Risk factors, Diagnosis and Outcomes of Management Strategies of Placenta Accreta Spectrum (PAS) Disorders in Low-resources Settings: Case Report

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Abstract

Background: Placenta accreta spectrum disorder (PAS), such as placenta accreta, placenta increta, and placenta percreta are causes of post-partum hemorrhage causing maternal morbidity and mortality. The major risk issues are prior caesarean section, placenta previa, advanced maternal age, multiparity, and preeclampsia. A reliable antenatal diagnosis is required for this serious condition. To reduce the incidence of maternal morbidity and mortality due to massive bleeding, it is necessary to make an early diagnosis in order for the surgical approach can be planned in the future. High birth rates and cesarean delivery are the cause of an increase in the incidence of PAS in middle / low-income countries. Additional diagnostic methods, advanced surgical methods, and other interventional radiological methods can greatly contribute to reducing maternal morbidity and mortality in high-income countries but are frequently not available in low-resource settings. Therefore, an inexpensive management strategy is an important issue. *Methods*: This is a retrospective case series. The patients suspected of PAS are reassessed histologically for the diagnosis confirmation. The information about risk factors, time to decide a definite diagnosis, monitoring vital signs, resuscitation, blood transfusions, surgical management, and maternal outcomes are detailed in a table. *Result*: We reported five women with PAS, diagnosed and managed in our hospital, with different conditions at admission and a different risk factor for PAS. All of the patients undergoing subtotal hysterectomy and uterine tissue samples were sent to the anatomical pathology department for histopathological examination. Red blood cell transfusions were used in all patients and transfer of patients to the intensive care unit was carried out postoperatively. Complications related to monitoring occurred in one patient such as acute kidney injury. There was one maternal death that occurred. *Conclusion*: Antenatal diagnosis is essential in outlining the best management strategy in patients with PAS. The clinical approach was able to prove valuable when PAS is suspected before delivery. In low-resource settings, lack of interventional radiology services and prenatal diagnostic may probably impact patients management with PAS.

Keywords: placenta accreta spectrum, abnormal placentation, PAS

Introduction

Placenta accreta spectrum disorder (PAS) is a placentation disorder characterized by invasion of trophoblast tissue and abnormal adhesions through the myometrium and serosa.[1] the incidence of PAS is increasing. This may be due to an increase in the cesarean delivery rate, which is one of the main risk factors for PAS in subsequent pregnancies.[3,4]

Bleeding from the placental bed after attempted placental extraction is the most common complication, which can be a major cause of maternal morbidity and ultimately lead to maternal death.[3,4] The severity of the complications and the morbidity acquired depends largely on the capacity of the health care team to diagnose antenatal PAS disorders, because it is possible to planning the

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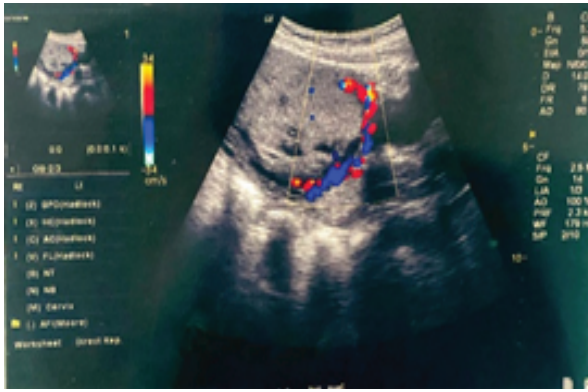
Figure 1. Ultrasound images antenatally showed placenta previa, diffuse placenta accreta spectrum on the lower anterior uterine wall.

Figure 2. Intraoperative of hysterectomy. The placenta was invaded to the serosa.

labor and management experts in the most severe cases.[4,5,6] Therapeutic strategies already developed by and for high-income settings require adjustment for low-resource settings where access to neonatal care, anesthetists, surgeons, and intensive care units (ICU) is limited.[6,7] The purpose of this review is to discuss and discuss the difficulties of diagnosing and managing PAS in low-resource settings.[8,9]

Case Presentation

Case 1: A 30-year-old woman (gravida 4, para 1, alive 1, abortus 2) admitted for routine antenatal care at our antenatal clinic, 38 weeks gestational age. She had history of two curettage due to incomplete abortion. She also had history of one previous caesarean deliveries (CD) due to haemorrhagic placenta previa at 7 years ago. Ultrasound examination illustrates a single fetus pregnancies life breech, the fetal biometry according to gestational age approximately 38 weeks, with the presence of placenta previa and placenta accreta are diffuse spectrum in the lower anterior uterine wall. **(Fig. 1).**

The examination found a normotensive patient with blood pressure (BP) 116/68, Heart rate (HR) 80x/min and slightly discolored conjunctiva. She was found to have a hemoglobin (HB) concentration of 9,4 g/dl. The patient is treated with monitoring for uterine contractions, fetal heart sounds, and vaginal bleeding. The patient will be scheduled to undergo an elective cesarean hysterectomy. At the time of intraoperatively the obstetrician can confirm the placenta percreta in the anterior uterine wall of the lower uterine segment **(Fig. 2)**, but the pathologic examination of the operative specimen was not examined. Blood loss was estimated at 1000 cc, the patient received 4 red blood cells transfusion. She left the hospital after 6 days.

Case 2: A 30-year-old woman (para 3, alive 3, abortus 1). She had received antenatal care in primary medical facility with general practitioner and midwife. She had history of two curettage due to incomplete abortion and retention placenta. The patient admitted to the emergency department due to post partum hemorrhage. The admission examination found lethargy with BP 90/75 mmHg, HR 130x/min, and CRT >3 sec. the Hb count was 3,9 g/dl which diagnosed as hemorrhagic shock grade III. The patient received intravenous fluid
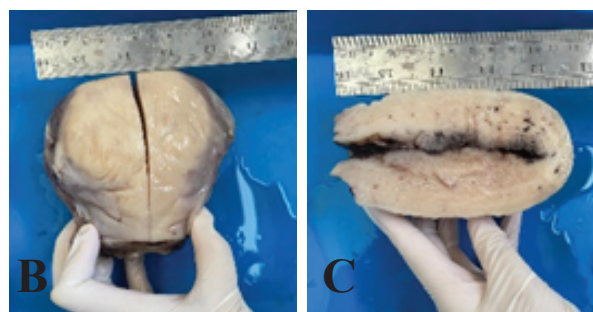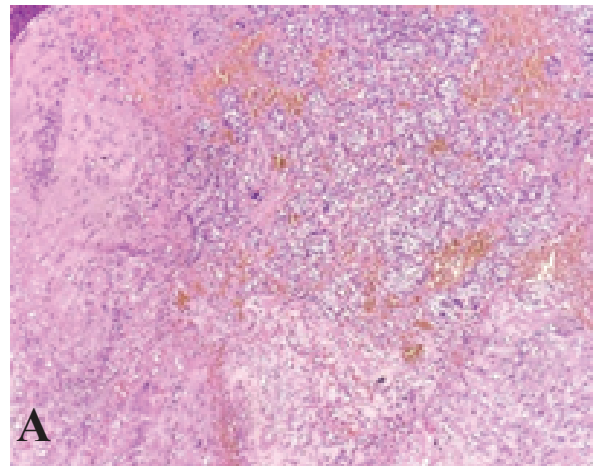

Figure 3. Postoperative pathologic examination of the operative specimen case 2. **A.** Microscopic specimen, chorionic villi and trophoblastic cells infiltrated less than half the thickness of the myometrium. **B.C.** Macroscopic specimen, in the uterine cavity lamellation contain blood clots.
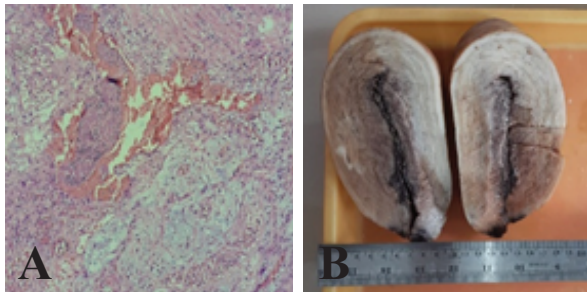
Figure 4. Postoperative pathologic examination of the operative specimen case 3. **A.** Microscopic specimen, necrotic villi on the mucosa and attach to the myometrium. The stromal of the connective tissue appears edematous with capillary proliferation of blood vessels, **B.** Macroscopic specimen, in the uterine cavity lamellations contain blood clots.

resuscitation with 1500 cc of crystalloid. The placenta appears to be firmly attached to the uterine wall so that the method of extraction of the placenta was unsuccessful because of the suspicion of

placenta accreta. The patient was directly referred to the operating room for an emergency subtotal hysterectomy. The blood loss intra-operative was estimated at 1500 cc. The patient was transferred to the ICU and was transfused with 8 red blood cells. Post-operative pathologic examination of the operative specimen confirmed the presence of placenta increta **(Fig. 3)**. The outcome was favorable, she left the hospital after 6 days.

Case 3: 37-years-old patient (gravida 3, para 2 with 2 live children). She had received antenatal care in primary medical facility with general practitioner and midwife. She also had received ultrasound examination with obstetrician once. The patient admitted for high blood pressure and confirm of covid-19 disease based on polymerase chain reaction (PCR) test. The examination had found a conscious, BP was 179/102 with discolored conjunctiva. The patient was planned for vaginal delivery with medical induction. The vaginal delivery was succeed. The placenta appears to be firmly attached to the uterine wall so that the method of extraction of the placenta was
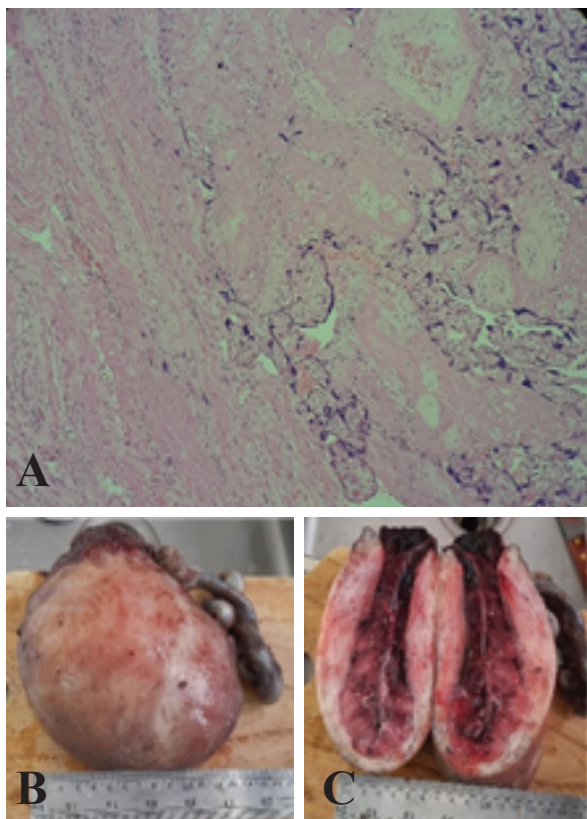

Figure 5. Postoperative pathologic examination of the operative specimen case 4. **A.** Microscopic specimen, the chorionic villi appear attached to the surface of myometrium. **B&C.** Macroscopic specimen, the uterine cavity consists of a placenta measuring 14x6x3 cm.

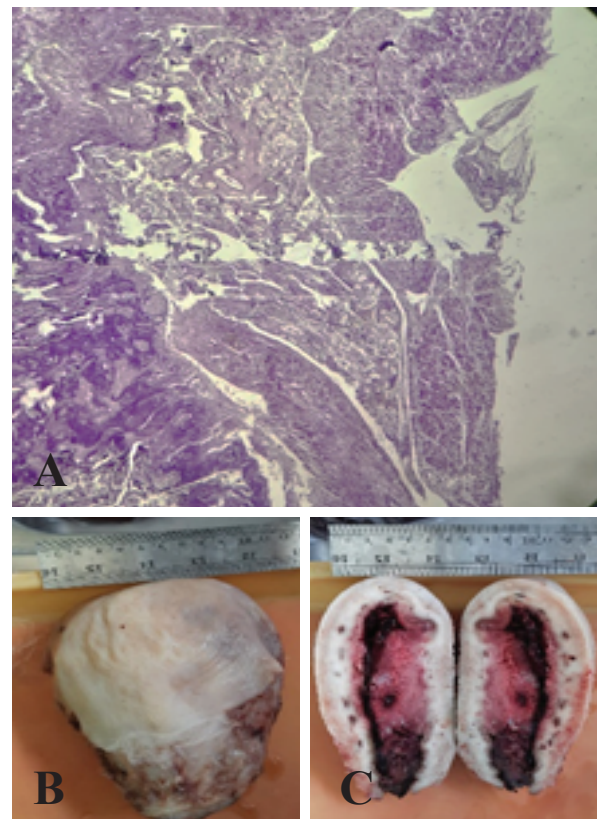**Figure 6.** Postoperative pathologic examination of the operative specimen case 5. **A.** Microscopic specimen, Microscopic specimen, chorionic villi on the mucosa and attach to the myometrium. The stromal of the connective tissue appears edematous with capillary proliferation of blood vessels. **B&C.** Macroscopic specimen, in the uterine cavity lamellation contain blood clots and residual placenta.

unsuccessful because of the suspicion of placenta accreta and diagnosed post-partum hemorrhage due to suspected placenta accreta spectrum. The patient was directly referred to the operating room for an emergency hysterectomy. But because of the patient had confirm covid-19 status, the surgical was delay due to preparation of all the device. The patient's condition before surgical was lethargy with BP 85/60 mmHg, HR 135x/min, CRT >3 sec which diagnosed as hemorrhagic shock grade III. The Hb count was 4.5 g/dl. A subtotal hysterectomy was performed. Post-operative pathologic examination of the operative specimen confirmed the presence of placenta accreta with venous thrombotic **(Fig. 4)**. The blood loss intraoperative was estimated at 1500 cc. The patient was transferred to intensive care and was transfused with 6 red blood cells. Patient was diagnosed acute kidney injury. The outcome was favorable and the patient left the hospital after 7 days.

Case 4: 32-years-old patient (para 3 with 3 live children). She had received antenatal care in primary medical facility with general practitioner and midwife. She also had received ultrasound examination with general practitioner. She had history of vaginal hemorrhage post-partum due to retention placenta and successfully treated with manual placenta. The patient admitted to the emergency department due to post-partum hemorrhage.

The admission examination found lethargy with BP 80/60 mmHg, HR 130x/min, CRT >3 sec, and conjunctiva discolored which diagnosed as hemorrhagic shock grade III. The patient received intravenous fluid resuscitation with 2 liters of crystalloid. The placenta appears to be firmly attached to the uterine wall so that the method of extraction of the placenta was unsuccessful because of the suspicion of placenta accreta. The patient was directly referred to the operating room for an emergency total hysterectomy. Post-operative pathologic examination of the operative specimen confirmed the presence of placenta increta **(Fig. 5)**. The blood loss was estimated at 2000 cc, the patient received 4 red blood cells. The outcome was favorable, she left the hospital after 6 days.

Case 5: 35-years-old patient (para 5 with 5 live children). She had received no antenatal care. The patient admitted through the emergency department due to profuse vaginal bleeding post spontaneous delivery without medical assistant. The admission examination found somnolen with BP 87/62 mmHg, HR 145x/min, CRT >3 sec, and conjunctiva discolored which diagnosed as hemorrhagic shock grade IV. The patient received intravenous fluid resuscitation with 2 liter of crystalloid. The placenta appears to be firmly attached to the uterine wall so that the method of extraction of the placenta was unsuccessful because of the suspicion of placenta accreta. The patient was directly referred to the operating room for an emergency total hysterectomy. Post-operative pathologic examination of the operative specimen confirmed the presence of placenta increta **(Fig. 6)**. The blood loss was estimated at 2000 cc, the patient received 4 red blood cells. The patient was transferred to ICU. Three hours after the surgical procedure, the patient was declared dead.

Discussion

Placenta accreta spectrum (PAS) disorders is a condition in which impaired placentation is characterized by abnormal adhesions, and invasion of trophoblast tissue passes through to the uterine myometrium and serosa. PAS can be life-threatening and thus requires proper treatment, and can significantly increase maternal morbidity, due to uncorrected post partum hemorrhage, hysterectomes, postoperative complications and more severe organ damage.[10]

The placenta accreta spectrum is influenced by several risk factors. a history of previous cesarean delivery is a frequent risk factor. In a systematic review, the incidence of placenta accreta spectrum increased from 0.3% in women with a history of one previous cesarean delivery compared to 6.74% for women with five or more cesarean sections.[6,11]

A report from another systematic review suggests that the risk of placenta accreta in a second pregnancy is increased in women who have had a cesarean delivery in a previous pregnancy compared to women who have had vaginal delivery (OR 3.02; 95% CI, 1.50-6.08).[12] Other risk factors, including elderly patients, can occur after any procedure that can damage the endometrium, including myomectomy, uterine artery embolization, uterine curettage, endometrial ablation, manual removal of the placenta, and also multiparity..[5,6] In all of our cases, there are risk factors such as multiparity, which three of them also have a history of curettage. But just one of all the case have history of caesarean delivery. This suggests that although some literature reported that previous cesarean delivery is one of the major risks, not all patients who do not have a history of cesarean delivery will be exempt of PAS. Therefore it is very important to be attention to other risk factors when doing antenatal care examinations. Placenta previa is another significant risk factor. The incidence of placenta accreta spectrum in women diagnosed with placenta previa and no previous cesarean delivery was 3%.[6,13] In our cases, there was one case who diagnosed placenta accreta spectrum from the ultrasound imaging

Table 1: Clinical presentation and outcome of all patients

Case	Age (years)	Parity	Risk factor	Clinical sign and symptoms	Hemodynamic at admission	Relevant Comorbidity	ANC history	USG of PAS	Histopatology diagnosis	Treatment (Non-surgical and surgical)	Outcome
1	30	G4P1A2	History of curettage twice, History of cesarean sections. Multiparity	Fully conscious, Discoloured conjunctiva	BP 116/68 mmHg, HR 80x/min, CRT <3 sec Hb 9,4 g/dl	No	Routin with obstetri-cian	PAS with placenta previa totalis	NA	Blood transfusion, elective cesarean hysterectomy	Mother was stable and no complication
2	30	P3A1	History of curettage due to abortion, History of curettage due to placenta retention, Multiparity	Hemorrhage post partum, lethargy, Discoloured conjunctiva hemorragic shock gr III	BP 90/75 mmHg, HR 130x/min, CRT >3 sec Hb 3,9 g/dl	No	Primary medical facility	Un-diagnosed	Placenta Inccreta	Resuscitation Blood transfusion, Emergency subtotal hysterectomy	Mother was stable and no complication
3	37	P3A0	Multiparity	Hemorrhage post partum, lethargy, Discoloured conjunctiva hemorragic shock gr III	BP 85/60 mmHg, HR 135x/min, CRT >3 sec Hb 4,5 g/dl	Confirm Covid-19, Severe Preeclamsia,	Primary medical facility	Un-diagnosed	Placenta accreta with vein thrombotic	Blood transfusion, Emergency subtotal hysterectomy	Acute kidney injury
4	32	P3A0	Multiparity	Hemorrhage post partum, lethargy, Discoloured conjunctiva hemorragic shock gr III	BP 80/60 mmHg, HR 130x/min, CRT >3 sec Hb 7,9 g/dl	No	Primary medical facility	Un-diagnosed	Placenta Inccreta	ResuscitationBlood transfusion, Emergency total histerectomy	Mother was stable and no complication
5	35	P5A0	Multiparity	Hemorrhage post partum, lethargy, Discoloured conjunctiva hemorragic shock gr IV	BP 87/62 mmHg, HR 145x/min, CRT >3 sec Hb 4,8 g/dl	Delivery without medical assistant	No History	Un-diagnosed	Placenta accreta	ResuscitationBlood transfusion, Emergency total histerectomy	Mother was died.

G: gestation, P: parity, A: abortus, BP: blood pressure, HR: heart rate, CRT: capillary refill time, Hb: Hemoglobin, NA: not avalaible.

also with placenta previa.

The decision to diagnose PAS antenatally has been shown to improve maternal outcome, with an appropriate risk assessment and a well-planned delivery by an experienced multidisciplinary team at a tertiary referral center. It has been reported from several studies that have conducted research on the predictive value of various ultrasound markers of PAS. The main problem that occurs is that the results of all diagnostic techniques are very dependent on the subjective operator who will be able to show varying results according to their experience. Because PAS is still a rare condition in pregnancy, there are still many doctors who do not have as much experience with ultrasound images compared to obstetricians.[10] Therefore, the limited access to experts and high-resolution Doppler machines are still the main problems faced by health services dealing with worker obstetric problems in low resource settings. Furthermore, it was not screened antenatally in patients with high

risk factors or who had been screened but was performed by inexperienced health care workers due to the absence of a gynecologist round the clock in low-resources place.[13] Four patient in our cases received antenatal ultrasound, however, an additional concern is that the diagnosis of placenta accreta is not demonstrated in three cases on antenatal scan. Antenatal ultrasound identified in one case who undergoing antenatal care routine with obstetrician.

In high-income countries a large proportion of pregnant women are routinely screened around 20 weeks of gestation for fetal abnormalities and placental status using trans-abdominal ultrasound. If the patient is suspected of having PAS disorder, then the patient should be referred to a special center that has more facilities where the diagnosis can be confirmed by an imaging specialist. However, in some areas of low resource settings with limited antenatal care (ANC) programs, most pregnant women are discouraged from

having routine ultrasound examinations so that the location and status of the placenta are not frequently evaluated.[16]

Based on a systematic review reported in 2013, prenatal ultrasound examination has a high degree of accuracy for the diagnosis of PAS especially in women with anterior placenta previa and a history of previous caesarean section, achieving a sensitivity rate of 91% and a specificity of 97% .[10] This is appropriate to our case who have previous cesarean delivery identified as a placenta accreta spectrum with placenta previa from the ultrasound imaging. The most typical features to be identified using gray-scale ultrasonography are loss of the hypoechoic space, placenta lacunae, abnormalities of the uterine-bladder interface, thinning of the myometrium, focal exophytic mass, and protrusion of the placenta with a sensitivity of between 50-87%. Examination performed simultaneously with Doppler color abnormalities such as uterovesical and sub-placental hypervascularity, connecting vessels, placental lacunae vessels, and the presence of intrapacental hypervascularity on 3D images increases the diagnostic sensitivity by 90%. However, the advantages of increasing the sensitivity of this ultrasound approach may be too costly in low-income countries due to the unavailability of machines with 3D power Doppler.[16]

Patients should be referred to a specialized center with facilities for a multidisciplinary team and access to interventional radiology, blood bank facilities, and a neonatal unit once the antenatal diagnosis of PAS has been established. When the diagnosis is confirmed and the patient is in a stable condition and there is no active bleeding, then the patient will be treated as an outpatient with regular follow-up and a planned delivery in a well-resourced setting. However, due to poor social conditions in low-resource settings, especially with difficult access conditions (eg distance from specialist centers, availability of emergency transportation, and patient education), doctors will decide more to be hospitalized until the patient undergoes the labor. The main burden in places with low resources to decide on hospitalization for these patients is the high costs involved, these costs are very important to consider against the possibility of emergency surgery in worsening conditions, and resulting in increased morbidity and mortality of the maternal. [13]

The gold standard for the treatment of abnormal placentations is caesarean hysterectomy. In a recent systematic review and meta-analysis, approximately 90% of suspected antenatal PAS underwent cesarean hysterectomy. However, this condition is also associated with a relatively high incidence of maternal morbidity, reaching 40-50%, most commonly associated with bleeding and organ disorders during surgery, and leading to a mortality rate of around 7% due to untreated massive bleeding.[6] There are only one case that received scheduled cesarean hysterectomy. Because this case can be diagnosed PAS during antenatal care. Also, in this case the maternal outcome was very good if compared to other patients.

The availability of an experienced gynecologist should be held immediately and a hysterectomy carried out immediately. With this effort, it becomes a live-saving for patients with PAS conditions, especially in low resource settings when multidisciplinary teams are not available or there are geographic problems due to difficult access to transportation, especially in emergency situations.[16] The four patient was successfully resuscitated and recovered well post-operatively. It is very important to carry out a proper method to control intra-operative bleeding is important for the patient. The presence of massive untreated bleeding can cause organ damage such as failure of the heart, lungs, brain, liver, kidneys, and other vital organs.[15] However, one of our series was survived, she was diagnosed acute kidney injury (AKI) due to prolonged shock. Because of the patient had confirm covid-19 status, the surgical was delay due to preparation of all the device.

Histopathology evaluation is performed on hematoxylin and eosin-stained sections. In the recent years, the International Federation of Gynecology and Obstetrics (FIGO) suggested classification of the placenta accreta spectrum cases according clinical and histological criteria.[9] The diagnosis of placenta accreta is made in the absence of a decidual layer between the placental villi and the myometrium. Whereas in the diagnosis of cases of placenta increta and percreta if there is found in the presence of deep myometrial invasion and myometrial perforation.[14]

Conclusion

Antenatal diagnosis is essential in outlining the best management strategy in patients with PAS. The clinical approach was able to prove valuable when PAS is suspected before delivery. In low-resource settings, lack of interventional radiology services and prenatal diagnostic may probably impact patients management with PAS.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient has given her consent for her images and other clinical information to be reported in the journal. The patient understands that name and

initials will not be published and due efforts will be made to conceal identity, but anonymity cannot be guaranteed.

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Author contribution

References :

1. Yu FNY, Leung KY. Antenatal diagnosis of placenta accreta spectrum(PAS) disorders. Best Practice & Research Clinical Obstetrics and Gynaecology. 2020.

2. Slaoui A, Talib S, Nah A, et al. Placenta accreta in the department of gynaecology and obstetrics in Rabat, Morocco: case series and review of the literature. Pan African Medical Journal. 2019;33:86.

3. Morlando M, Collins S. Placenta Accreta Spectrum Disorders: Challenges, Risks, and Management Strategies. International Journal of Women's Health 2020:12 1033–1045

4. Fonseca A, Campos DAD, Maternal morbidity and mortality due to placenta accreta spectrum disorders. Best Practice & Research Clinical Obstetrics and Gynaecology. 2020.

5. Silver RM, Branch DW. Placenta Accreta Spectrum. N engl j med. 2018. 378;(16):1529-36

6. Cahill AG, Beigi R, Heine RP, Silver RM, Wax JR. Placenta Accreta Spectrum. Obstetric Care Consensus of The American College of Obstetricians and Gynecologists and the Society. 2018. B2-16

7. Jauniaux E, Bhide A. Prenatal ultrasound diagnosis and outcome of placenta previa accreta after cesarean delivery: a systematic review and meta-analysis. American Journal of Obstetrics & Gynecology. 2017. 27-36

8. Morlando M, Collins S. Placenta Accreta Spectrum Disorders: Challenges, Risks, and Management Strategies

9. Jaraquemada JMP, Fiorillo A, Hamer J, et al. Placenta accreta spectrum: a hysterectomy can be prevented in almost 80% of cases using a resective-reconstructive technique. The journal of maternal-fetal & neonatal medicine. 2020. 1-8

10. Yu FNY, Leung KY. Antenatal diagnosis of placenta accreta spectrum (PAS) disorders. Best Practice & Research Clinical Obstetrics and Gynaecology. 2020

11. Jauniaux E, Grønbeck L, Bunce C, et al. Epidemiology of placenta previa accreta: a systematic review and meta-analysis. BMJ. 2019;9:e031193.

12. Mucio1 BD, Serruya S, Aleman A, Castellano G, et al. A systematic review and meta-analysis of cesarean delivery and other uterine surgery as risk factors for placenta accrete. Int J Gynecol Obstet 2019; 1–11

13. Escobar MF, Gallego JC, Nasner D, Gunawardana K. Management of abnormal invasive placenta in a low- and medium-resource setting. Best Practice & Research Clinical Obstetrics and Gynaecology. 2020. 1-12

14. Jiang X, Lin X, Han X, Ma Y, Zhao F. Successful resuscitation of a patient with pernicious placenta previa and placenta accrete who had massive life-threatening bleeding during cesarean section: A case report. Medicine. 2019. (98):14

15. Tan SG, Jobling TW, Wallace EM, Mcneilage LJ, et. al. Surgical management of placenta accreta: a 10-year experience. Acta Obstet Gynecol Scand 2013;92:445–450.

16. Hussein AM, Kamel A, Elbarmelgy RA, et al. Managing Placenta Accreta Spectrum Disorders (PAS) in Middle/Low-Resource settings. Curr Obstet Gynecol Rep. 2019