

Placenta accreta spectrum disorder in a primigravida with angular pregnancy: a case report

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ABSTRACT

Placenta accreta spectrum (PAS) is characterized by abnormal invasion of placental tissue into the underlying uterine muscles and has an incidence of 1/533–1/251. The incidence of complications includes uterine rupture (14–29%), PAS (6–10%), and retained placenta or incomplete placenta removal (4%). Here, we described a rare case of PAS and angular pregnancy, including how to diagnose and manage it preoperatively. A 32-year-old primigravida diagnosed at 24 weeks of gestation with a right angular pregnancy was admitted due to preterm premature rupture of membrane (PPROM) with a singleton fetus. We decided to perform hysterotomy because of the PPRM and intrauterine infection. Intraoperatively, we found PAS in the right angular pregnancy; therefore, we performed uterine conservative management with wedge resection on the right uterine fundus. Intraoperative bleeding was 1,600 cc. Histopathological examination revealed placenta increta. The maternal prognosis was good, while the fetus was poor, with an APGAR score of 1/1/0.

KEYWORDS angular pregnancy, case report, placenta accreta

Angular pregnancy is a rare condition in which the embryo is implanted in the lateral angle of the uterine cavity, medial to the uterotubal junction and round ligament. It causes life-threatening obstetric complications, such as uterine rupture, placental retention, and postpartum hemorrhage, which may need further surgery and hysterectomy.¹ Placenta accreta spectrum (PAS) is a disorder in which either a part or all of the abnormal trophoblasts in the placenta invade the myometrium or areas further away from the uterine wall.^{2,3} Several pathological abnormalities of the placenta exist, including placenta accreta, increta, and percreta.^{2,4} The incidence of PAS disorder has dramatically increased over the last few decades.^{5,6} A cohort study in Italy showed an increased incidence of PAS from 0.12% during the 1970s to 0.31% during the 2000s. During the same period, the number of

cesarean sections (CSs) increased from 17% to 64%. The increased incidence rates of PAS and CS were similar to those in Ireland and Hong Kong; meanwhile, in Surabaya, Indonesia, there were 156 such cases (4% of total deliveries) from January 2013 to October 2018. Moreover, the incidence of PAS has increased in women with a history of prior CS.^{2,4,5,6–9}

Maternal morbidity and mortality can occur due to heavy bleeding and even lead to life-threatening conditions that require a blood transfusion. Mortality rates have increased in mothers with PAS, with them likely to require management such as hysterectomy at delivery or during the postpartum period and a subsequent longer hospital stay.^{2,3} The complications of angular pregnancy include uterine rupture (14–29%), placenta accreta/increta/percreta (6–10%), and retained placenta or incomplete placenta removal

(4%).¹⁰ Therefore, herein we discussed a rare case of intraoperative PAS in a primigravida with angular pregnancy without a history of operation penetrating the endometrium, *in vitro* fertilization (IVF), and placenta previa.

CASE REPORT

A 32-year-old pregnant patient from an urban area visited the Mohammad Hoesin Hospital, Palembang. She was referred from another private hospital with a diagnosis of G₁P₀A₀ at 24 weeks of gestation with preterm premature rupture of membrane (PPROM) and oligohydramnios. She complained about amniotic leakage 16 hours before being admitted to the hospital with changing undergarments twice. She denied a history of bleeding or abdominal pain (cramping). She had a history of laparotomy myomectomy due to subserous uterine myoma and cystectomy 11 months ago. Her histopathological examination revealed uterine leiomyoma and endometriosis cysts in both ovaries. It is worthy of note that no penetration of the endometrium occurred when performing laparotomy myomectomy for subserous uterine myoma. She routinely monitored her pregnancy by visiting her obstetricians once a month.

On the initial physical examination, the vital signs were within normal limits. Obstetric examination showed a fundal height as high as 16 cm with external ballottement. There were no contractions, and the fetal heart rate was normal (142 beats/min). We did not find any signs or symptoms of PAS in this patient.

Laboratory results showed a white blood cell (WBC) count of 13,590/mm³. Serial ultrasound examination revealed a single live intrauterine fetus with no signs of placenta accreta (Figure 1). Recent ultrasound results showed normal fetal growth with biometry biparietal diameter of 5.70 cm, head circumference of 21.43 cm, abdominal circumference of 17.87 cm, femur length of

3.95 cm, and estimated fetal weight of 538.70 g (Figure 1). In addition, the placenta was located in the uterine fundus, with decreased amniotic fluid due to PPRM (single deepest pocket of 0.72 cm) (Figure 1). As per ultrasound findings, there were no signs of PAS such as no lacuna, thin myometrium, bridging vessels, and placenta located in the uterine fundus, except for hypervascularization in the right uterine horn with dilatation. Thus, we suspected an angular pregnancy in this patient.

We decided to perform conservative management by administering fluid, antibiotics, and corticosteroids with routine laboratory examinations to detect and evaluate the possibility of intrauterine infection due to PPRM; antibiotics (ampicillin 1 g q.i.d intravenous [IV] and gentamicin 80 mg b.i.d IV) were administered subsequently. On the 4th day of admission, laboratory results showed quantitative C-reactive protein (CRP) levels to be 11, indicating the presence of intrauterine infection. Therefore, we decided to perform abdominal termination. During surgery, a Pfannenstiel incision was made, and multiple subserous uterine myomas measuring 1–3 cm in diameter were found in the anterior corpus. A hysterotomy was performed, and a live neonate was born with a birth weight of 600 g, body length of 23 cm, and an APGAR score of 1/1/0. The baby died soon after hysterotomy (Figure 2a).

However, the placenta was not delivered after the neonate was born; therefore, the uterus was removed from the abdominal cavity. We observed a thin and fragile uterine horn with spontaneous and active bleeding at the placental implantation site. We performed the tourniquet technique by tying a catheter 20 Folley on the uterine isthmus away from the ascending and descending branches of the uterine artery. We then decided to perform wedge resection by incising the uterus far away from placental implantation; 200 g of additional placental tissue was obtained. We decided not to perform

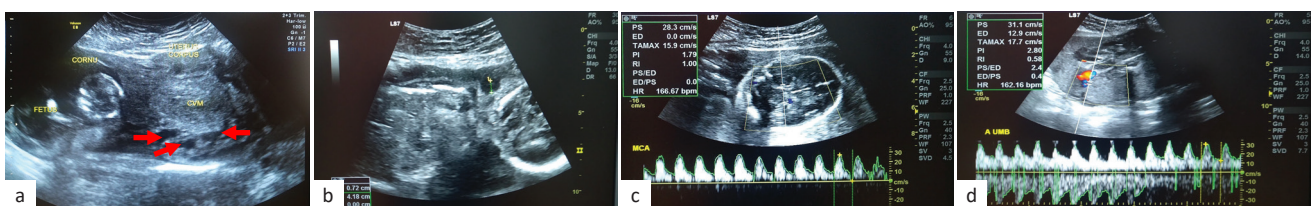


Figure 1. Ultrasound examination results showed angular pregnancy. There were no signs of placenta accreta. (a) Angular pregnancy was suspected (shown by hypervascularization and dilatation [arrows]), (b) SDP was 0.72 cm, (c) PI MCA was 1.79, (d) S/D umbilical artery was 2.4. MCA=middle cerebral artery; PI=pulsatility index; SDP=single deepest pocket; S/D=systolic/diastolic

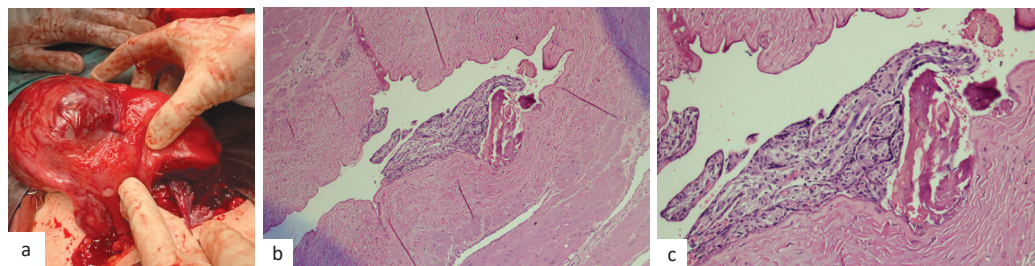


Figure 2. Postoperative findings. (a) A hysterotomy was performed. The histopathological examination showed placenta increta. Chorionic villi were lined with cytotrophoblast and syncytiotrophoblast cells between the myometrial layers. Extravillous trophoblast cells were present. (b) Magnification 100 \times ; (c) magnification 400 \times

a myomectomy because of profuse bleeding. The surgery was continued by inserting a stab wound drain to monitor postoperative bleeding. Her postoperative condition was stable, with no signs of active bleeding. Postoperative laboratory results showed a WBC count of 21,450/mm³ (leukocytosis), while the other parameters were within normal limits. She was administered antibiotics (ampicillin 1 g q.i.d IV and gentamicin 80 mg b.i.d IV), analgesics (ketorolac 30 mg t.i.d IV), and antifibrinolytics (tranexamic acid 500 mg t.i.d IV). Three days after hysterotomy, we re-performed the laboratory examination and found a decrease in the WBC count to 10,690/mm³. Histopathological examination revealed placenta increta (Figure 2, b and c). During follow-up, she exhibited a good response and only complained of postoperative pain with a visual analog scale score of 6 on postoperative day-1, which decreased to 1 on postoperative day-5. She was discharged and asked to monitor her health with a regular follow-up. Six months after the surgery, she had no complaints, and the multiple subserous uterine myomas did not enlarge. We advised her to plan a spontaneous pregnancy 1 year after the surgery, and she went through routine antenatal care with obstetricians. There were no ethical issues in this case report, and the ethical exemption was declared (No. 12/kepkrsmh/2022). Informed consent for publication was obtained from the patient and her family.

DISCUSSION

Considering the increased incidence of PAS, this case report can help provide insight into ways to deal with PAS in angular pregnancy. Angular pregnancy is a rare condition in which the embryo is implanted in the lateral angle of the uterine cavity, medial to the

uterotubal junction and round ligament. There are only a few reports on the term angular pregnancies, while angular pregnancy with PAS is rarely reported. We found only one case involving the term angular pregnancy with placenta accreta reported in Korea that was diagnosed with ultrasonography and computed tomography.¹¹

The pathogenesis of PAS is still unknown. A hypothesis proposed the inclusion of developmental disorders of the decidua, excessive trophoblast invasion, or a combination of both in the pathogenesis of PAS. Damaged decidualization, abnormalities in maternal vascular remodeling, excessive trophoblast invasion, or combinations of these factors are thought to have an impact on PAS due to previous instrumentation. In addition, PAS was thought to be secondary due to the wound dehiscence, which led to the development of chorionic villi deeper in the uterine wall, thereby causing extravillous trophoblasts (EVTs) to have access to the deeper myometrium.¹² Predisposing factors that could cause placenta accreta include surgical procedures in the endometrial lining, placenta previa, uterine malformation, endometriosis, and previous manual placental detachment process. Additional risk factors include maternal age, multiparity, previous uterine surgery and curettage, endometrial ablation, Asherman's syndrome, leiomyomas, uterine anomalies, gestational hypertension, and smoking.¹³⁻¹⁵

The definitive diagnosis of PAS is based on the pathological specimens obtained after hysterectomy. This definitive diagnosis depends on the visualization of the chorionic villi attached between the myometrium in the absence of the decidual layer.¹⁶ Based on histopathology, PAS is classified into three types, namely (1) placenta accreta, where placental villi invade directly into the myometrium, (2) placenta increta,

where a part of parietal decidua that lies between the myometrium and placenta is lost with direct contact between the trophoblast cells and myometrium, and (3) placenta percreta, a condition of placental villi that invade deeper from the myometrium to the serosa and even to other intra-abdominal organs such as the urinary bladder.¹⁵ In this case, histopathological results indicated PAS with a placenta increta type. There were chorionic villi in the intervillous space lined by cytotrophoblasts and syncytiotrophoblasts. The EVT cells were also observed, while in the basal plate, anchored villi and vessels were observed. The myometrium consisted of myocytes, in which chorionic villi were found.

Antenatal ultrasound examination could help establish the diagnosis of placenta accreta. The presence of vascular lacuna, loss of the retroplacental zone, the relationship between the urinary bladder and the thin and irregular uterus, and the presence of blood vessels crossing from the placenta to the urinary bladder are the typical features of placenta accreta. Overall, grayscale ultrasonography is sufficient to diagnose placenta accreta, with a sensitivity of 77–87%, specificity of 96–98%, positive predictive value of 65–93%, and negative predictive value of 98%.¹⁶ Before the surgery, the PAS diagnosis was missed because this was a rare case of PAS with angular pregnancy occurring in a primigravid woman. Due to its rarity and our limited experience in diagnosis, it was challenging to diagnose this case. In the future, a better and more detailed examination and recognition of warning signs and symptoms could prevent similar cases.

The ultrasound examination results showed no signs of PAS, such as lacuna, clear zone, or bridging vessels. In addition, the patient was primigravid, had no previous CS or curettage, no history of IVF, and no placenta previa. Thus, in this patient, the cause of placenta accreta was idiopathic because it could not be identified.

In general, the ideal management for PAS was a total hysterectomy. For patients who still wanted to maintain fertility, uterine conservative management could be performed, namely, performing a low transverse CS without hysterectomy.^{16,17} Timmersmans et al,¹⁸ who compared all articles about conservative management of placenta accreta, found 48 articles reporting good and effective results of conservative management. However, it was only performed in patients with minimal blood loss and those who wanted

to maintain their fertility. Conservative management could be performed for placenta accreta by leaving the placenta in the uterus accompanied by administration of drugs such as methotrexate, oversewing the placental bed, wedge resection, coagulation with argon laser, and hypogastric artery balloon occlusion or ligation.^{19,20} In this case, we decided to perform conservative management for PAS considering the intraoperative finding, which showed that the location and extension of placental implantation were localized. Thus, it was still possible to perform wedge resection and hysterorrhaphy, considering her future fertility. We performed the tourniquet technique on the uterine isthmus and wedge resection with the incision made away from the placental implantation to prevent further bleeding. Hysterorrhaphy was then performed. Intrauterine infection, also known as chorioamnionitis, is an infection and inflammation of any combination of the amniotic fluid, placenta, fetus, fetal membranes, or decidua.²⁰ The clinical findings of chorioamnionitis include maternal fever ($\geq 38^{\circ}\text{C}$), maternal (>100 beats/min) and/or fetal tachycardia (>160 beats/min), maternal leukocytosis on complete blood count examination ($>15,000$ cells/ mm^3), and uterine tenderness and/or purulent and/or foul-smelling amniotic fluid.^{21,22} Confirmed intraamniotic infection is based on a positive amniotic fluid test result (Gram stain, glucose level, or culture results consistent with infection) and a placental pathology demonstrating histologic evidence of placental infection or inflammation.

The diagnosis of intrauterine infection in this case was based on the PPROM as a risk factor and laboratory examination showing leukocytosis and increased CRP. No other symptoms were observed. We also did not perform Gram staining and culture of the amniotic fluid. Thus, this case was of an atypical intrauterine infection.

A recent population-based study on placenta accreta did not demonstrate any association between chorioamnionitis and abnormal placentation. Nevertheless, the study was likely underpowered to detect a significant relationship as only three cases of chorioamnionitis were identified among 128 patients with placenta accreta (odds ratio 0.88, confidence interval 0.28–2.78, and $p = 0.83$). In addition, some evidence suggest that intra-amniotic inflammation may be associated with certain placental abnormalities, such as placental edema and terminal villous immaturity.²³

The antibiotics used were in accordance with the guidelines followed in a previous study. The recommended antibiotic regime is ampicillin 2 g IV every 6 hours and gentamicin 2 mg/kg IV load followed by 1.5 mg/kg every 8 hours or 5 mg/kg IV every 24 hours.^{19,20} Other antibiotics alternatives are ceftriaxone, metronidazole, and clarithromycin; ampicillin-sulbactam and azithromycin, ampicillin-sulbactam, piperacillin-tazobactam, cefotetan, ceftiofex, and ertapenem.²² Besides, tranexamic acid is important to prevent and treat traumatic and perioperative bleeding and can reduce the consequent blood transfusion requirements.²⁴

The patient was primigravid; therefore, conservative management was performed to maintain her fertility. In this patient, the intraoperative complication was intraoperative bleeding, with a total volume of 1,600 cc. However, this bleeding could be managed and did not endanger the patient's life. She was discharged after 5 days of hospitalization. Her reproductive prognosis was good because the incision did not penetrate the endometrium, and the uterine myoma was subserous.

The limitation of this study was that only one case of PAS in angular pregnancy complicated by PPRM was included, and a follow-up was only done for 6 months after the surgical procedure. In addition, this case was undiagnosed preoperatively because of its rarity and the authors' knowledge and experience. Furthermore, a case series should be performed to compare our findings with other studies.

In conclusion, this case of PAS in angular pregnancy complicated by PPRM is a unique case because it did not rupture in the usual time as predicted, did not show any symptoms or signs of PAS, and had no risk factor for PAS. Prompt diagnosis and treatment were required to prevent maternal and fetal morbidity and mortality. Besides anamnesis and physical examination, antenatal ultrasound and laboratory examination played a role in diagnosing this case. The treatment depended on the patient's condition, intraoperative findings, available resources, and future fertility outcomes.

Conflict of Interest

The authors affirm no conflict of interest in this study.

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