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MATERNAL-FETAL MEDICINE

Self-reported physical, mental, and reproductive sequelae after treatment of abnormally invasive placenta: a single-center observational study

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Abstract

Objective To analyze the types of treatment of abnormally invasive placenta (AIP) and to investigate the self-reported physical and mental short- and long-term sequelae.

Methods This single-center observational study was performed between 2003 and 2017. Women with prenatal or intrapartum diagnosis of AIP were identified through the departmental database. Classification was performed according to the time of diagnosis establishment and the type of treatment. Medical complications overall and according to the type of treatment were analyzed. Data about women's perception of diagnosis, treatment, and short- and long-term sequelae were gathered by questionnaire.

Results Cases were classified into four groups: prenatal diagnosis, cesarean hysterectomy (A, $n=10$); prenatal diagnosis, expectant management (B, $n=19$); intrapartum diagnosis, cesarean hysterectomy (C, $n=6$); intrapartum diagnosis, conservative therapy (D, $n=20$). Depth of invasion, total units of transfused red blood cells, and the need for reoperation differed between the treatment groups. Expectant management was successful in 94.7% of cases. Irrespective of the treatment group, 73.3% of women perceived the condition as serious or life-threatening; 30.0% utilized psychological support; and 36.7% reported persistent pain or problems. 37.5% of women after uterine preservation had another live birth, AIP recurred in 44.4% of cases.

Conclusion Conservative management of AIP is feasible in selected cases. The condition is perceived as life-threatening and has a lasting impact on the physical, mental, and reproductive health of those affected. This finding merits further investigation. AIP continues to be a condition with high morbidity.

Keywords Cesarean hysterectomy · Abnormally invasive placenta · Accrete · Inreta · Percreta · Placenta · Expectant management · Conservative management

Introduction

As a result of rising cesarean delivery rates, abnormally invasive placenta (AIP) has become a commonly encountered problem in today's obstetric work. Numerous reports have been published on incidence, diagnosis and treatment; consensus statements for standards of care and management recommendations have evolved [1–11]. The depth of villous invasion, prenatal diagnosis, and planned delivery in specialized centers by a multidisciplinary team are predictors of good outcome [12, 13, 11].

Cesarean hysterectomy remains the gold standard treatment for high-grade AIP (placenta in- and percreta). Rising prenatal detection rates have allowed for the development of alternative treatment options, particularly as cesarean

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hysterectomy is associated with considerable operative morbidity and an inevitable loss of fertility. Conservative approaches include excision of the affected area and simultaneous uterine reconstruction, often in combination with surgical or radiological devascularization, and an expectant approach [14, 15, 3, 16–22].

The basic principle of expectant management of AIP consists of the operative delivery of the fetus leaving the abnormally invasive placenta in place, awaiting loss of perfusion and ultimately its resorption. Various additional procedures have been reported, aiming to decrease uterine blood flow or to expedite resorption. These include ligation or embolization of the feeding vessels and methotrexate administration. None of the procedures has been investigated and compared in randomized controlled trials. Complications of the expectant management approach include infection and sepsis, bleeding or coagulation disorders, and secondary loss of organ [23–27, 18, 17, 10, 28, 29].

Self-reported data about the physical, mental, and reproductive impact of diagnosis and treatment of AIP are not available.

Expectant management of AIP for patients with prenatal diagnosis of high-grade AIP was introduced at our institution, a tertiary referral center, in 2003. Here, we report our experience with diagnosis and treatment of AIP at our institution over a 14-year period. Additionally, we report the results of a questionnaire sent to all women who had undergone treatment for AIP at our institution. In this questionnaire we asked the women about their perception of the condition and its severity, and the physical, mental, and reproductive short- and long-term sequelae of the treatment they had received.

Methods

We searched our departmental database for all cases of AIP who delivered between 1 July 2003 and 31 May 2017. In case of prenatal diagnosis, investigations included gray scale and color Doppler ultrasound, applying established criteria [30–35]. Patients with suspected AIP involving the posterior uterine wall underwent MR imaging. For selected women (suspected bladder invasion) cystoscopy was performed. Treatment options were extensively discussed with the women, and a joint decision was made, taking women's preferences into consideration. Major points included loss of fertility versus extended treatment and follow-up times. In case of expectant management, serial clinical, serological, and ultrasound investigations were performed from delivery until completion of treatment.

In women without prenatal suspicion of AIP diagnosis was established during delivery utilizing clinical criteria. Based on severity of hemorrhage and depth of invasion a decision for or against uterine preservation was taken by the attending surgeon. In case of hysterectomy the diagnosis was confirmed by histopathology. Data on diagnosis and treatment of 15 cases have been published previously [36].

In October 2017 (6 months–14 years after delivery) a questionnaire was sent to all women (see Supplement). It covered the following topics: perception of the diagnosis and its severity; satisfaction with the choice of treatment (at the time of the survey); impact of diagnosis and treatment on the relationship to the newborn; physical and mental sequelae of the respective treatment; reproductive history; and quality of life. Patients who did not respond were contacted by phone, and information was gathered by telephone interview.

Data analysis was performed using statistical software package SPSS 24 (SPSS Inc., Chicago, IL, USA). Between group comparisons of normally distributed variables were performed by *t* test for independent samples, otherwise Kruskal–Wallis- or Mann–Whitney *U* test was used.

The University Bonn Institutional Review Board does not require formal approval for retrospective observational studies, therefore, ethics approval was not sought. For the questionnaire, written informed consent was obtained from all women.

Results

During the study period 55 cases of AIP occurred. They were classified into four categories as follows: (A) prenatal diagnosis, planned cesarean hysterectomy ($n=10$); (B) prenatal diagnosis, planned expectant treatment ($n=19$); (C) intraoperative diagnosis, cesarean hysterectomy ($n=6$); (D) intraoperative diagnosis, uterine preservation ($n=20$). Characteristics of the study population are listed in Table 1. Pregnancy was a result of assisted reproduction in 12.7% of patients, and 78.2% of women had a history of previous uterine surgery, with no difference between the four subgroups. Compared to groups A, B and C, placenta previa was less common in group D (80% vs. 30%, $p<0.002$). Mean gestational age at delivery was 34 weeks (range 21–41), and six women delivered vaginally.

Treatment details are summarized in Table 2. Two thirds of women in group D (intraoperative diagnosis with preservation of the uterus) had minor degrees of AIP, whereas partial or complete placenta increta or percreta constituted the majority of patients in the remaining treatment groups. In the entire study group there was no maternal or perinatal death. Maternal morbidity consisted of the following: Relaparotomy ($n=4$, two in patients after cesarean hysterectomy, and two in women with planned conservative treatment); urinary bladder lesion ($n=4$); unilateral salpingo-oophorectomy ($n=4$). Transfusion of packed red blood cells (median 6 units, range 1–24) was necessary in 32.7%

Table 1 Demographic and obstetric details of the women with abnormally invasive placenta ($n=55$)

Age (years), mean (range)	34.9 (21–51)
Parity, median (IQR)	1 (1.5)
Assisted reproduction, *n* (%)	7 (12.7)
Previous uterine surgery, *n* (%)	43 (78.2)
Number of previous uterine surgeries, median (IQR)	1 (1)
Placenta previa, *n* (%)	35 (63.6)
ToP for fetal congenital malformations, *n* (%)	3 (5.5)
GA at delivery (weeks + days), mean (range)	34 + 2 (21 + 0 to 40 + 6)
Vaginal delivery, *n* (%)	6 (10.9)
Prenatal diagnosis, *n* (%)	29 (52.7)
GA at prenatal diagnosis (weeks + days), mean (range)	27 + 3 (16 + 3 to 37 + 4)
Prenatal diagnosis, planned cesarean hysterectomy, *n* (%)	10 (34.5)
Prenatal diagnosis, planned expectant treatment, *n* (%)	19 (65.5)
Part of or complete placenta left in place, *n* (%)[a]	11 (57.9)
Uterine cavity emptied, *n* (%)[a]	8 (42.1)
Intraoperative diagnosis, *n* (%)	26 (47.3)
Intraoperative diagnosis, hysterectomy, *n* (%)	6 (23.1)
Intraoperative diagnosis, uterus preserved, *n* (%)	20 (76.9)
Part of or complete placenta left in place, *n* (%)[b]	4 (20.0)
Uterine cavity emptied, *n* (%)[b]	16 (80.0)
Type of abnormal invasion[c]	
Placenta accreta, *n* (%)	14 (25.5)
Placenta increta, *n* (%)	24 (43.6)
Placenta percreta, *n* (%)	17 (30.9)

GA gestational age, *ToP* termination of pregnancy

[a]Women with planned expectant treatment

[b]Women with intraoperative diagnosis and preserved uterus

[c]Confirmation by histopathology in cesarean hysterectomy, otherwise clinical diagnosis

($n=18$) of cases. Bilateral uterine artery embolization was successfully performed in four patients with planned cesarean hysterectomy.

In group B (prenatal diagnosis, planned expectant management), one patient with placenta percreta required hysterectomy 10 days after delivery for intractable intravesical bleeding from the invaded urinary bladder wall, giving a 94.7% success rate. Two patients developed hyperfibrinolysis which was successfully treated with tranexamic acid. Septic complications did not occur. Treatment lasted 1–26 weeks (mean 7.6). Various medical and surgical treatment modalities were applied in patients in group D (uterus preserved): insertion of Bakri catheter ($n=12$); placental bed suture; B-Lynch suture; and Chitosan tamponade insertion (one case each).

Table 3 contains a selection of the questionnaire results. The mean time interval between delivery and interview was 76.7 months. Thirty patients (54.5%), representing 32 cases, responded. Respondents were equally distributed between the treatment groups.

No significant differences were found in the responses between the four treatment groups. The majority of women (73.3%) had perceived the condition as very severe or even life-threatening, and 70% indicated that diagnosis and treatment had created an emotional burden. Seven women (23.3%) reported that establishing a relationship to the newborn had been disturbed. Across the four groups, 30% of respondents required psychological support after completion of treatment. One third of patients (36.7%) was suffering from persistent problems or pain at the time of follow-up, and 50% of women after hysterectomy reported difficulties to accept the loss of fertility. All women with prenatally diagnosed high-grade invasive disease were satisfied with their choice of treatment. AIP recurrence was observed in 50% of the live births that occurred.

Discussion

Compared to other reports the success rate of our expectant management approach is high. The self-reported physical and mental impact and long-term sequelae of diagnosis and therapy of AIP are profound across all treatment groups.

Table 2 Treatment and outcome details, women with abnormally invasive placenta ($n=55$)

	A ($n=10$) (prenatal diagnosis, cesarean hysterectomy)	B ($n=19$) (prenatal diagnosis, expectant management)	C ($n=6$) (intraoperative diagnosis, cesarean hysterectomy)	D ($n=20$) (intraoperative diagnosis, uterine preservation)	p value
Type of AIP					$p<0.001$
Accreta, n (%)	1 (10.0)	0 (0)	0 (0)	13 (65.0)	
Increta, n (%)	1 (10.0)	12 (63.2)	4 (66.7)	7 (35.0)	
Percreta, n (%)	8 (80.0)	7 (36.8)	2 (33.3)	0 (0)	
Units of RBCs transfused at delivery, mean (range)	7 (0–16)	1.3 (0–13)	5.6 (0–20)	0.3 (0–2)	$p<0.01$
Total units of RBCs transfused, mean (range)	11 (0–24)	2.8 (0–13)	6.4 (0–20)	0.3 (0–2)	$p<0.01$
Second operation required, n (%)	3 (30)	11 (57.9)	3 (50)	4 (20)	$p<0.05$
Curettage, n (%)	0 (0)	8 (42.1)	0 (0)	4 (20)	
Hysterectomy, n (%)	1 (10)	1 (5.3)	1 (16.7)	0 (0)	
Other, n (%)	2 (20)	2 (10.5)	2 (33.3)	0 (0)	
Treatment duration (weeks) mean (range)[a]	1.4 (1–2)	7.6 (0–26)	1.3 (1–2)	1.7 (0–8)	$p<0.05$
Inpatient treatment (days) mean (range)[a]	9.5 (6–14)	9.3 (4–33)	9.5 (7–12)	5.6 (2–17)	$p<0.001$

[a]From the date of delivery until completion of treatment

Table 3 Questionnaire results, women after treatment for abnormally invasive placenta ($n=30$)

	Entire group	Group A ($n=10$) (prenatal diagnosis, cesarean hysterectomy)	Group B ($n=19$) (prenatal diagnosis, expectant management)	Group C ($n=6$) (intraoperative diagnosis, cesarean hysterectomy)	Group D ($n=20$) (intra-operative diagnosis, uterine preservation)	p value
Response rate, n (%)	30 (54.5)	4 (40.0)	13 (68.4)	2 (33.3)	11 (55.0)	$p<0.5$
Time between delivery and questionnaire, months, mean (range)	75.1 (5–171)	46.5 (7–158)	76.1 (5–171)	141.5 (125–158)	72.3 (6–133)	$p<0.5$
Condition perceived as serious or life-threatening, n (%)	22 (73.3)	3 (75.0)	11(84.6)	1 (50.0)	7 (63.6)	$p<0.6$
Condition evoked emotional stress, n (%)	21 (70.0)	2 (50.0)	9 (69.2)	1 (50.0)	9 (81.8)	$p<0.6$
Psychological support utilized, n (%)	9 (30.0)	2 (50.0)	4 (30.8)	1 (50.0)	2 (18.2)	$p<0.5$
Persistent pain / problem, n (%)	11 (36.7)	2 (50.0)	3 (23.1)	1 (50.0)	5 (45.5)	$p<0.7$
Further live birth[a], n (%)	8 (26.7)		4 (30.8)		4 (36.4)	
Recurrent AIP[b], n (%)	4 (50.0)		3 (75.0)		1 (25.0)	

[a]Women with preserved uterus

[b]Women with subsequent pregnancies

Success rates for expectant treatment range between and 14 and 85% [23–25, 15, 16, 28]. We attribute the high success rate of our expectant treatment approach (94.7%) to the following factors: (a) patient selection: since complications may occur any time after delivery, adherence to follow-up visits for prolonged times is essential. (b) Monitoring

interval: our schedule entails weekly controls, allowing for prompt action in case of an abnormal finding. (c) Type of investigations: on each follow-up visit, clinical assessment and serological tests (full blood count, C-reactive protein, prothrombin time, activated partial thromboplastin time, fibrinogen, antithrombin, D-dimers) are complemented by ultrasound and color Doppler examination with analysis of the perfusion to the AIP. (d) Interventions during follow-up: (1) curettage is performed after cessation of placental perfusion. This reduces follow-up time and risk of further complications, infection and hemorrhage in particular. (2) In case of ensuing hyperfibrinolysis, treatment with tranexamic acid is initiated; with this approach, hyperfibrinolysis could be reverted in two women [37].

The comparison of treatment results is hampered by the inconsistencies in the classification of the various degrees of abnormal invasion, and the inherent lack of histological confirmation in the expectant management approach [10, 11, 38, 33, 27]. The high morbidity of our study group, illustrated, e.g., in the transfusion rate and number of additional procedures serves as an indicator that minor forms of AIP, placenta adherens in particular, were not included.

In patients with most severe forms of AIP, i.e., placenta percreta involving the entire placentation site, our results confirm previous observations of a reduced blood loss and higher frequency of additional interventions in the expectant treatment group [15].

We explored women's perception of diagnosis and treatment of AIP. Our investigations revealed a high mental, physical, and reproductive morbidity and profound long-lasting sequelae after diagnosis and treatment of AIP.

Several questionnaires for patient-reported outcome measures with respect to physical and mental health, including mother-to-infant bonding are available [39–42]. They capture information on women's perspective covering the preceding 1–4 weeks. Our aim was to explore various physical, mental, and reproductive health-related outcome measures exploring the transition from pregnancy to parturition and motherhood. We, therefore, designed a questionnaire which covered the entire time period. Its validation is pending, but might prove difficult due to the topic's peculiarity. Women reported a severe and sustained impairment of their mental, physical, and reproductive health, illustrated by the fact that nearly one third of women required psychological support, and reported persistence of problems or pain. Loss of fertility after hysterectomy, even though a life-saving procedure in this circumstance, was hard to accept for half of the women. On the other hand, the 44% recurrence rate of AIP in women with subsequent pregnancies underscores the lasting effect of AIP after its initial diagnosis. These self-reported outcomes were present despite the women's satisfaction with their choice of treatment, and irrespective of the type of treatment they had received.

Limitations

Our study group is heterogeneous with respect to the type of abnormal placental invasion, the type of treatment, and the time diagnosis was established. Additionally, histopathological confirmation of the diagnosis is available only for the subgroup of patients who underwent cesarean hysterectomy. However, these limitations are inherent to the subject.

The classification into four treatment groups according to the time of diagnosis establishment and severity of AIP reduces the number of cases in each treatment group. We used this approach since it is a reflection of the clinical situations in which AIP is encountered.

The response rate to the questionnaire was moderate but distributed equally between the four treatment groups. Recall bias cannot be excluded particularly as the follow-up time covers an extended time period and range.

Conclusion

AIP continues to carry a high maternal morbidity. Prenatal diagnosis allows a choice between surgical and expectant treatment approach. With careful patient selection and meticulous follow-up, high success rates of expectant management can be achieved.

Self-reported short- and long-term physical and mental sequelae are substantial and arise across all treatment modalities. To our knowledge these are the first data of women's perception after having received the diagnosis of AIP. If confirmed in larger studies the incorporation of mental health services to the multidisciplinary team attending to women with AIP merits further investigation.

Author contribution JW: data collection and management; data analysis; manuscript writing and editing; final approval; agreement to be accountable. M-DK-P: data collection; manuscript editing; final approval; agreement to be accountable. UG: project development; data collection and management; manuscript editing; final approval; agreement to be accountable. WMM: data collection and management, data analysis; manuscript writing and editing; final approval; agreement to be accountable.

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Compliance with ethical standards

Conflict of interests The authors declare that they have no conflict of interest.

Ethical approval The University Bonn Institutional Review Board does not require formal approval for retrospective observational studies, therefore, ethics approval was not sought. For the questionnaire, written informed consent was obtained from all women.

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