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Research article

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Placenta accreta spectrum: Is placental invasion real?

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The study was approved by the Institutional Review Board of Harran University's School of Medicine (HRU/21.18.24).
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Abstract

Background/Aim: The description of placenta accreta spectrum disorder (PAS) has undergone significant changes. However, its association with obstetric morbidity and mortality has become even more important. Therefore, we aimed to assess the histopathologic evaluation of PAS patients who underwent a hysterectomy.

Methods: We conducted a retrospective study of all pathology reports from patients with peripartum hysterectomies at Sanliurfa Training and Research Hospital diagnosed with PAS. The study included 45 patients with a cesarean hysterectomy due to a preoperative placenta accreta spectrum disorder diagnosis. Hysterectomy specimens were evaluated based on placental invasion and myometrial defect at the site of the placenta.

Results: Out of 45 patients diagnosed with placenta accreta spectrum disorder who underwent a hysterectomy, only 17 (37.8%) had a histological diagnosis supporting the placental invasion. The histological diagnosis was consistent in 20 (44.4%) patients, indicating that the placenta protruded from a uterine wall defect without placental invasion. In eighth (17.8%) patients, the histopathological diagnosis was consistent with a histologically normal placenta.

Conclusion: The primary pathology of the disorder is variable, and the main issue is the association of the placenta with defective myometrium. Although a more alarming definition, such as invasion, should be avoided, PAS should not be underestimated due to its high mortality.

Keywords: adherent placenta, cesarean hysterectomy, placenta accreta

Introduction

Under a new definition, a class of placental adhesion anomalies is referred to as placenta accreta spectrum (PAS); the common feature of this class is the presence of a scar in the uterus, with the placenta attaching to this scar. However, the prognosis of these conditions varies considerably, making the most crucial feature of this class the differences in prognosis [1].

Over the past decade, there has been a significant increase in the diagnosis of PAS, with a tremendous increase in publications in this field [2]. Although the increase in cesarean rates has been cited as the primary cause, accepting this as the only factor is inaccurate. More than 90% of PAS cases are associated with placenta previa, with the combination of placenta previa on a previous cesarean section scar, and PAS is the leading factor of maternal morbidity and mortality due to massive peripartum hemorrhage [3]. However, Carusi et al. [4] reported their experience with PAS cases not associated with placenta previa in 2020 and found that these cases were less severe.

Ultrasonography and magnetic resonance imaging (MRI) are primarily used for the prenatal diagnosis of PAS. Findings described with both ultrasonography and MRI include placental "bulge", loss of the retroplacental clear or hypoechoic zone, imperceptible myometrium, and bladder wall interruption or irregularity. Vascular findings include sub-placental or ureterovesical hypervascularity and intraplacental abnormal vascularity or cavities [5].

In more than half of the literature on PAS, authors do not provide detailed information on the macroscopic clinical description at birth or histopathologic confirmation of the placenta accreta, even though hysterectomy is the primary treatment for PAS cases diagnosed prenatally or during labor [6]. In addition, very few studies differentiate these cases histopathologically from other adherent placentas.

This study evaluated cases diagnosed as PAS prenatally and who underwent a hysterectomy, including the histopathological results and the presence of placental invasion in the hysterectomy specimens. The primary aim was to determine whether the primary pathology in PAS cases is a placental invasion or another factor.

Materials and methods

We conducted a retrospective cohort study using Şanlıurfa Training and Research Hospital (Şanlıurfa, Turkey) and obtained Institutional Review Board approval from Harran University's School of Medicine (HRU/21.18.24). From May 2017 to September 2021, we included all patients who had undergone peripartum hysterectomy and were diagnosed with PAS. Preoperative diagnoses were made for all patients using sonography (Voluson E8, GE Healthcare, Milwaukee, WI) or MRI. Cases managed with uterine-sparing approaches that did not undergo hysterectomy were excluded from the study. Only cases with prior cesarean sections were included, and patients without any prior cesarean sections were excluded during patient selection. Patients provided verbal and written informed consent for using their data in studies in this area.

The antepartum diagnosis of PAS was made based on sonographic findings and, when necessary, MRI. Ultrasound examinations were performed centrally prenatally, and a single maternal-fetal medicine physician (Author 2: Ekmekci E.) confirmed all PAS findings. All patients were followed, and deliveries were planned electively at 35 weeks of gestation if there was no need for emergency delivery before that time. The same surgical team performed all elective deliveries, while several physicians at the same hospital performed emergent operations. Decisions regarding conservative management or hysterectomy were made based on multiple factors, such as disease severity, intraoperative surgical conditions, and patients' preferences. However, only subjects who underwent hysterectomy were included in the study, and these results did not affect our findings.

Collected outcome data included maternal age, gravidity, number of cesarean deliveries, gestational age at delivery, red blood cell unit transfusion, the occurrence of planned or incidental cystotomy, operation time, and the need for hospital readmission. The presence of placenta previa was also recorded. The final pathological diagnosis was determined from pathology reports, and a pathologist reevaluated the histopathologic diagnosis of all cases microscopically (Author 3/Coskun F.). Placental tissue invasion and myometrial tissue condition on the scar line were reevaluated. Trophoblastic tissue between myometrial fibers was defined as invasion and the loss of myometrial tissue, and the unrestricted presence of trophoblasts within the placental integrity was defined as placental protrusion.

Statistical analysis

The Statistical Package for Social Sciences (IBM SPSS Statistics for Windows, Version 22.0, IBM Corp., Armonk, NY, USA) was used for statistical analyses. The normality of distribution was assessed using the Kolmogorov-Smirnov test. Mean or median values were used to describe normally distributed data, while categorical data were presented as percentages. The chi-square and Fisher Exact tests were used for categorical data, and a t-test was used to determine two independent means. The significance level for all tests was set at $P<0.05$.

Results

Over 4 years, a retrospective analysis of medical records identified 45 cases of peripartum hysterectomy due to PAS. The average age of mothers was 35 years (range: 24–42), and all patients had a history of previous cesarean sections. No hysterectomy cases due to PAS were observed in patients without a prior cesarean section. On average, patients had undergone four previous cesarean sections (range: 3–7). Of the 45 pregnancies, 44 were singletons, and one was a twin pregnancy. Placenta previa was absent in only three cases, while 42 cases had total placenta previa. Only two cases had posteriorly located placentas, while 43 had placentas on the anterior uterine wall. Patient and pregnancy characteristics are presented in Table 1.

Table 1: Demographic characteristics of patients.

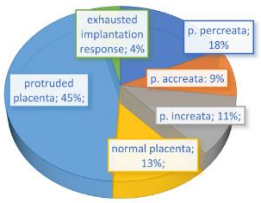
	n=45
Maternal age (years)	34.78 (3.63)
Previous cesarean section	3.96 (0.85)
Multiple gestations	1/45
Placenta previa	42/45
Placental localization	Anterior: 43
	Posterior: 2
Gestational age at delivery	35 (4.4) weeks
Mean operation time	137 (22) min
Red blood cell transfusion	4.6 (1.66) units

Thirty-four cases underwent elective surgery at 35–37 gestational weeks, with a median gestational age at the time of operation of 35 weeks (range: 21–37 weeks). Eleven cases underwent surgery before the 34th gestational week due to emergencies such as obstetrical hemorrhage or uterine rupture. Three cases underwent an emergency hysterectomy due to uterine rupture from a previous uterine scar, and eight (17.8%) underwent surgery for obstetrical hemorrhage.

The mean surgical time was 137 (22) min (range: 70–180). The median red blood cell transfusion was 4 units (range: 2–10), with seven cases requiring a transfusion of 5 or more units. Intraoperative cystotomy and bladder wall repair were required in seven cases. One maternal death occurred 36 h postoperatively due to disseminated intravascular coagulation induced by massive transfusion. After the operation, each patient was monitored in the hospital for 3 to 7 days before discharge, with no patient requiring hospital readmission after discharge.

Histopathology results are presented in Figure 1. Regarding invasion, materials with pathological diagnoses of placenta accreta, increta, and percreta were reevaluated. Of the 45 patients diagnosed with PAS who underwent a hysterectomy, only 17 (37.8%) had a histological diagnosis supporting placental invasion. Histological diagnosis was compatible with protrusion without invasion in 20 patients (44.4%), and eight patients (17.8%) had a histopathological diagnosis consistent with normal placentas.

Figure 1: Pathology reports of placenta.



In the histopathological examination, the mean surgical time of patients with normal placentas was 118.75 (29.97) min. In contrast, the mean surgical time was 139.51 (21.95) min in other patients, and the difference in operation time was significantly shorter in the group with normal placentas compared to the other groups (P=0.02). However, there was no significant difference in the amount of transfusion between the groups (P=0.05).

Upon examination of histopathology specimens, some specimens previously interpreted as placental invasion intraoperatively were evaluated as placental dehiscence or usual rather than invasion. The histopathological diagnosis of 12 (26.7%) of the 17 (37.8%) cases previously diagnosed as placental invasion was interpreted as an abnormal appearance consisting of a thinned or absent myometrium and a placenta located on abnormal decidua rather than placental invasion. These cases revealed that the previously considered placental invasion areas resulted from abnormal choriodecidual relations formed by the placement of the placenta on a damaged, insufficiently healed myometrium and decidua.

In the remaining five patients, a clear interpretation for the histopathological diagnosis was not made despite inadequate findings to describe placental invasion, as the presence of chorionic villi extending between myometrial fibers could not be distinguished from chorionic villi invasion or an inadequately healed myometrial defect (Figures 2 and 3).

Figure 2: Protrusion of placenta from the myometrial defect seen in cesarean section, Arrow: Protrusion of placenta out of the myometrial defect.

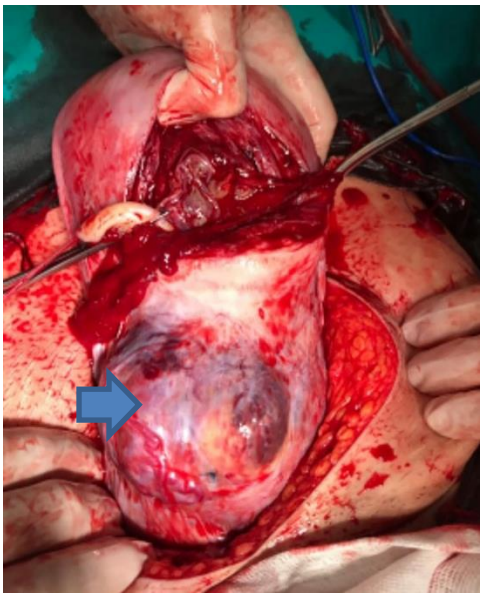
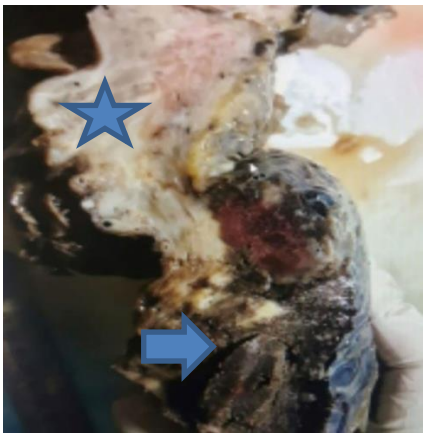


Figure 3: The macroscopic specimen of the hysterectomy material of placenta accreta spectrum, Asterisk: Macroscopic specimen of myometrial part, Arrow: Protrusion of placenta from the myometrial defect.



Discussion

Although risk factors for PAS are well-known, the underlying mechanisms that cause abnormal placentation remain unclear. Human placentation is a unique and highly invasive developmental process that occurs exclusively in the decidua and superficial myometrium of the uterus [7]. Several theories have been proposed to explain the aberrant placentation in placenta accreta. Initially, emphasis was placed on abnormal trophoblast function, leading to excessive invasion of the uterine myometrium [8]. Later, the other prevailing hypothesis suggested that abnormally deep trophoblastic infiltration results from the failure of decidua basalis formation in the uterine scar area [8,9]. Finally, localized hypoxia and abnormally vascularized scar tissue have been suggested to cause

decidualization disorder and increased trophoblastic invasion [10].

Tseng et al. [11] suggested that increased VEGF and EGFR expression from trophoblasts due to excessive angiogenesis are involved in the pathogenesis of PAS. Conversely, Earl et al. [12] argued that extravillous trophoblasts in PAS have the same immunophenotype as those in normal placentas and that overactive trophoblastic invasion is unlikely to be the cause of PAS. Instead, they emphasized that the absence of decidua plays a more significant role in the pathogenesis. Tantbirojn et al. [8] proposed that cracking and separation in the existing myometrial scar area in PAS are more likely to lead to trophoblastic invasion of the great vessels in the myometrial outer layer and serosa than trophoblastic growth defects or other immunologic factors. They presented the view in 2008 that anatomical factors, rather than immunohistochemical factors, are the main features in the pathophysiology of PAS.

Our results indicate that placental invasion was not detected in 40 (88.9%) of the 45 patients who underwent hysterectomy with a PAS diagnosis. Thus, the primary pathology was anatomical defects in the myometrium.

Although this study is retrospective, the antepartum diagnosis of the placenta accreta spectrum was confirmed by ultrasound in all included cases. All cases required a hysterectomy, indicating their severe and challenging nature. Therefore, subjective variations in diagnosing PAS were eliminated. However, only five (11.1%) cases showed evidence of placental invasion when pathological diagnoses were examined. In 20 (44.45%) cases, the pathological diagnosis was consistent with a normal placenta protruding from a uterine wall defect without invasion. In eight (17.8%) cases, both placenta and myometrial areas were histopathologically normal.

Maternal morbidity associated with PAS, such as massive transfusion, urinary tract injury, intensive care unit admission, hysterectomy, and maternal death, is linked to various factors. However, the results of our study do not align with the widely accepted notion that the severity of placental invasion is the primary factor associated with morbidity. The fact that 43 out of 45 cases had total placenta previa suggests that its presence is a critical factor in morbidity. Additionally, the size of the myometrial defect and the severity of the anatomical defect are also important factors related to morbidity.

In our histopathologically normal cases, the operation time was shorter than the remaining group, but there was no significant difference between the groups regarding transfusion units. The lack of significant difference in transfusion units between the groups may be due to the low preoperative hemoglobin counts of the patients, which could increase the need for blood. Additionally, the decision to perform a hysterectomy based on macroscopic appearance and previous surgeries may have increased the need for transfusion in patients with normal results. The use of hemostatic methods other than hysterectomy becomes controversial, as there is no reduction in blood use in normal cases. In our case series, the median history of previous cesarean sections was 4. A higher number of previous cesarean sections and more severe associated adhesions seem to be essential factors in morbidity.

Einerson et al. [4] identified the most critical factors associated with morbidity in cases of PAS, including the degree of uterine scar dehiscence, the degree and location of pelvic adhesions, and the extent of abnormal vasculature in and around hysterectomy planes.

Abnormal vasculature in and around the previous uterine scar area, particularly in the parametrial region, is a poor prognostic factor in PAS surgery. During the antepartum period, this abnormal vascularization appears as “lacunae” with irregular borders and low resistance flow in sonography. The presence of more lacunae is associated with a higher degree of difficulty in the operation. These cavities are often interpreted as evidence of placental invasion, but extravillous trophoblasts invading the uterine spiral arteries during normal placentation behave similarly in the case of an abnormal or damaged decidua. They penetrate the myometrium and access deep myometrial vessels, adhesions, and deeper pelvic vessels, causing dramatic uterine scar dehiscence. However, this trophoblastic behavior should not be considered an invasion of the placenta, such as in choriocarcinoma. Although cavities are associated with the severity of PAS cases, they should not be taken as an indicator of placental invasion. Placental lacunae are more common in placenta previa cases without a myometrial scar and are linked to postpartum bleeding, possibly due to insufficient decidual development in the lower uterine segment and the invasion of extravillous trophoblasts into deep myometrial arteries.

The first important factor related to the severity of the surgery is a defective decidual layer and pelvic hypervascularity resulting from the extension of extravillous trophoblasts into deep myometrial arteries. The second factor is the progressive scar dehiscence causing placental extension into the niche of the uterine scar in the first trimester and extending to the serosa as it progresses in later pregnancy. Cesarean scar pregnancy is considered a precursor of the placenta accreta spectrum, and the two conditions are histopathologically indistinguishable [14]. According to Timor-Tritsch et al. [14], the leading pathology and process of PAS is an abnormal attachment, abnormal recruitment of uterine vasculature, and slow progressive uterine scar dehiscence.

Limitations

The retrospective design of our study is a significant limitation. Furthermore, more data on conservatively managed PAS cases are necessary to improve our understanding of the condition. However, the advantage of our study is that all cases required a hysterectomy, indicating that we included cases with severe features. Additionally, the fact that the same physician diagnosed all cases during the antenatal period and the same pathologist evaluated all pathology materials prevented variations in diagnosis, which is advantageous for diagnostic accuracy.

Conclusion

While our findings suggest that anatomical defects and inadequate healing of the myometrium are the primary pathologies rather than placental invasion, it does not diminish the severity of PAS. It is crucial to always consider these cases’ as at high risk of morbidity and mortality and manage them individually.

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