Clinical Article

A Clinico-pathological study of Placenta percreta

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Key Words: Invasive placentation; placenta increta; placenta percreta; prenatal diagnosis; Ultrasound imaging; MRI

Synopsis: Placenta percreta can be accurately diagnosed prenatally with ultrasound and is associated with good outcomes when managed by a multidisciplinary team.

Word Count: 2497

Abstract

Objective: We aim to review a series of placenta percreta (PP) managed in the same centre of excellence and to evaluate the risk factors and the impact of prior caesarean delivery (CD) surgical techniques used.

Methods: Retrospective cohort study of 19 pregnancies with placenta percreta managed by a multidisciplinary team between January 2002 and March 2017 at Saint Luc University Hospital. Data reviewed included demographics, outcome, inter-pregnancy interval (IPI) and surgical techniques used for prior CD uterine closure. A series of non-accreta placenta praevia was used as control group.

Results: The most commonly found ultrasound signs in the study group were loss of clear zone (n=14 out of 17 cases; 82.4%), placental lacunae (n=17; 100%) and subplacental hypervascularity (n=11 out of 14 cases); 78.6%). Median gravidity, parity and number of prior CD were significantly (P< 0.05) higher and IPI significantly (P<0.05) longer in the PP group than in the control group. There was no difference between the groups for the surgical techniques used for the prior CD.

Conclusion: The prenatal ultrasound diagnosis of PP is accurate allowing for optimal management by a specialised multidisciplinary team. Multicentric studies are required to further evaluate the impact of prior CD surgical techniques used on the risks of PP in subsequent pregnancies.

Word count: 200

Introduction

Placenta percreta (PP) is the most invasive form of the placenta accreta spectrum (PAS) where the villous tissue is found to invade the full thickness of uterine wall through the serosa [1-4]. In many cases of PP, the villous tissue also invades surrounding pelvic tissues and organs such as the bladder. The first case of PP was probably described by Alexandroff in 1900 and by 1956, only eight cases had been reported in the medical literature, all associated with uterine rupture [5]. The patient described by Cuthbert had a prior caesarean delivery (CD) but none of the other previous cases he reviewed had one [5]. Similarly, out of the 20 PAS cases reported by Irving and Hertig and the 86 case reports that they reviewed, only two were found in patients with a previous CD [6]. Until the 1960s, the vast majority of PAS was associated with a previous endometritis, manual removal of the placenta or uterine curettage [5,6].

The vast majority of PAS are now found in women presenting with a prior of CD [7]. In case of large caesarean scar defects, there is permanent focal myometrial degeneration, as well as a reduced or absent re-epithelialisation of the scar area. Uterine scars have an impact on both implantation and placentation. Recent epidemiological studies have found that the risk of placenta praevia increases by 50% after one CD and doubles after two prior CD [8] whereas there is a 3.2-fold increased risk of PA after more than one CD in women presenting with placenta praevia [9]. There are only limited data on the different surgical techniques for entering and closing the uterus during CD and no data on pregnancy interval and the risks of PAS in the next pregnancy.

Around 25% of the 203 cases included in the cohort studies on the prenatal

diagnosis of PAS were reported as PP [8]. PP is the most complex form of PAS and is associated with a high maternal morbidity [9]. In a recent review of the literature, it was found that 70 women out of 119 presenting with PP had intra- and post-operative complications including major haemorrhage, bladder injury and pulmonary embolism or cardiopulmonary arrest [10]. There is increasing evidence that specialist care in centre of excellence with access to a multidisciplinary team (MDT) is superior to standard obstetric care management in patients with suspected PAS [11,12]. In particular, cases of PP are likely to require additional blood products, intensive care admission and have a higher incidence of urologic complications, including cystotomy and ureteral injury [13,14].

Previous cases series of PP published in the international literature are multicentric or small case series with presenting variable diagnostic techniques and management protocols and no data on previous CD. We present here a large series of PP managed using a standardized protocol by a specialist MDT in a single centre and we have evaluated the possible impact of previous surgical techniques used for the uterine closure on the development of PP.

Materials and Methods

This is retrospective cohort study of cases of PP managed by the same MDT between January 2002 and March 2017 at Saint Luc University Hospital. In all cases the diagnosis of PP was confirmed clinically at delivery [15] and by a detailed histopathological examination. Demographic data included maternal age, gravidity, parity, inter-pregnancy interval (IPI) between the last delivery and start of the case pregnancy, prior surgery including CD and the surgical techniques used for the uterine closure in previous CD including suture material use, number of layers and locking of suture. The study was approved by the ethical committee of Cliniques Universitaires Saint Luc. Retrospective patient consent was not required as all data were collected using a standard clinical audit protocol and all data were anonymised for data analysis.

In all cases but one, the diagnosis of PAS was made prenatally with ultrasound using both transabdominal and transvaginal transducers (GE Voluson® 730, GE Medical System, Zipf, Austria). Magnetic resonance imaging (MRI) was also performed in 14 cases when lateral extension of villous tissue outside the uterine wall was suspected on ultrasound. Ultrasound still images and video recording of the examination which lead to the prenatal diagnosis of PP were reviewed using the standardized descriptions proposed recently by the European Working Group on Abnormally Invasive Placenta (EW-AIP) and the AIP international expert group [16,17].

A specialist perinatal pathologist performed all the macroscopic and microscopic examinations and confirmed PP. For the histopathologic examination, a standard methodology was used as previously described by placental pathologists

[1-3]. Between 10 and 15 samples were taken from the accreta area, as identified by the clinical and macroscopic examination. All samples were processed as per the protocol of the Department of Histopathology at Saint Luc University Hospital and slides were stained with Haematoxylin and Eosin (H&E) for microscopic examination.

The ultrasound results were compared to those of the literature. The clinical characteristics were compared with those of an equivalent series of major placenta praevia with one or more prior CD and no evidence of PAS managed during the same period of time (control group). The diagnosis of placenta praevia was defined as a placenta reaching and/or lying directly over the internal os of the cervix on transvaginal sonography (TVS). For our data analysis of uterine closure and suture material we used the first suture parameters in case of double suture.

Statistical analysis

The data were analysed using StatGraphics- plus version 3 statistical software package (Station, TX, USA). The standard Kurtosis analysis indicated that some values were not normally distributed and therefore the data are presented as median and inter-quartile range (IQR). Mann-Whitney W test to compare the medians of the study and control groups. The data of the operative protocols of previous CD in the study and control group were compared using chi-square test after matching for the number of previous CD. A P value <0.05 was considered significant.

Results

The study included 19 cases of PP. All but one presented prenatally and at delivery as placenta praevia covering the scar area of a prior CD. This patient had a posterior PP implanted on a large area of scar tissue following synechia removal surgery after previous D&C. In three cases, the patients had also a prior curettage. Table 1 displays the prenatal ultrasound findings at the time of diagnosis in the study group. In all cases, the patient had more than one ultrasound examinations. The median (IQR) gestational age at diagnosis of PP was 33 weeks (26;34). In all cases, grey-scale ultrasound was used. Ultrasound images were available for review in 17 cases and data from both 2D grey-scale ultrasound and CDI were available in 14 cases. The most commonly found signs were: loss of clear zone in 14 (82.4%) cases and placental lacunae in 17 (100%) cases for grey-scale imaging and uterovesical hypervascularity in 11 (78.6%) cases, lacunae feeder vessels in 5 (35.7%) cases for CDI. In eight out of 14 (57.1%) cases who had an MRI, a clear surgical plane could be identified between the bladder and uterus allowing non-traumatic reflection of the urinary bladder at hysterectomy whereas in 6 cases placenta villi were found to have invaded into the bladder (n= 5) and/or pelvic side (n=1).

Table 2 presents the management of the study group (n= 19) compared to data from the literature (n= 119). In all cases, the delivery management included a planned CD between 35 and 38 weeks using a midline abdominal skin incision under epidural anaesthesia. The fetus was delivered by transverse fundal uterine incision. Two cases were managed by primary caesarean hysterectomy due to massive intra-operative bleeding. In 17 cases, the placenta was left in situ and a secondary hysterectomy was performed in 15 cases. In the remaining 2 cases, a partial myometrial resection or placentectomy was performed 4 weeks post-delivery,

preserving the uterus. Interventional radiology (IR) by embolization of the uterine and intern iliac artery was used in 17 cases prophylactically after the delivery of the fetus. Peri-operative complications included bladder injury (26%) in five cases and major obstetric haemorrhages (MOH) define as blood loss in excess 1500 ml, requiring blood transfusions in 13 cases (68.4%).

The clinical data and surgical historical data of the 18 cases presenting with placenta previa percreta are presented on Table 3 and are compared with those of control group of placenta praevia without evidence of PAS prenatally and at delivery. The first CD in the study group was performed as an emergency procedure in 10 cases (52,7%) and electively in the remaining 9 patients (47.3%). Median gravidity, parity and number of prior CD were significantly (P= 0.028) higher in the PP series than in the control group of placenta praevia. The IPI between the last CD and the start of the next pregnancy was significantly (P= 0.049) longer in the study group than in the control group. There was no significant difference between the groups for maternal age. Four patients in the study group had their previous CD abroad and thus detailed surgical operative protocols could only be obtained for 15 cases. The types of closure techniques included continuous single versus double layer and for the first layer continuous locked stich versus interrupted stiches. Absorbable synthetic sutures were used for closing hysterotomy of the prior CD included copolymers (Vicryl ®) and polyglycolic acid (Dexon ®) in the study group and (Vicryl ®) and monofilament (Monocryl ®) in the control group. There was no statistical difference for the surgical techniques used for uterine closure of the previous CD between the study group of placenta previa percreta (n=18) compared to control group of non-accreta placenta previa.

Discussion

Our series is the largest single series of PP diagnosed and managed by the same MDT in the centre of excellence indicates that the diagnosis of this subgroup of PAS is accurate allowing for optimal management. In addition our evaluation of the use of different surgical techniques used for the previous CD suggest that the types of closure techniques and suture materials used has no impact on the incidence of PP the subsequent pregnancy

Regionalization of care for women in centre of excellence by MDT [11,12] requires an accurate prenatal diagnosis of PAS. The sensitivity and specificity of ultrasound imaging in diagnosing placenta previa accreta in women with prior CD, presenting with anterior low placenta or placenta previa as in the present series are 88 and 90% and 97 and 97% in retrospective and prospective series, respectively [9]. Only in 72 cases out of 1078 published in the literature up to 2016 include detailed correlations between ultrasound findings and PAS grading [18]. When analyzed for the depth of villous myometrial invasion, the presence of placental lacunae and subplacental hypervascularity are the most common sign found in cases of PP. In the present series, placenta lacunae were found in all cases and hypervascularity of the uterovesical junction was present in 11 out of 14 cases for which CDI was used (Table 1). On grey-scale imaging, we found a higher incidence of loss of the clear zone, myometrial thinning to <1mm or undetectable, bladder wall interruption or loss, placental bulge and focal exophytic mass of placental tissue extending beyond the uterine serosa than in the literature.

A recent systematic review found that around 90% of women diagnosed prenatally with placenta previa accreta have been managed by elective or emergent caesarean hysterectomy [9]. In the present series, two cases only were managed

with primary caesarean hysterectomy and 15 had a conservative management with secondary hysterectomy (Table 2). In only two cases we were able to excise the myometrium with PAS tissue and to reconstitute the uterine defect without removing the uterus. Despite our management protocol including systematic post-CD embolization, the rates of MOH was higher in our series than those reported in a review of 119 PP cases published in the international literature [10]. The incidence of bladder damage or resection was also much higher, probably because of the lateral extension of the placental invasion in most of our cases. A recent cohort study of 71 women has recently shown that a MDT stepwise surgical approach, including bilateral ligations of the anterior division of the iliac arteries before removing the placenta can be successful in controlling the bleeding and preserving the patient's uterus in around 90% of the cases with 14% urinary tract complications, most of which can be identified and repaired during CD [19].

The impact of IPI on obstetric outcomes varies depending on the population studied. In China, following the end of the one-child policy and independently of maternal age, longer IPIs have been associated with higher risks of preterm delivery and term low birthweight in the second pregnancy [20]. By contrast, in the USA, short IPI was found to be at risk factor for poor neonatal outcomes in socially disadvantaged women [21]. In the present study, we found that the IPI between the last CD and the start of the next pregnancy was significantly (P<0.05) longer in women presenting with PP than in those with a non-accreta previa. The risk factors in women presenting with PP include one or more previous CD associated with an increased IPI to next pregnancy and a higher gravidity and parity (Table 3).

In the present study, we found no impact of the surgical techniques used for the previous CD uterine closure on the incidence of placenta praevia percreta

compared to a control group of placenta praevia non-accreta (Table 3). Compared with double-layer closure of the uterine incision, single-layer closure is associated with a reduction in mean blood loss, a shorter operating time and no increase in composite complications for the subsequent pregnancy [22,23]. Women with a single-layer closure have a significantly thinner residual myometrial thickness on ultrasound compared to double-layer closure [23]. A case-control study of 98 women presenting with placenta praevia including 38 PAS and with a history of one or more prior CDs found no difference in single-layer versus double-layer closure in the incidence of PAS [24]. The corresponding multivariate logistic regression analysis showed that continuous suture was associated with a higher risk of PAS than interrupted sutures. For chromic catgut versus polyglactin-910 (Vicryl ®) sutures for uterine repair, there is no significant difference in adverse pregnancy outcomes in a subsequent pregnancy, such as uterine rupture [24]. A retrospective case-control study of 53 cases and 157 controls found that the use of monofilament suture for hysterotomy closure in prior caesarean reduces the risks of having a placenta praevia and thus PAS in future pregnancies [25].

Limitations of this study include the retrospective design, the relatively small number of cases of PP. However, cases of PP are rare and despite these limitations, the strengths of our study include the use of standardized protocols for prenatal diagnosis and management by the same MDT allowing for better outcomes. Multicentric studies and randomised control trials are required to evaluate the impact of the different surgical used to close the uterus at CD on the risks of invasive placentation in PP for subsequent pregnancies.

Author contributions

All authors contributed to the study design. MM and CH performed the data collection. EJ and CH carried out the data analysis and drafted the manuscript. PB analysed and reviewed all placental histology. All authors were involved in the critical discussion and approved this final version for publication. CH is the guarantor of the study.

Acknowledgments

Conflict of interest

The authors have no conflicts of interest to declare.

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Table 1: Distribution of the ultrasound signs in PP series compared with those from cases reports and cohort studies published in the literature [18].

Ultrasound signs	Study group	Literature review
	n (%)	n/no cases (%)
Grey-scale Parameters (n=17)		
Loss of clear zone	14 (82.4)	8/17(47.1)
Myometrial thinning	12 (70.6)	4/17(23.5)
Placental lacunae	17 (100)	14/17(82.4)
Bladder wall interruption	15 (88.2)	5/17(29.4)
Placental bulge	14 (82.4)	2/17(11.8)
Focal exophytic mass	11 (64.7)	2/17(11.8)
CDI Parameters (n=14)		
Uterovesical hypervascularity	11 (78.6)	2/11(18.2)
Subplacental hypervascularity	3 (21.4)	6/11(54.5)
Bridging vessels	2 (14.3)	2/11(18.2)
Lacunae feeder vessels	5 (35.7)	5/11(45.5)

PP = Placenta percreta   CDI= Color Doppler Imaging

Table 2: Surgical management and perioperative complications in PP series compared with those reported in the literature [10].

Variables Literature review (%)	Study group n (%)	n
No of cases	19	119
Mode of CD		
Elective (64.7)	9 (47.3)	77
Emergency (20.2)	10 (52.7)	24
Unknown (15.1)	0	18
Intraoperative management		
Primary CD-hysterectomy (82.4)	2 (10.5)	98
Secondary hysterectomy (17.6)	15 (78.9)	21
PMR	2 (10.5)	
Interventional radiology (70.6)	17 (89.4)	84
Complications (58.8)		70
MOH (19.3)	13 (68.4)	23
Bladder injury/resection (14.3)	5 (26.3)	17

PP = Placenta percreta ; CD= Caesarean delivery; PMR= Partial myometrial resection; MOH: Major obstetric haemorrhage

Table 3: Comparison of the clinical characteristics between the study group and control placenta previa group.

Variables	Study group (n=18)	Control group (n=18)	P value
Patient characteristics (median and IQR)			**W test**
Maternal age (Years)	34 (32;37)	36 (32;39)	0.202
Gravidity	3 (3;4)	3 (2;3)	0.028
Parity	2 (2;3)	1 (1;2)	0.016
No of prior CD	2 (1;2)	1 (1;2)	0.021
IPI (months)	36 (24;60)	26 (14;36)	0.049
Prior CD characteristics (n=15)			**Chi-square**
Uterine closure - Single layer	9 (60%)	8 (53.3%)	
- Double layer	6 (40%)	7 (46.7%)	0.713
First layer - Continuous locked	9 (60%)	9 (60%)	
- Interrupted	6 (40%)	6 (40%)	1
Suture material - Copolymer	13 (86.7%)	12 (80%)	
- Others	2 (13.3%)	3 (20%)	0.624

CD= Caesarean delivery; IPI= inter-pregnancy interval
W test= Mann-Whitney (Wilcoxon) test