

## PAPER DETAILS

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# Conservative management of two cases of morbidly adherent placenta

## İki adet morbid yapışık plasentalı olguda konservatif tedavi

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### Abstract

To present two cases of placenta percreta which were treated with conservative management in our clinic. Two cases of retained placenta percreta are presented. Treatment was failed in the first case because of haemorrhage. The second one was treated successfully with the procedures which consisted of caesarean section with midline abdominal and classic incision in the uterine fundus, internal iliac artery ligation, prophylactic broad-spectrum antibiotic treatment, suppression of menstrual cycle, use of methotrexate until the achievement of rapid downtrend of human chorionic gonadotropin, and monitoring the patient until spontan expulsion or resorbtion of placenta. It may be better to treat the cases of placenta percreta with conservative management, if the patients are hemodynamically stable and desirable for future fertility.

**Keywords:** Placenta percreta, methotrexate, conservative, ligation.

### Özet

Plasenta perkratada konservatif tedavi uygulanan iki olgu sunuldu. Kliniğimizde plasenta perkrata tanısı konan iki olguya konservatif tedavi uygulandı. İlk olguda kanamadan dolayı tedavide istenilen başarı elde edilemedi. İkinci olguda; abdominal orta hat ve uterin fundusda klasik insizyon, internal iliak arter ligasyonu, profilaktik geniş spektrumlu antibiyotik kullanımı, menstruel siklus supresyonu, human koryonik gonadotropin seviyesinde hızlı düşüş trendi elde edene kadar metotreksat uygulaması ve plasental atılım gerçekleşene kadar hastanın haftalık izlemi ile başarılı bir sonuç elde edildi. Hemodinamik olarak stabil ve fertilitate isteği olan plasenta perkrata olgularında konservatif yaklaşım daha uygun bir seçenek olabilir.

**Key Words:** Placenta percreta, methotrexate, conservative, ligation

### Introduction

Placenta percreta is a rare but most severe form of abnormal adherence of the placenta to the uterine wall, with invasion of the myometrium and the uterine serosa (1). The increasing rate of cesarean

deliveries seems to be a significant contributor to the increasing incidence of abnormal adherence of the placenta. In the event of invasive placentation, the third stage of labour may be complicated by severe uterine haemorrhage that may lead to life-threatening

condition. There are different approaches in managing placenta percreta such as cesarean section with hysterectomy, resection of parts of the uterus and uterus conserving surgery leaving the placenta behind. However, the optimal treatment has not yet been determined (2). We report two cases of placenta percreta in which we tried to avoid hysterectomy. Follow up was different for each of them.

### **Case reports**

#### **Case 1**

First case is a 31 years old, gravida (G) 5/para (P) 4 woman, with one previous cesarean section. She was referred to emergency room with abdominal pain and vaginal bleeding. She complained of having spontaneously expelled the twin fetuses at home twenty-five days ago, at about 14 weeks gestational age. Upon examination, she had moderate vaginal bleeding and retained placenta inside. She had a history of prior one cesarean section and no medical problems. Her vital signs on admission were stable and hemoglobin (Hb) was 7,65 mg/dL. Her ultrasound and magnetic resonance imaging findings were consistent with placenta percreta (Figure 1). After counseling, the patient and her husband made a decision to retain the uterus. She was given one unit of red blood cells and prophylactic broad-spectrum antibiotics (combination of 2,000 mg ceftriaxone every 24 h, and 500 mg metronidazole every 8 h). She received methotrexate 100 mgr intramuscular by weekly intervals for two times. At the first dose of methotrexate therapy, patient's  $\beta$  human chorionic gonadotropin ( $\beta$ -hCG) level was 814 IU/L, and it was 419 IU/L at the second dose. Three days after the second dose of methotrexate she had heavy uterine bleeding. Hb level was 6,5 g/dL. Her general condition was satisfactory, and

she received three units of red blood cells. After counseling again she did not want to go on to take the risks and she requested surgery. A laparotomy with midline abdominal incision was made. Her uterus was relatively large with prominent and bulging isthmic portion, suggestive of placenta percreta. The total blood loss during the hysterectomy was 1,5 L. The histopathological examination was also consistent with placenta percreta, and showed placental villi extending deeply into and through the myometrium to the serosa (Figure 2). Patient recovered uneventfully. She was discharged on the tenth post-operative day.

#### **Case 2**

A 31-year-old G7P4 woman with three previous cesarean sections was diagnosed with placenta previa totalis at the 37th week of gestation with uterine contractions. Ultrasound examination showed the absence of a normal subplacental sonolucent layer and the anterior lower uterine wall was deeply invaded by the placenta. Abnormal blood vessels connecting from placenta to the serosa were seen on color Doppler imaging. Because of her strong desire to retain the uterus, conservative management was decided. An emergency caesarean section was performed under general anesthesia with midline abdominal and classic uterine incision. Placenta previa percreta was confirmed visually at surgery. Focal thinning was noted in the lower segment of the anterior uterine wall and placental tissue was visible through the serosal layer. The lower segment was totally adhered. The fetus was delivered via a vertical incision in the uterine fundus. The umbilical cord was ligated proximally and the placenta left in situ. There was no bleeding from the undisturbed placental site, and then the uterine incision was closed. The main trunks of both internal iliac arteries were ligated as a prophylactic procedure to prevent heavy bleeding.

The estimated blood loss was 1000 mL and the operating time was 55 minutes. The hemoglobin count was 9.1 g/dL preoperatively and 8.0 g/dL postoperatively. She was given one unit of blood cells. Intravenous oxytocin infusion was administered for 24 h and prophylactic antibiotics (combination of 2,000 mg ceftriaxone every 24 h, and 500 mg metronidazole every 8 h) for 10 days. The woman's recovery was uneventful. She received methotrexate (100 mg, i.m.) by weekly intervals for three times starting one week after cesarean section on the ward. She was discharged on the tenth post-operative day. Two antibiotics (amoxicillin-clavulanic acid and ciprofloxacin) were prescribed to reduce the risk of infection.

At the first dose of methotrexate therapy, patient's  $\beta$ -hCG level was 6146 IU/L, at the second dose 5839 IU/L, and it was 2108 IU/L at the third dose of methotrexate. After achievement of rapid downtrend we performed a dose more and then stopped methotrexate treatment and monitored the  $\beta$ -hCG levels weekly. Level of  $\beta$ -hCG gradually decreased and 50 days after the first dose of methotrexate therapy it was less than 5 IU/L. Outpatient management consisted of monitoring C-reactive protein, hemogram, creatinin, aspartate aminotransferase, alanine aminotransferase,  $\beta$ -hCG, and ultrasound weekly. We planned two doses of 150 mg depot medroxyprogesterone acetate with an interval of one month for suppressing the cycle to avoid potential menstruation-associated hematometra while anticipating sloughing of the placenta(3). She received the first dose three weeks after the operation, but she did not accept to receive the second dose. Presence of abundant maternal vascularization of the retained placenta continued until the 12th week of postpartum period, and then

began to reduce. The patient reported expulsion of the placenta with mild vaginal bleeding four months after the delivery, and a subsequent ultrasonographic examination documented an empty uterine cavity. Her regular menstruation returned 5 months after delivery.

### Discussion

Invazive placentation is a severe pregnancy complication that may be associated with massive and potentially life-threatening intrapartum and postpartum haemorrhage(2). Unfortunately, placenta percreta presents significant challenges at cesarean section even for highly skilled surgeons. Conservative approach to therapy may provide a reduction in the need for transfusion and preservation of reproductive capabilities. Moreover, delayed surgery may also provide a reduction in uterine blood flow and the opportunity for thorough preoperative planning, if hysterectomy is still needed (4). So conservative management of placenta percreta may be a choice in hemodynamically stable patients, especially who desires future fertility.

Conservative management can be combined with selective embolization of the uterine arteries or ligation of the internal iliac arteries(4). Conservative management was failed in our first case because of haemorrhage, in the second case we performed bilateral internal iliac artery(IIA) ligation to avoid haemorrhage. We preferred to perform IIA ligation prior to selective arterial embolization, because we do not have the available trained personnel to perform selective arterial embolization at our institute. In placenta previa percreta, the descending cervical and vaginal arteries also supply blood to the placental site. Therefore, uterine artery ligation may not be satisfactory for control of hemorrhage in this region and IIA ligation may be preferred to diminish the blood flow. In the cases of percreta, IIA ligation

may be a haemorrhage control procedure and may also preserve fertility. Several studies have shown that recanalization of the IIA, normal blood flow in the uterine, arcuate, and ovarian arteries can occur after IIA ligation and, then subsequent fertility is not affected(5).

Another choice for preventing haemorrhage may be avoiding early attempt to remove the placenta. In the case of conservative management is successful, it results in gradual resorption or delayed delivery of the placenta(6). We realized that levels of  $\beta$ -hCG became negative many weeks before expulsion or resorption of placenta in our second case and in several cases which published (2,4). Any attempt to remove the placenta just after undetectable levels of  $\beta$ -hCG may be resulted in massive haemorrhage. Zepiridis et al suggested that placental expulsion or involution occurred just after decreased of human placental lactogen (hPL) to undetectable levels whereas placental expulsion or resorption occurred much later than undetectable levels of  $\beta$ -hCG. Production of  $\beta$ -hCG and hPL from distinct placental cell subpopulations seems to be the most plausible explanation for this disparity(2). Moreover, Masuzaki et al measured placental mRNA in plasma of a woman with placenta percreta to evaluate residual placenta, and found that HCG mRNA might reflect the methotrexate induced apoptotic activity in dividing cytotrophoblasts directly, and the hPL mRNA concentration might reflect the resorption of syncytiotrophoblasts(7). Thus evaluating hPL levels may be a valuable additional monitoring criteria before intervention to the placenta, and methotrexate adjuvant therapy may come into question again.

In the literature, there is controversy that

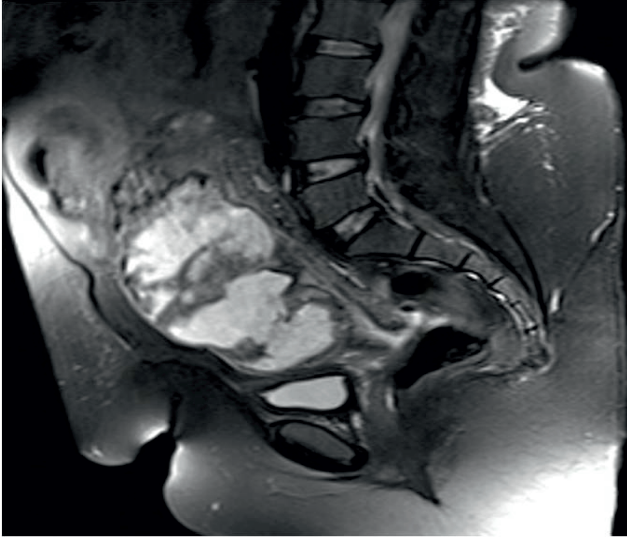
methotrexate should be used in the treatment of placenta percreta. A few number of case reports have been published on this issue(2,4,6). The sensitivity of chorionic tissue to methotrexate is well documented by its use in gestational trophoblastic neoplasia and ectopic pregnancy, but there are no studies evaluating the sensitivity of invasive placentation to methotrexate(6). It has been argued that there is no further cell division of placental tissue after delivery of the fetus, and therefore methotrexate may not be valuable(6). The placenta is a normal tissue, but the ability of trophoblast cells to proliferate and then to migrate and invade the uterine wall, as well as the many common characteristics shared by normal trophoblast cells and malignant cells(8). The differentiation, proliferation, and invasion of trophoblast cells require a proper regulation of growth factors and receptors, cell adhesion molecules, extracellular matrix proteins, hormones, and transcription factors(9). Several investigations suggest that abnormal invasive placentation may be related with aberrant regulation of these molecular changes (9,10). We think that progress of invasive placentation after the birth may be different from the uncomplicated cases. So, methotrexate may be useful in the conservative treatment of placenta percreta. However, appropriate trophoblast model systems and experimental approaches are needed to find out whether methotrexate has a role in treatment or not.

In conclusion we suggest that it may be better to treat the cases with placenta percreta conservatively, if the patients are hemodynamically stable and desirable for future fertility. Caesarean section with midline abdominal and classic incision in the uterine fundus, internal iliac artery ligation, prophylactic broad-spectrum antibiotic treatment, suppression of menstrual cycle, use of methotrexate until the achievement of rapid downtrend, and monitoring the

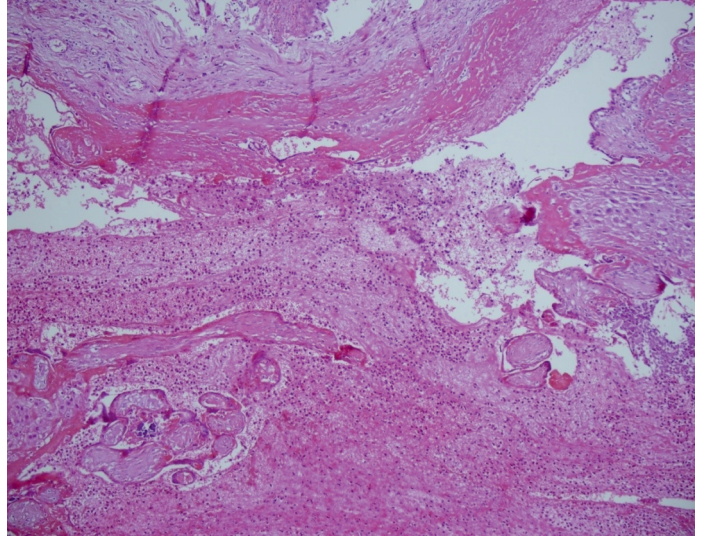


patient until spontaneous expulsion or resorption of placenta are the procedures that we performed in the second case. Of course conservative management carries the risk of intrauterine infection and delayed hemorrhage; hence the patients must be informed of the importance of

close and consistent outpatient follow-up for many weeks. The incidence of pathologically adherent placentae seems to be increasing much more with the increasing number of cesarean deliveries, so further experiences may be shared to reveal an exact consensus on this issue.



**Figure 1 :** Sagittal T2WI image shows heterogeneous placental signal and thin serosal bladder interface.



**Figure 2 :** Placenta penetrated through the myometrium to the serosa.

*Yazarlarla ilgili bildirilmesi gereken konular (Conflict of interest statement) : Yok (None)*

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