Asia-Pacific Journal of Science and Technology: Volume: 29. Issue: 04. Article ID.: APST-29-04-06. Research Article

APST

Asia-Pacific Journal of Science and Technology

https://www.tci-thaijo.org/index.php/APST/index

Published by the Research and Graduate Studies,
Khon Kaen University, Thailand

Uterine pathology of women with antenatally diagnosed placenta accreta spectrum (PAS) disorders

Thanyathorn Eakpinitpitaya[1], Chumnan Kietpeerakool[1], Piyamas Saksiriwuttho[1], Naratassapol Likitdee[1], Pilaiwan Kleebkaow[1], Nittaya Panphet[2] and Yuwadee Itarat[1,*]

[1]Department of Obstetrics and Gynecology, Faculty of Medicine, Khon Kaen University, Khon Kaen, Thailand
[2]Department of Nursing, Faculty of Medicine, Khon Kaen University, Khon Kaen, Thailand
[*]Corresponding author: maymae1626@hotmail.com

Received 21 April 2023
Revised 18 July 2023
Accepted 17 August 2023

Abstract

To determine the rate of women with antenatally diagnosed placenta accreta spectrum (PAS) who are pathologically unconfirmed and associated factors. This study was conducted in the Department of Obstetrics and Gynecology, Faculty of Medicine, Khon Kaen University, Thailand. Medical records of women with an antenatal diagnosis of PAS who underwent hysterectomy between January 2015 and July 2022 were reviewed. Records of 50 women were reviewed. All women had placenta previa, and most (94.0%) had a prior history of cesarean delivery. Four women were found to have no PAS on pathological examination, accounting for a false-positive rate of 8.0% (95% confidence interval 2.20%-19.2%). Coexisting adenomyosis was more likely to be noted among women without PAS on pathologic examination than among those with pathologically confirmed PAS (50.0% versus 17.8%, respectively). Among women with clinically suspected extensive myometrial involvement, grade 3 PAS was pathologically diagnosed in only 57.1% with coexisting adenomyosis, that was lower than that in women without adenomyosis (84.6%). The false-positive rate of prenatal PAS diagnosis in this study was 8.0%. Coexisting adenomyosis appeared to affect the accuracy of the antenatal diagnosis of PAS.

Keywords: Placenta accreta spectrum, Hysterectomy, False positive, Adenomyosis

1. Introduction

Placenta accreta spectrum (PAS) disorders, formerly known as morbidly adherent placenta, are conditions in which the placenta is unable to spontaneously separate from the uterine wall during delivery [1]. PAS is believed to develop due to a defect in the endometrial-myometrial interface, leading to a failure of normal decidualization of the endometrium. This allows for abnormally deep anchoring of placental villi within the underlying myometrium [1,2].

PAS disorders are associated with massive obstetric hemorrhage, peripartum hysterectomy, intensive care unit (ICU) admission, surgical site infection, reoperation, and prolonged hospitalization [3,4]. PAS contributes to maternal mortality at a rate as high as 7% [3,4]. The major risk factor for PAS is prior cesarean delivery [1]. In a secondary analysis of the World Health Organization Multicountry Survey on Maternal and Newborn Health, pregnant women with prior cesarean delivery were 2.6 times (95% confidence interval (CI) 1.98 to 3.40) as likely to develop PAS as those without prior cesarean delivery [5]. Thus, the global increase in cesarean delivery rates has been accompanied by a consecutive increase in PAS.

Scheduled caesarean hysterectomy without attempting placental removal is the standard management for PAS disorders [4]. The placenta was left untouched inside the uterus to avoid catastrophic hemorrhage. Conservative management, defined as procedures aimed at avoiding cesarean hysterectomy, should be reserved for a well-selected group of women with a strong desire for fertility [4]. Cesarean hysterectomy for PAS is a technically challenging procedure. Bulky lower uterine segments, pelvic neovascularization, and possible extrauterine involvement may complicate the operation, resulting in massive obstetric hemorrhage or adjacent organ injury in some cases [4].

However, in antenatally suspected PAS, PAS may be absent histologically in some cases [6,7]. Therefore, information regarding the uterine pathology of antenatally suspected PAS is of utmost importance for counselling regarding the management options. This study reviewed the uterine pathology of women with PAS with the aim of determining the rate of women antenatally suspected PAS but pathologically undiagnosed and associated factors.

2. Materials and methods

This cross-sectional study was conducted in the Department of Obstetrics and Gynecology, Faculty of Medicine, Khon Kaen University, Thailand. The medical records of pregnant women antenatally diagnosed with PAS who underwent cesarean hysterectomy between January 2015 and July 2022 were reviewed. Abstract data included baseline characteristics, gestational age (GA) at diagnosis and delivery, methods of PAS diagnosis, antenatal assessment results, detailed pathology of uterine specimens, coexisting uterine pathology, and perinatal outcomes.

At our institute, all pregnant women with placenta previa and/or previous cesarean delivery, the common clinical risk factors for PAS, will undergo prenatal ultrasound performed by Maternal-Fetal Medicine Subspecialists. Magnetic resonance imaging (MRI) may be performed at the discretion of attending physicians. Antenatally suspected PAS disorder encompasses three categories: (1) placenta creta (the placenta attaches to but does not invade the myometrium); (2) placenta increta (the placenta invades the myometrium, but not beyond); and (3) placenta percreta (the placenta invades through the uterine serosa and potentially beyond) [8].

At our institute, surgical specimens were submitted as hysterectomy specimens with the placenta in situ. Tissue sections for pathological assessment were made as recommended in the Manual of Surgical Pathology [9]. Briefly, at least three full-thickness sections of the placental disc and four additional sections of the disrupted maternal surface were sampled [9]. Maternal surfaces with an abrupt transition in the myometrial thickness were also sampled. Gross hysterectomy specimens and pathological slides were examined by a perinatal pathologist (P.K). All pathological slides were reviewed to grade the severity of PAS disorders according to the current classification system proposed by the International Federation of Gynecology and Obstetrics (FIGO) [2,10]. Table 1 summarizes the FIGO histological subcategories of PAS disorders [2,10].

Table 1 Histologic criteria of PAS grading according to the FIGO classification system.

PAS grade	Description
Grade 1: Noninvasive	Smooth placental-myometrial interface and uniform myometrial thickness without thinning
Grade 2: Superficial invasion	An irregular placental-myometrial interface without involvement of the outer myometrium
Grade 3: Deep invasion	3A: An irregular placenta-myometrial interface with involvement of the outer myometrium. The serosa is intact. 3D: Deeply invasive placenta with disruption of the uterine serosa 3E: Invasion into adjacent organs or extra-uterine fibroadipose tissue (confirmed by microscopy)

PAS, placenta accreta spectrum; FIGO, International Federation of Gynecology and Obstetrics.

Coexisting uterine adenomyosis was categorized according to the degree of myometrial involvement; grades 1, 2, and 3 corresponded to involvement of the inner third (superficial adenomyosis), two-thirds (deep adenomyosis), and entire myometrium [11].

Descriptive statistics were used to summarize the baseline characteristics of the study participants. Characteristics of women whose surgical specimens did not pathologically demonstrate PAS were narratively presented. A 95% confidence interval (CI) for the rate of women who had no PAS on pathological examination was calculated to represent the precision of the main study results.

3. Results

During the study period, the records of 50 women with antenatally diagnosed PAS disorders were reviewed. Table 2 presents the baseline characteristics of the women in the study cohort. All women had placenta previa. Almost all women (94.0%) had a history of cesarean delivery. Twin pregnancies were noted in one woman. Eleven women (22.0%) underwent cesarean delivery more than once and fifteen women (30.0%) underwent emergency cesarean section hysterectomy.

Table 2 Characteristics of the cases.

Characteristics	All (n=50)
Mean (SD) maternal age (years)	34.1 (5.1)
Mean (SD) GA at first diagnosis (weeks)	28.4 (5.5)
Median (IQR) GA at delivery (weeks)	34 (33 - 36)
Prior history of cesarean delivery	
None	3 (6.0%)
One time	36 (72.0%)
≥ two times	11 (22.0%)
Type of diagnostic procedure	
Ultrasound alone	5 (10.0%)
Both ultrasound and MRI	45 (90.0%)
Setting of operation	
Emergency cesarean hysterectomy	15 (30%)
Elective cesarean hysterectomy	35 (70%)

Data are presented as number (percentage), unless stated otherwise. SD, standard deviation; IQR, interquartile range; GA, gestational age; MRI, Magnetic resonance imaging.

The details of the preoperative findings and the reviewed histopathological results are shown in Table 3. The number of pathological slides examined ranged from 10 to 37, with a median of 18 slides. Of the 50 hysterectomy specimens assessed, we were unable to determine the degree of placental invasion in one specimen because detailed pathologic examination was limited to an area of potential surgical disruption. Of the 49 surgical specimens for which pathological examination was clinically feasible, 35 and 2 specimens were classified as having PAS grade 3A and 3D, respectively.

Four women were found to have no PAS disorders on pathologic examination, accounting for the rate of 8.0% (95% CI 2.20% to 19.2%) of women with antenatally diagnosed PAS but were pathologically unconfirmed (Table 3).

Coexisting adenomyosis in the hysterectomy specimens was noted in 10 (20.0%) women, including grade 1 (four women), grade 2 (one woman), and grade 3 (five women). Coexisting adenomyosis was more likely to be noted among women who found no PAS on pathologic examination than among those with pathology-confirmed PAS (50% vs. 17.8%, respectively) (Table 3).

Among women with a prenatal diagnosis of placenta increta, myometrial involvement (grade 2-3 PAS) was pathologically confirmed in 80% of women without coexisting adenomyosis. In contrast, myometrial involvement was not confirmed by pathology in all women (0%) with coexisting adenomyosis (Table 3).

Among women with clinically suspected placenta percreta, extensive myometrial involvement of PAS (grade 3 PAS) was pathologically confirmed in 57.1% of women with coexisting adenomyosis, that was lower than women without coexisting adenomyosis (84.6%) (Table 3).

Table 3 Preoperative assessment results and detailed histopathology by presence of coexisting adenomyosis.

Presence of coexisting adenomyosis on pathologic examination (10 women)				
Antenatal assessment results	PAS grading			
	No PAS	Grade 1	Grade 2	Grade 3
Placenta creta (n=0)	0 (0)	0 (0)	0 (0)	0 (0)
Placenta increta (n=3)	2 (66.7)	1 (33.3)	0 (0.0)	0 (0.0)
Placenta percreta (n=7)	0 (0.0)	1 (14.3)	2 (28.6)	3A: 4 (57.1)
No coexisting adenomyosis on pathologic examination (39 women)				
Antenatal assessment results	Antenatal assessment results			
	No PAS	Grade 1	Grade 2	Grade 3
Placenta creta (n=1)	0 (0)	0 (0)	0 (0)	3A: 1 (100)
Placenta increta (n=10)	1 (10.0)	1 (10.0)	0 (0)	3A: 8 (80.0)
Placenta percreta (n=26)	1 (3.8)	3 (1.5)	0 (0)	3A: 19 (73.1) 3D: 3 (11.5)
Unknown (n=2)	0 (0)	1 (50.0)	1 (50.0)	0 (0)

Data are presented as number (percentage); PAS, placenta accreta spectrum.

Table 4 shows the characteristics of the four cases in which PAS was not found on pathological examination. In two pregnant women who were suspected to harbor placenta percreta and placenta increta during antenatal work-up, PAS was pathologically unconfirmed; however, grades 1 and 3 coexisting adenomyosis were noted in the surgical specimens.

Table 4 Characteristics of four cases being pathologically unconfirmed PAS.

Characteristics	Case 1	Case 2	Case 3	Case 4
Year of diagnosis made	2017	2018	2019	2019
Maternal age (years)	30	36	34	38
Prior uterine surgery	CD: one time	CD: one time	CD: two times	None
GA at first diagnosis (weeks)	26	28	36	33
GA at CD (weeks)	33 $^{5/7}$	36 $^{6/7}$	36 $^{5/7}$	35 $^{4/7}$
Setting of CD	Emergency	Elective	Elective	Elective
Type of diagnostic procedure	US and MRI	US and MRI	US and MRI	US and MRI
Type of antenatally diagnosed PAS	Increta	Percreta	Percreta	Increta
Number of pathology slides examined (slides)	22	34	22	24
Coexisting uterine adenomyosis	Absence	Presence	Absence	Presence
Grade*	NA	1	NA	3
Number of foci/LPF**	NA	1-3	NA	4-9

GA. Gestational age, PAS: placenta accreta spectrum, CD: cesarean delivery, MRI, Magnetic resonance imaging, LPF: low-power microscopic field, NA: not applicable.
*Grades 1, 2, and 3 correspond to involvement of the inner third, two-thirds, and entire myometrium, respectively.
**The number of foci as 1-3, 4-9 and ≥10 foci/low-power microscopic field, respectively, indicated mild, moderate, and severe.

4. Discussion

The findings of the present study were based on the experience of a single tertiary care referral institution in Thailand over an 8-year period. Previous cesarean deliveries and placenta previa were noted in most of the women. Of the 50 cesarean hysterectomy specimens reviewed, most were classified as having grade 3 PAS. Four women, however, were found to have no PAS disorders on pathologic examination. They accounted for the rate of 8.0% (95% CI 2.20% to 19.2%) of women with antenatally diagnosed but pathologically absent of PAS. The presence of coexisting adenomyosis appeared to affect the accuracy of the antenatal diagnosis of PAS.

Antenatal diagnosis of PAS is mandatory, enabling tailored management. Pregnancy complicated by PAS disorders should be managed by a multidisciplinary team at a specialist center to reduce adverse perinatal outcomes [12]. Prenatal ultrasound and pelvic magnetic resonance imaging (MRI) are tools used to investigate PAS disorders [12]. In a review of 3889 pregnant women who presented in the second trimester with placenta previa or low-lying placenta and had a history of cesarean deliveries, the pooled sensitivity and specificity of ultrasound for diagnosing PAS were 88.0% (95% CI, 81.0% to 93.0%) and 90.0% (95% CI, 88.0% to 93.0%), respectively [13]. Prenatal ultrasound, when performed by skilled operators, is therefore highly sensitive and specific for screening PAS during the second trimester among women at risk of PAS [13]. Although MRI seems to yield similar diagnostic performances, it is superior to ultrasound in diagnosing PAS occurring in the posterior uterine wall and provides additional information regarding the degree of myometrial involvement and extension of the lesion [14]. In our study, most women (90.0%) underwent prenatal ultrasound followed by MRI.

Accurate prenatal diagnosis of PAS remains challenging. A false-positive prenatal diagnosis of PAS disorders can lead to unnecessary obstetric hysterectomy and nontraditional surgical incisions performed during the operation (i.e., midline vertical skin incision, vertical uterine incision, fundal uterine incision), that results in a loss of future fertility and increased risk of perioperative complications. A false diagnosis of antenatal PAS can also lead to neonatal compromise secondary to iatrogenic preterm birth.

In a study conducted in two teaching hospitals in the United States, nine of 40 (22.0%) antenatally suspected cases were noted to have no PAS during pathological evaluation of the uterus and placenta [6]. In this study, all women underwent antenatal ultrasound and 31(77.5%) women underwent MRI. Recently, a prospective multicenter study assessing the use of third-trimester ultrasound for the diagnosis of PAS in pregnancies complicated by placenta previa observed that three of 82 (3.7%) pregnant women undergoing hysterectomy for PAS were found to have no PAS on pathological examination [15]. In the present study, four women, although undergoing both ultrasound and MRI for diagnosing PAS, were found to have no PAS disorders on pathologic examination (8.0%; 95% CI 2.20%-19.2%) (Table 4). These findings highlight the possibility of false-positive results for prenatally diagnosed PAS despite the meticulous investigation undertaken. Therefore, this vital issue should be discussed with patients and family members during planned treatment counseling.

Limited evidence exists for factors related to false-positive results for antenatally diagnosed PAS. Researchers from Chiang Mai University Hospital reported a case with a false-positive diagnosis of PAS, that might be related to coexisting adenomyosis. In this report, a 34-year-old woman was diagnosed with placenta previa accompanied by PAS based on ultrasound and MRI findings. Cesarean delivery followed by hysterectomy was performed at 35 weeks. Pathological examination of the uterus and placenta revealed no trophoblastic villi invasion of the

myometrium. However, there are multiple lesions of adenomyosis with marked stromal decidualization and intervening myometrial bundles of the uterine wall beneath the placental attachment area [7].

The findings of the present study also suggest that the presence of coexisting adenomyosis might affect the accuracy of the prenatal diagnosis of PAS. Coexisting adenomyosis was more likely to be noted among women without PAS on pathologic examination than among those with pathologically confirmed PAS (50.0% versus 17.8%, respectively) (Table 3). Additionally, the degree of myometrial involvement was less accurate if the underlying adenomyosis was present. Among women with clinically suspected extensive myometrial involvement, grade 3 PAS was pathologically confirmed in only 57.1% of women with coexisting adenomyosis, that was remarkably lower than that in women without coexisting adenomyosis (84.6%). Therefore, our findings reaffirm the false-positive diagnosis of PAS using prenatal ultrasound and MRI, which might be related to coexisting adenomyosis. The results of a previous case report [7] together with the present study remind clinicians of the false-positive results of antenatal PAS diagnosis due to coexisting adenomyosis.

Adenomyosisis characterized by the presence of endometrial glands and stroma ectopically embedded in the myometrium, causing myometrial smooth muscle hyperplasia and hypertrophy [16]. During pregnancy, a thickened myometrium secondary to adenomyosis can cause a mass effect on the placental attachment site [7,16]. Thus, it can lead to difficulty in distinguishing between the myometrium and placenta because of a poorly defined interface. Hormonal changes during pregnancy have been reported to alter the appearance of adenomyosis. Adenomyosis increases in size during pregnancy owing to stromal decidualization [16]. Increased uterine blood flow during pregnancy induces adenomyosis becoming hypervascular [7]. These changes likely mimic the imaging findings of PAS [7,16].

The strengths of the present study are that all pathology slides were re-examined by a perinatal pathologist (P.K.) to revise the pathological diagnosis of PAS disorders according to the of FIGO classification [2,10]. This would allow further comparisons across studies. A relatively high number of sectioned pathological slides might indicate the adequacy of surgical pathology tissue sampling in the present study. Additionally, the present study evidently underlines that, even among women who underwent extensive investigations for diagnosing PAS in a large referral institution, the possibility of false-positive result remains.

A major limitation of the present study is its potentially low generalizability, as the data were obtained solely from women undergoing obstetric hysterectomy. A relatively small sample size secondary to the rarity of the disease has resulted in a wide confidence interval of the main finding and also precludes the ability to assess the detailed characteristics of prenatal imaging related to the pathology grade of PAS and other coexisting uterine pathology. In addition, this study could not determine the correlation between intraoperative findings and false-positive diagnosis of PAS. Surgical specimens were submitted as hysterectomy specimens with the placenta in situ. Intraoperative specimen examination was not carried out to avoid damaging specimens that might interfere further pathological examination.

5. Conclusion

The rate of false-positive results for prenatal diagnosis of PAS in the present study was 8.0% (95% CI 2.20%-19.2%). The presence of coexisting adenomyosis appeared to affect the accuracy of antenatal PAS diagnosis. Coexisting adenomyosis limits the assessment of myometrial involvement among women with an antenatal diagnosis of PAS disorders.

6. Acknowledgements

We are grateful to the Faculty of Medicine, Khon Kaen University, Khon Kaen, Thailand (Grant Number IN66035).

7. References

[1] Jauniaux E, Chantraine F, Silver R, Langhoff-Roos J. FIGO consensus guidelines on placenta accreta spectrum disorders: Epidemiology. Int J Gynaecol Obstet. 2018;140(3):265-273.

[2] Hecht JL, Baergen R, Ernst LM, Katzman PJ, Jacques SM, Jauniaux E, et al. Classification and reporting guidelines for the pathology diagnosis of placenta accreta spectrum (PAS) disorders: recommendations from an expert panel. Mod Pathol. 2020;33(12):2382-2396.

[3] Jauniaux E, Bunce C, Grønbeck L, Langhoff-Roos J. Prevalence and main outcomes of placenta accreta spectrum: A systematic review and meta-analysis. Am J Obstet Gynecol. 2019;221(3):208-218.

[4] Allen L, Jauniaux E, Hobson S, Papillon-Smith J, Belfort MA. FIGO consensus guidelines on placenta accreta spectrum disorders: nonconservative surgical management. Int J Gynaecol Obstet. 2018;140(3):281-290.

[5] Kietpeerakool C, Lumbiganon P, Laopaiboon M, Rattanakanokchai S, Vogel JP, Gülmezoglu AM. Pregnancy outcomes of women with previous caesarean sections: Secondary Analysis of World Health Organization Multicountry Survey on maternal and Newborn Health. Scientific Reports. 2019;9(1).
[6] Eller AG, Porter TF, Soisson P, Silver RM. Optimal management strategies for placenta accreta. BJOG. 2009;116(5):648-654.
[7] Tongsong T, Khunamornpong S, Sirikunalai P, Jatavan T. Adenomyosis in pregnancy mimicking morbidly adherent placenta. BMJ Case Rep. 2014;1-5.
[8] Garmi G, Salim R. Epidemiology, etiology, diagnosis, and management of placenta accreta. Obstet Gynecol Int. 2012;2012:1-7.
[9] Lester SC. Manual of surgical pathology. 3rd ed. Pennsylvania: Elsevier; 2010.
[10] Jauniaux E, Ayres-de-Campos D. FIGO consensus guidelines on placenta accreta spectrum disorders: Introduction. Int J Gynaecol Obstet. 2018;140(3):261-264.
[11] Kepkep K, Tuncay Y, Göynümer G, Tutal E. Transvaginal sonography in the diagnosis of adenomyosis: Which findings are most accurate? Ultrasound Obstet Gynecol. 2007;30(3):341-345.
[12] Pegu B, Thiagaraju C, Nayak D, Subbaiah M. Placenta accreta spectrum-a catastrophic situation in obstetrics. Obstet Gynecol Sci. 2021;64(3):239-247.
[13] Jauniaux E, Bhide A. Prenatal ultrasound diagnosis and outcome of placentapreviaaccreta after cesarean delivery: A systematic review and meta-analysis. Am J Obstet Gynecol. 2017;217(1):27-36.
[14] D'Antonio F, Iacovella C, Jaraquemada PJ, Bruno CH, Manzoli L, Bhide A. Prenatal identification of invasive placentation using magnetic resonance imaging: systematic review and meta-analysis. Ultrasound Obstet Gynecol. 2014;44(1):8-16.
[15] Fratelli N, Prefumo F, Maggi C, Cavalli C, Sciarrone A, Garofalo A, et al. Third-trimester ultrasound for antenatal diagnosis of placenta accreta spectrum in women with placenta previa: results from the ADoPAD study. Ultrasound Obstet Gynecol. 2022;60(3):381-389.
[16] Jensen KK, Pyle C, Foster BR, Sohaey R, Oh KY. Adenomyosis in pregnancy: diagnostic pearls and pitfalls. Radiographics. 2021;41(3):929-944.