodynamic instability mandating hysterectomy. We hereby, report a multigravid woman with two previous cesarean deliveries who was diagnosed to carry a fetus with Exencephally at thirteen weeks gestation. After the second dose of Misoprostol, she started to have intractable vaginal bleeding. Evacuation and Curettage failed to stop this hemorrhage. At emergent laparotomy, no hemoperitoneum was found and the uterus was intact. A bluish transparent area in the previous cesarean scar, covered with serosa and lodging a blood clot was identified. Total abdominal hysterectomy was done to secure hemostasis. To our surprise, histo-pathologic examination disclosed the presence of placenta Percreta. Sonographic screening of all pregnancies at high clinical risk for development of PAS should start as early as possible. Furthermore, termination of early pregnancy with the use of either medical or surgical methods should not be performed before the precise and certain exclusion of PAS done by experienced sonographers.

Keywords: First-Trimester PAS, Scarred uterus, Misoprostol, TOP

Corresponding author: J. Darido
Department of Obstetrics and Gynecology, Rafik Hariri University Hospital, Beirut-Lebanon.
E-mail: jesydarido@hotmail.com

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Introduction
PAS is commonly asymptomatic before delivery, though, it might less often, give rise to antepartum bleeding during variable times in pregnancy.[1] The most frequent presentation remains massive hemorrhage upon attempting to remove an adherent placenta at delivery.[2] Cases of First-trimester PAS are extremely rare, predominantly belonging to the severest form of invasion (PAS grade-3). These reports, described early-PAS complicating low, as well as, fundal placental implantation.[3, 4] Few common features were noted; a tendency for uterine rupture/perforation, involvement of scarred and intact uterus,[5-6] excessive utilization of hysterectomy, all of which reflecting the gravity of the condition. Finally, early-PAS was scarcely identified prior to the development of catastrophic complications. The most frequent complication of 1st trimester PAS was heavy vaginal bleeding upon suction evacuation or surgical curettage.[7] Less frequently, massive intraperitoneal hemorrhage as a consequence of uterine rupture/perforation was reported to occur spontaneously[8] or following the use of Misoprostol.[8] We hereby, describe the clinical findings of a multigravid lady with two previous cesarean deliveries. At first trimester scan (13 weeks) the fetus was discovered to have Exencephally. The patient consented for medical termination of pregnancy. Following administration of Misoprostol, the patient started to have heavy vaginal bleeding. At exploratory laparotomy no uterine rupture and no hemoperitoneum was encountered but hysterectomy was done to control vaginal hemorrhage. Pathology revealed the presence of placenta percreta involving the previous cesarean scar.
Case Presentation

This patient was a 31-year-old healthy G8P6A1 lady, with negative medical and surgical history. Her obstetric history disclosed 4 normal vaginal and two cesarean deliveries. The last cesarean section was 2 years prior to current presentation. At 13 weeks' gestation ultrasound showed cranial defect with protruding brain tissue, consistent with Exencephally. (Figure-1) The patient was counseled and consented for feticide with KCL, to be followed by medical termination with Misoprostol.

Upon admission one week later, she was hemodynamically stable. Misoprostol was initiated at half the dose suggested by FIGO for first trimester termination.[9, 10] Following the second Misoprostol dose, the patient started to experience heavy vaginal bleeding estimated at about 1.5 liters, though, she had no unusual pain. Her pulse became 150 BPM and blood pressure 100/60 mm/HG, while, pelvic exam revealed a thick long cervix of one finger dilation. A bedside ultrasound revealed normal uterus, no interruption of myometrial continuity, a lifeless fetus in the uterine cavity and no free fluid in Douglas pouch. No suspicion of uterine rupture due to absence of severe pain and absence of hemoperitoneum.

Owing to the profuse and massive vaginal bleeding, the patient was rushed to OR after starting fluid therapy while blood preparation was in progress. Vacuum-aspiration was started under ultrasound guidance and surgical evacuation of the Products of Conception (POC) was undertaken using Bierer Forceps. Despite uterine evacuation she continued to bleed heavily, losing another 1.5 liters. Transfusion with blood and blood products was started. Uterine revision disclosed a myometrial gap/thinning in the lower anterior segment of the uterus corresponding to the previous cesarean scar. During emergency exploratory laparotomy, we found no hemoperitoneum and the uterus was intact. We could identify a 5 cm rounded area in the anterior lower uterine wall covered only by serosa, with the remaining POC and a blood clot visible underneath. (Figure-2) Total abdominal hysterectomy was done to secure hemostasis. Another 5 units of PRBC and 1 FFP were provided intra and postoperative.

The patient’s post-operative course was smooth. She was discharged home on day 3 post-op after an uneventful recovery. Histo-Pathology revealed the presence of placenta Percreta at the cesarean scar.
Discussion

Misoprostol, a potent PGE1 analogue has been frequently used for medical termination of pregnancy (TOP) among other obstetric indications. Its use during first trimester was intended to ripen the cervix before surgical dilation and curettage or to induce labor and expulsion of fetuses with lethal anomaly with success rates reaching 80-90% when used alone in intact uterus and 70-80% in scarred uterus.[6, 20] Uterine rupture following the use of Misoprostol has been reported to involve scarred, as well as, intact uterus during second trimester.[20,22] As a result of the contemporary increasing rate of cesarean delivery, obstetricians are required to manage TOP on scarred uterus more frequently than ever. Patients with previous cesarean delivery are at increased risk for placenta previa and accreta.[20] Uterine rupture might, though less often, occur spontaneously due to defective or thinned-out myometrium due to Mullerian anomaly or created by placental invasion of a scarred myometrium.[16-18]

The timing of invasive placentation is not clear, nevertheless, the current prevailing concept is that cesarean scar pregnancy might be a precursor of PAS if untreated,[9, 10] though, not all CSP will evolve into PAS.[10, 12] Ballas et al, after studying 10 cases of late first trimester PAS (8-14 weeks) concluded that signs of placenta accreta may be present in the first trimester. [20] The placenta can be readily seen and assessed sonographically by week 10 of gestation, [21] In spite of this fact; most diagnosis of PAS is only made during 2nd and 3rd trimesters. [8,9] It is not precisely known what percentage of first trimester PAS can give rise to complications. Spontaneous uterine rupture/perforation is extremely rare as this requires deep infiltration of the villi and extreme thinning of the myometrium, a condition consistent only with placenta which forms ≤7% of all PAS. With placenta percreta, the invasion and unrestricted growth continue through the myometrium into the serosa or adjacent organs, and the reduced stability of the scar can lead to subsequent rupture of the scar tissue even in the absence of uterine contraction.[20,22] Hence, rupture/perforation can occur in scarred or intact uterus both spontaneously or initiated by an uterotoninc medication. Other cases described massive bleeding upon disrupting the PAS during D&C.[23-24] Severe intraperitoneal hemorrhage following the use of Misoprostol was reported previously in few cases complicated by PAS during second trimester when uterine rupture occurred due to thinned-out (infiltrated) myometrium.[25]

In spite of the strong-risk factor for developing PAS (two prior cesarean deliveries), this abnormal placentation was not identified by our team, possibly because the placenta was not previa. Actually the placenta was anterior covering the previous cesarean scar. To our knowledge, this is the only reported case of first-trimester PAS giving rise to torrential vaginal bleeding following the use of Misoprostol without inflicting uterine rupture. In this case, massive bleeding in the absence of uterine rupture could only be explained by Misoprostol-induced myometrial contractions at the placental bed provoking disruption of large engorged vessels supplying the abnormal placenta. A similar case reported a woman but at more advanced pregnancy (20 weeks) with PPROM. The placenta was previa and Gemeprost was used for TOP. Their patient experienced severe hemorrhage that mandated cesarean-hysterectomy. The placenta was found to be previa/accreta. They advocated the use of other modalities for TOP if PAS is suspected as prophylactic UAE and scheduled hysterectomy to minimize bleeding.[27]

Screening for abnormal placentation has moved from term for patients presenting with antepartum bleeding to screening at routine mid-pregnancy anomaly-scan done at18-22 weeks for high-risk patients (placenta previa and previous cesarean delivery). But the appearance of PAS complicating younger gestational age pushed screening further earlier during 1st trimester scan (11-14 weeks). Currently, the performance of 1st trimester screening with ultrasound has been less favorable than screening done later (2nd/3rd trimester).[28-29] Nevertheless, identification of PAS with ultrasonography in the first trimester is possible and reliable.[29-30] Furthermore, identifying PAS in early pregnancy provides gynecologists with many management options. It might allow the use of less invasive modalities of treatment as Uterine Artery Embolization, E&C plus Balloon-tamponade, Methotreaxate and most importantly, it might probably eliminate the need for hysterectomy which carries an end to women's fertility aspirations. Sonographic screening of all pregnancies at high clinical risk for development of PAS should start as early as possible. Furthermore, termination of early pregnancy with the use of either medical or surgical methods should not be performed before the precise and certain exclusion of PAS done by experienced sonographers.

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