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Case Series

Unmasking the elusive: an early gestational age placenta accreta case series to illuminate the path towards avoiding missed diagnosis

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ABSTRACT

Placenta accreta is a condition characterized by the abnormal invasion of the placenta into the uterine wall, leading to torrential hemorrhage. This case series, highlights the importance of accurate diagnosis and early detection of this life-threatening complication. The incidence of this iatrogenic complication is rising due to increased caesarean deliveries. While in advance stages of pregnancy the chances of missing accreta are less but in early pregnancy the diagnosis may be elusive. Timely detection by using imaging modalities like ultrasound both 2D and colour Doppler, provide valuable clues. Misdiagnosis may be fatal, especially in the first trimester. The present case series presents 3 cases where initial diagnosis of missed abortion followed by repeated curettage and gestational trophoblastic disease (GTD) was made respectively. The agony of suffering leads the patient to our tertiary care center where the diagnosis of accreta was made. Accurate diagnosis and early detection of placenta accreta are vital to optimize patient outcome. Detecting the niche and an anteriorly situated low lying placenta with history of previous birth by caesarian section should raise suspicion, and vigilance on the part of treating obstetrician is must.

Keywords: Placenta accreta, Misdiagnosis, Early gestational age

INTRODUCTION

Placenta accreta is a condition characterized by an abnormally invasive placenta that poses a significant risk of hemorrhage. It occurs when the placenta attaches firmly to the uterine wall.¹ In placenta accreta, the normal layers that separate the placenta from the uterus, such as the decidua basalis and fibrinoid or Nitabuch layer, are absent or underdeveloped. As a result, the placental villi become embedded in the myometrium, making it difficult for the placenta to separate after delivery and potentially leading to severe bleeding. The prevalence of placenta accreta is estimated to be around 1 in 2500 pregnancies, and its incidence has been increasing due to rising rates of caesarean deliveries.² Early detection of placenta accreta

is crucial to guide clinical management and prevent immediate complications.³ Ultrasound is the primary diagnostic tool during pregnancy and is particularly useful in evaluating obstetric hemorrhage.⁴ By examining the morphometric data of the uterine wall, especially the niche area and trophoblast structure, ultrasound can provide valuable clues for diagnosing placenta accreta in the early stages of pregnancy.⁵ Grayscale and color Doppler ultrasound can be combined to assess the uterine cavity and blood flow. In cases where there is suspicion of gestational trophoblastic disease, beta-human chorionic gonadotropin (β -hCG) levels can also be used as a diagnostic marker.⁶ Misdiagnosis of placenta accreta often occurs during the early stages of pregnancy, especially when the gestational age is low.⁵ Variability in diagnostic

outcomes can be attributed to several factors that may contribute to misdiagnosis, and it is essential to address these issues.

In this case series, we present three cases of placenta accreta in early pregnancy. One case was initially misdiagnosed as a missed abortion, another case was misdiagnosed as gestational trophoblastic neoplasia (GTN), and the third case was correctly diagnosed as placenta accreta based on our previous experience.

CASE SERIES

Case 1

A 36-year-old woman, who has given birth thrice and experienced two miscarriages (para 3 abortus 2), was referred to a hospital due to vaginal bleeding. Uncertain about her pregnancy status, she expressed concerns about severe abdominal pain that had begun two weeks prior. The patient had a history of two previous caesarean deliveries and two previous curettages, the most recent one being in March 2020 for a blighted ovum. Following the first curettage, she was discharged but noticed spotting a week later. Despite receiving treatment, the spotting persisted, prompting her referral to a second hospital. During an ultrasound examination, an intrauterine mass was detected, leading to a second curettage in April 2020. However, a week after this procedure, the patient developed fever and worsening spotting, which led to her presentation at the emergency room (ER). Internal medicine provided her with antibiotics and analgesics, but after six days of therapy, her condition did not improve. Consequently, she was referred to another healthcare facility due to suspected pelvic infection and possible intestinal adhesions.

Upon arrival at the new ER, the patient exhibited grade I hypovolemic shock and complained of abdominal pain. After stabilizing her condition, an ultrasound examination was performed, revealing an enlarged uterus with irregular and discontinuous endometrial lining. These findings raised concerns about uterine perforation, particularly at the anterior corpus uteri near the isthmus, where a measurement of 11.24 mm indicated a potential breach. The presence of fluid, suspected to be blood, was also observed within the lesion, extending into the Douglas cavity. Based on these findings, the medical team planned an exploratory laparotomy once the patient's vital signs had stabilized. During the exploratory laparotomy, the suspected uterine perforation was confirmed, prompting the decision to proceed with a hysterectomy. Subsequent histopathology examination of the hysterectomy sample revealed placenta accreta, confirming the diagnosis (Figure 1).

Following the surgery, the patient's postoperative condition remained stable. She received a course of antibiotics and was discharged on the fourth day after the procedure.

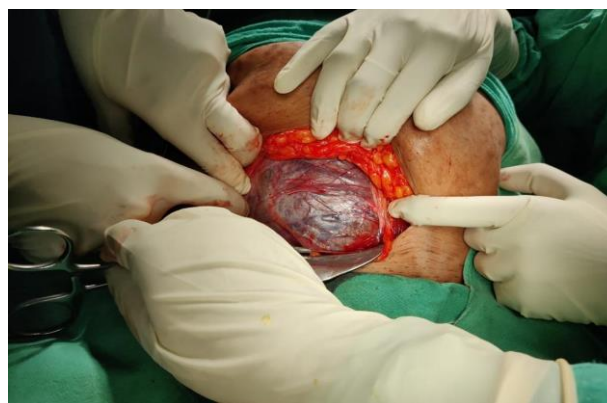


Figure 1: Histopathology examination of the hysterectomy sample revealed placenta accreta, confirming the diagnosis.

Case 2

A 35-year-old woman, who has given birth three times via caesarean section and has not experienced any previous miscarriages (para 3), was admitted to a primary healthcare facility due to sudden vaginal bleeding. The obstetrician/gynecologist suspected a spontaneous abortion but opted against performing curettage based on ultrasonography findings of a myometrial mass. Instead, the patient received medication and was advised to continue therapy as an outpatient for further follow-up. During the subsequent one-month follow-up, the patient reported a sensation of her abdomen becoming larger, although no vaginal bleeding or abdominal pain was present. Seeking further evaluation, she consulted with an obstetrician/gynecologist who referred her to a gynecologic oncologist at a different hospital. A series of examinations, including physical assessments and imaging, were conducted. Ultrasonography revealed the presence of a mass in the uterine corpus, prompting the doctors to measure β -human chorionic gonadotropin (β -hCG) levels to support the diagnosis. The initial β -hCG examination showed significantly elevated levels, leading to a diagnosis of gestational trophoblastic neoplasia (GTN). The recommended treatment plan involved 4 cycles of chemotherapy with regular β -hCG monitoring throughout. The patient agreed to undergo chemotherapy using methotrexate, but despite a reduction in β -hCG levels during follow-up examinations, the tumor did not resolve. Subsequently, the patient was referred to our hospital for further management.

Upon arrival at our hospital, a re-examination was conducted to confirm the diagnosis. Ultrasonography revealed enlargement of the lower uterine corpus, displaying a nonhomogeneous opacity. Doppler imaging indicated a color score of 4, providing sufficient information to diagnose the patient with placenta accreta and guide appropriate treatment. Advanced imaging modalities such as computed tomography (CT scan) or magnetic resonance imaging (MRI) were deemed unnecessary.

DEPARTMENT OF PATHOLOGY BUNDELKHAND MEDICAL COLLEGE & ASSOCIATED HOSPITAL Shivaji Ward, Tili road, Sagar (M.P.)		
HISTOPATHOLOGY SECTION		
Name : Jayanti Lodhi	Age : 28 years, Female	
IPD/UHID No. : 240145/294983	Date of sample collection : 19.12.2022	
HPE No.: 5678-5689/2022	Date of report dispatch : 31.12.2022	
Department : Obstetrics & Gynecology		
Specimen labeled as :uterus with placenta		
HISTOPATHOLOGY REPORT		
Gross Findings:-		
Specimen consists of gravid uterus, with attached placenta. Uterus measuring 17x11x6.5 cm. Endometrium 0.5 cm, Myometrium measuring 4 cm. Myometrium 1.5 cm at upper segment, 2cm in middle segment. Placenta is attached to the upper middle and lower segment of uterus. Placenta measuring 14x13x6 cm. On cut grayish brown. Umbilical cord is attached eccentrically and measures 12cm in length and 1 cm in maximum diameter with three vessels. Feta surface is smooth shiny, maternal surface is fragmented grayish brown with retroplacental hemorrhage. Number of cotyledons are approximately 12.		
Microscopic Examination:- H & E stained sections studied shows		
Endometrium- Myometrium- Chorionic villi are seen invading in one third of myometrium. Placenta is attached to lower segment of Myometrium. Features are suggestive of Placenta accreta with placenta previa. Placental tissue-		
Advice:- Correlate clinically and radiologically.		
Dr. Amar Gangwani Prof. & HOD Department of Pathology	Dr. Santosh K. Gond Associate .Prof. Department of Pathology	Dr. Shikha Agrawal Asst. Prof. Department of Pathology

Figure 2: The results from the histopathology confirmed the presence of placenta accreta.

Based on our examination, we recommended operative therapy as the next course of action for the patient's management. With her consent, a total abdominal hysterectomy was performed, and the excised mass was sent to the pathology-anatomy department for histopathology examination. The results from the histopathology confirmed the presence of placenta accreta (Figure 2). The patient experienced an uncomplicated postoperative recovery and was discharged on the eight days after the procedure.

Case 3

A 33-year-old woman, who has given birth thrice via cesarean section (para 3), was referred to our facility due to vaginal bleeding. Uncertain of her pregnancy status, she reported experiencing irregular vaginal bleeding for approximately four months since December 2021. Following an ultrasound examination and a positive β -human chorionic gonadotropin (β -hCG) result, the obstetrician/gynecologist initially diagnosed the condition as gestational trophoblastic neoplasia (GTN).

Upon referral to our institution, a physical examination revealed a normal cervix with mild or inactive bleeding, as well as an enlarged uterus. Further ultrasonography revealed enlargement of the lower portion of the uterine corpus with an irregular opacity, while Doppler

examination showed neovascularization with a color score of 4.

Advanced imaging, such as magnetic resonance imaging (MRI), supported these findings, displaying a nonhomogeneous mass and enlargement of the lower uterine corpus with a suspected invasive bridging vessel towards the bladder. Based on these results, our initial impression still leaned towards malignant trophoblastic neoplasia. To differentiate between GTN (choriocarcinoma or placental trophoblastic tumor) and placenta accreta, we assessed the patient's β -hCG levels, which were measured at 2504. Drawing from our previous experience, where we encountered patients with similar presentations who were ultimately diagnosed with placenta accreta, we considered it the most probable diagnosis for this patient.

Treatment options included chemotherapy and surgical intervention, but we recommended a hysterectomy due to the inadequate response to chemotherapy and the patient's and her husband's preference to forgo future fertility. Consequently, the patient underwent a total abdominal hysterectomy. The excised specimen was sent to the pathology-anatomy department for a histopathology examination, which confirmed the presence of placenta accreta. The patient experienced an uncomplicated postoperative recovery and was discharged on the eight-day following the procedure.

Table 1: Summary of three cases.

Case	Clinical presentation	Previous cesarean deliveries	Ultrasonography findings	Elevated levels of β -hCG
1	Vaginal bleeding	2 prior C-sections	Enlarged uterus with an irregular, fragmented endometrial line measuring 11.24 mm. Presence of fluid, possibly blood, in the Douglas cavity	No β -hCG examination
2	Vaginal bleeding, abdominal distention	3 prior C-sections	Enlargement of the lower part of the uterus with heterogeneous opacity and a Doppler color score of 4	Elevated levels of β -hCG
3	Vaginal bleeding	2 prior C-sections	Enlargement of the lower part of the uterus with heterogeneous opacity and a Doppler color score of 4	Elevated levels of β -hCG

DISCUSSION

Placenta accreta is a condition characterized by the invasive attachment of the placenta to the uterine wall, posing a life-threatening risk of hemorrhage. It occurs when there is abnormal and firm adherence between the placenta and the uterine wall. In placenta accreta, the placenta infiltrates into the superficial layer of the uterine wall known as the basalis layer. Due to the partial or total absence of the decidua basalis and inadequate development of the fibrinoid or Nitabuch layer, the placental villi become attached to the myometrium. Consequently, the placenta cannot separate completely after delivery, leading to potential severe bleeding. Accurate diagnosis is crucial to determine the appropriate treatment and requires a precise understanding of the pathological structure involved. The prevalence of placenta accreta is estimated to be 1 in 2500 pregnancies, and its incidence has increased parallel to the rising rates of cesarean deliveries.² Placenta accreta remains a major cause of maternal morbidity and mortality, often necessitating postpartum hysterectomy.⁷

Early detection of invasive placentation is vital to decrease maternal complications. Ultrasonography is the primary diagnostic tool during the antepartum period and is particularly effective in evaluating obstetrical hemorrhage, with a sensitivity of 91% and specificity of 97%.⁸ In the first trimester, specific sonographic features such as a low-lying gestational sac and widespread dilation of intra-placental vessels (lacunae) in the lower uterine segment at the site of a previous caesarean section scar have been described.⁵ The Royal College of Obstetricians and Gynecologists (RCOG) guidelines outline various signs of placenta accreta on grayscale and color Doppler ultrasound, including the loss of the "clear zone," abnormal placental lacunae, interruption of the bladder wall, thinning of the myometrium, placental bulge, and focal exophytic mass.⁹ Uterovesical and sub placental hypervascularity, bridging vessels, and placental lacunae feeder vessels can be observed on color Doppler imaging. Combined grayscale and color Doppler ultrasound provide valuable information about the uterine cavity and its blood flow. MRI can be used as a complementary or adjunctive tool to ultrasound, especially in complex cases, to assess the depth and lateral extension of myometrial invasion.¹⁰

Gestational trophoblastic disease (GTN) encompasses a group of tumors characterized by abnormal trophoblastic proliferation and β -human chorionic gonadotropin (β -hCG) production. GTN includes invasive mole, choriocarcinoma, placental site trophoblastic tumor, and epithelioid trophoblastic tumor. Diagnosis and treatment of GTN rely on serum β -hCG levels combined with clinical findings, as histological examination of a specimen is not always required. In some cases, placenta accreta may mimic GTN due to similar sonographic and laboratory findings, such as high β -hCG levels.¹¹ However, GTN typically infiltrates the myometrium non-specifically, whereas placenta accreta shows a specific location of invasion, particularly in the anterior isthmus or niche area of the uterine lining.

This case series emphasizes the critical importance of considering placenta accreta as a potential diagnosis in patients who present with vaginal hemorrhage and have a history of previous caesarean delivery. To avoid misdiagnosis, it is essential to conduct a thorough histopathological examination.

In the first case, the niche and cervix were not evaluated, which is significant because it is the site where the trophoblast is implanted. Similarly, in the second case, the anterior wall of the uterus was not assessed. Although the patient was initially diagnosed with GTN, the invasion was limited to the anterior uterine wall. These findings, upon retrospective analysis, suggest that these cases were more likely to be placenta accreta rather than GTN. The histopathology results of the second case supported this conclusion. In the last case, having learned from the misdiagnoses of the first two cases, the history, physical examination, ultrasounds, and MRI findings indicated anterior uterine wall trophoblast invasion, leading to a diagnosis of placenta accreta, which was confirmed by histopathology. The missed diagnoses in the first and second cases resulted in unnecessary treatment and complications such as uterine rupture due to curettages and chemotherapy for the second patient. A crucial clue for accurate diagnosis is the presence of a niche and a low-lying placenta, which can be identified through histological analysis of imaging obtained from ultrasounds or MRI. It is crucial to carefully examine the anterior uterine wall, including the cervix, and evaluate the

trophoblast structure and invasiveness during ultrasound examinations. A meticulous evaluation is necessary to improve diagnostic accuracy, as caesarean scar pregnancies with extensive anterior uterine wall trophoblast invasion cannot be resected and require hysterectomy as the appropriate treatment.

CONCLUSION

In conclusion, placenta accreta is a life-threatening condition characterized by the invasive attachment of the placenta to the uterine wall. Early detection is crucial to guide clinical management and prevent complications. Ultrasound, combined with color Doppler imaging, is the primary diagnostic tool during pregnancy and can provide valuable clues for diagnosing placenta accreta. However, misdiagnosis can occur, especially in the early stages of pregnancy, leading to unnecessary treatments and complications. This case series highlights the importance of considering placenta accreta as a potential diagnosis in patients presenting with vaginal hemorrhage and a history of previous caesarean delivery. Thorough evaluation, including the examination of the niche and cervix, is essential for accurate diagnosis. Histopathological examination plays a critical role in confirming the diagnosis and avoiding misdiagnosis.

Missed diagnoses can result in adverse outcomes and complications for patients. Therefore, it is crucial to carefully assess the anterior uterine wall, including the cervix, and evaluate the trophoblast structure and invasiveness during ultrasound examinations. The presence of a niche and a low-lying placenta, detected through histological analysis of imaging, can provide important diagnostic clues. Improving diagnostic accuracy in cases of placenta accreta is vital to ensure appropriate management and reduce maternal morbidity and mortality. Clinicians should remain vigilant and consider placenta accreta as a potential diagnosis, especially in high-risk patients, to optimize patient care and outcomes.

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