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UROGENITAL

Novel MRI finding for diagnosis of invasive placenta praevia: evaluation of findings for 65 patients using clinical and histopathological correlations

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Abstract
Objective To review established magnetic resonance (MR) criteria and describe a new MR finding for the diagnosis of invasive placenta praevia.
Methods A retrospective review of prenatal MRI examinations of 65 patients (median age: 35 years) who underwent MR for the screening of invasive placenta praevia. All MRIs were performed on a 1.5-T unit, including axial, coronal and sagittal T2-weighted half-Fourier single-shot turbo spin echo imaging. Fifteen patients were diagnosed with invasive placenta praevia. Two experienced radiologists reviewed the MR images and evaluated a total of six MRI features of the placenta, including our novel finding of the placental protrusion into the internal os (placental protrusion sign). Inter-rater reliability was assessed by using kappa statistics. Features with a kappa statistic >0.40 were evaluated using Fisher's two-sided exact test for comparison of their capabilities for placental invasion assessment.
Results Interobserver reliability was moderate or better for the intraplacental T2 dark band, intraplacental abnormal vascularity, uterine bulging, heterogeneous placenta and placental protrusion sign. Fisher's two-sided exact test results showed all these features were significantly associated with invasive placenta praevia.
Conclusion The novel MRI finding of a placental protrusion sign is a useful addition to the established MRI findings for the diagnosis of invasive placenta praevia.
Key Points
- *Prenatal diagnosis for an invasive placenta is essential for perinatal planning.*
- *Magnetic resonance imaging provides useful information for the diagnosis of invasive placenta.*
- *The placental protrusion sign is a useful novel MRI finding for predicting invasive placenta.*

Keywords Placenta accreta · Placental invasion · Prenatal diagnosis · Placenta praevia · MRI

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Introduction

Women with placenta accreta, placenta increta and placenta percreta are at high risk of preterm delivery and massive bleeding. Abnormalities in the placental implantation may result in the attachment of the placenta directly onto the myometrium (placenta accreta), extension deeper into the myometrium (placenta increta), or invasion into or through the uterine serosa (placenta percreta). Prior caesarean delivery and placenta praevia are the two most important risk factors for placenta accreta. The risk of placenta accreta is reportedly 24 % for women with placenta praevia and one previous

caesarean delivery, and 67 % for women with placenta praevia and three or more previous caesarean deliveries [1]. On the other hand, the risk of placenta accreta is reported to be 3.3 % for women with placenta praevia and no history of caesarean deliveries [2]. The incidence of placenta accreta has increased and seems to parallel the increasing rate of caesarean deliveries. The rate of caesarean deliveries was 4.5 % in 1965 and increased to 32.8 % in 2010 [3]. According to previous reports, the incidence of placenta accreta was about 1 in 533 pregnancies for the period of 1982–2002 compared with 1 in 4,027 pregnancies in the 1970s and 1 in 2,510 pregnancies in the 1980s [4,5].

In clinical terms, placenta accreta becomes a critical problem during delivery when the placenta does not completely separate from the uterus and causes massive intrapartum or postpartum haemorrhage, sometimes leading to disseminated intravascular coagulopathy. This requires intrauterine balloon tamponade, embolisation or surgery to stem the bleeding, and in severe forms can lead to a hysterectomy or be fatal [6,7]. Maternal mortality associated with placenta accreta has been reported to be as high as 7 % [8,9]. Thus, optimal planning, transfusion management and medical care should be conducted before delivery to minimise potential maternal or neonatal morbidity and mortality. The prenatal diagnosis of placenta accreta thus assumes an important role in perinatal planning. Most commonly, the placenta is evaluated first by means of ultrasound because it is performed on all pregnant women as routine antenatal care, can be performed easily at the bedside, has low cost and high diagnostic accuracy [9,10]. However, for cases where posterior placenta accreta is suspected, ultrasound may be insufficient. Many authors have therefore recommended MRI for women with inconclusive ultrasound findings [10–15]. Thus, MR findings for placental invasion require further clarification for overall improvement of diagnostic performance, especially for patients with placenta praevia. Recently, we encountered some patients with abnormal placentation featuring placental protrusion into the internal os detected with MR, and this finding may be helpful for diagnosis of invasive placenta praevia. Therefore, this study aimed to determine whether the presence of placental protrusion in the internal os (placental protrusion sign) can be as effective as the established MRI criteria as an indicator for invasive placenta praevia. In addition, the physical and sociodemographic risk factors for invasive placenta praevia were investigated in this study.

Materials and methods

Patients

This retrospective study was approved by our Institutional Review Board, and written informed consent was waived. Our department's radiological records from January 2009 to April 2013 were searched to find all pregnant patients who had undergone prenatal MRI examination. During this period, ultrasound was used for 1,839 pregnant patients, 130 of whom were suspected of having gynaecological disorders, and 65 of these 130 patients were confirmed through MRI to have placenta praevia and enrolled in this study. The other 65 patients were excluded, as they underwent prenatal MRI for other reasons: 42 were suspected of having other uterine disorders, 10 of having ovarian disorders and 13 of having foetal disorders. Non-invasive and invasive placentations were differentiated by consulting pathological reports or clinical intrapartum findings.

Physical and sociodemographic data analysis

Physical and sociodemographic data of the patients enrolled in this study that were possible risk factors for invasive placenta praevia [9,10,16–20] were evaluated by consulting clinical records. The evaluated factors were as follows: age, gestational age at delivery, body mass index at booking, smoking status, number of previous caesarean deliveries, previous uterine surgery or procedure (includes myomectomy, dilation and curettage, surgical termination of pregnancy, uterine artery embolisation), and IVF pregnancy.

MR imaging

All MRI examinations were performed on a 1.5-T unit (Achieva; Philips Medical Systems, Best, The Netherlands) with body array coils, including axial, coronal and sagittal T2-weighted half-Fourier single-shot turbo spin echo imaging (ssh-TSE), T2-weighted true fast imaging with steady-state precession sequence (balanced-FFE) or T2-weighted turbo spin echo (T2W-TSE). The acquisition parameters for ssh-TSE, balanced-FFE and T2W-TSE images are shown in Table 1.

Imaging analysis

Two board-certified genitourinary radiologists, one with 8 years' (Y.U.) and the other with 6 years' experience (Y.S.), who had no knowledge of either the histopathological findings or the clinical data, retrospectively reviewed the MR images. A total of six MRI features of the placenta were assessed in terms of their presence or absence. These features comprised an intraplacental thick dark band on ssh-TSE, T2-TSE and balanced FFE images (intraplacental T2 dark band), intraplacental abnormal vascularity, uterine bulging, heterogeneous placenta and myometrial thinning, all of which were previously identified as features of placenta accrete [21–25], as well as our novel finding, that is, placental protrusion into the internal os (Fig. 1). An intraplacental T2 dark band was

Table 1 MR imaging parameters

Sequence	Ssh-TSE	Balanced FFE	T2W-TSE
TR/TE (ms)	-/70-80	4.0–4.5/1.5–2.5	3,700–5,400/60–90
Flip angle (degree)	90	90	60-90
TSE/TFE factor	64-72	80-92	16-18
SENSE factor	2	2.5	-
Band width (Hz)	450-460	624-630	370-380
FOV (mm)	420-480	420-480	340-380
Acquisition matrix	256×256	256×256	256×256
Slice thickness/ gap (mm)	5-8/1-2	5-8/1-2	5-8/1-2
Number of slices	35-46	35-46	35-46
Total acquisition time (s)	40-50	50-55	150-160

Ssh-TSE, T2-weighted half-Fourier single-shot turbo spin echo imaging; Balanced FFE, T2-weighted true fast imaging with steady-state precession sequence; T2W-TSE, T2-weighted turbo spin-echo; TR, repetition time; TE, echo time; TSE, turbo spin echo; TFE, turbo field; SENSE, sensitivity encoding; FOV, field of view

deemed positive when its longest diameter was more than 2 cm [24]. Intraplacental abnormal vascularity has been defined as tortuous enlarged flow voids observed on T2-TSE or ssh-TSE sequences deep within the placenta and measuring at least 6 mm in diameter [25]. Each data set was independently reviewed by the two readers with a minimum interval of 1 month to avoid any decision threshold bias due to reading-order effects.

Statistical analysis

Physical and sociodemographic factors for invasive placenta praevia were investigated by using Fisher's two-sided exact test for comparing the women with invasive placenta to those with non-invasive placenta. Interobserver agreement for the interpretation of MR images was assessed by means of kappa statistics with quadratic weighting. A kappa value of up to 0.20 was considered to indicate slight agreement, 0.21–0.40 fair agreement, 0.41–0.60 moderate agreement, 0.61–0.80 substantial agreement, and 0.81 or higher almost perfect agreement. Each correlation between MRI features with a kappa value >0.40 and placental invasion was analysed by using Fisher's two-sided exact test.

SAS software (version 9.2; SAS Institute, Cary, NC, USA) was used for all statistical analyses. A two-tailed P value of <0.05 was considered significant. For these analyses, placenta accreta, placenta increta and placenta percreta were all considered to indicate invasive placentas without distinction.

Results

Fifteen patients were pathologically or clinically deemed to have placental invasion, and 14 patients underwent caesarean hysterectomy. Seven of them were pathologically diagnosed with placenta accreta, six with placenta increta and one with placenta percreta. The placenta of one patient could not be fully removed during the caesarean section and was clinically diagnosed as placenta accreta.

This study found, as did previous studies [1,9,10,18,19], that a history of two or more caesarean deliveries with placenta praevia was a significant risk factor for placental invasion (Table 2). There were no significant differences between other physical and sociodemographic factors of patients with and without invasive placenta praevia.

The findings resulting from MRI analysis of the intraplacental T2 dark band, intraplacental abnormal vascularity, uterine bulging, heterogeneous placenta and placental protrusion into the internal os showed moderate or better interobserver reliability. The details of the findings are shown in Table 3.

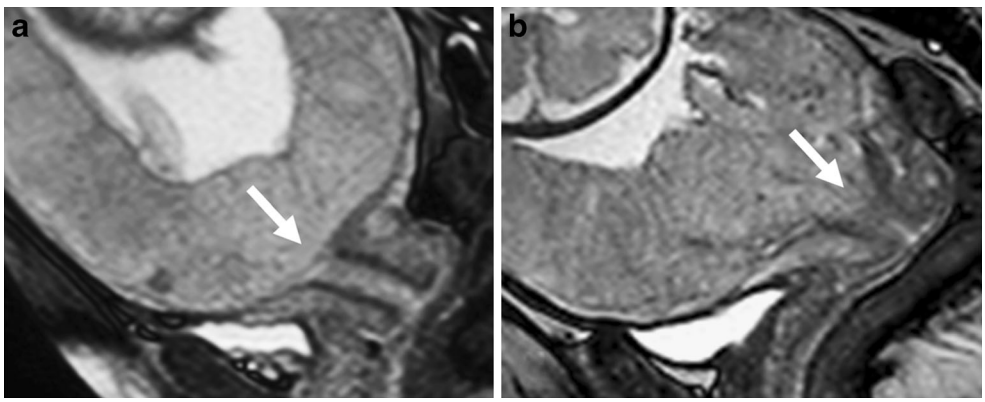

Fig. 1 Identification and definition of protrusion signs for patients with placenta praevia. (**a**) Sagittal T2 true fast imaging with steady-state precession sequence (balanced FFE) image shows that the placenta covers the internal os smoothly and does not project into the internal os. In such a case, the protrusion sign was defined as negative. (**b**) Sagittal balanced FFE image shows that the placenta pushes out and extends into the internal os. In such a case, the protrusion sign was defined as positive

Table 2 Physical and sociodemographic factors of patients studied

	Patients with non-invasive placenta praevia	Patients with invasive placenta praevia	*P* value
Number	50	15	
Age (years)			
Less than 35	29 (58 %)	8 (53 %)	
35 or older	21 (42 %)	7 (47 %)	0.61
Gestational age at delivery (weeks)			
Less than 27	0	0	
27-34	16 (32 %)	6 (40 %)	0.64
34-37	31 (62 %)	7 (47 %)	0.62
38 or more	3 (6 %)	2 (13 %)	0.78
Body mass index at booking			
Less than 25	40 (80 %)	10 (67 %)	0.60
25-29.9	9 (18 %)	4 (27 %)	0.68
30 or more	1 (2 %)	1 (6 %)	1
Smoking status			
No	48 (96 %)	14 (93 %)	
Yes	2 (4 %)	1 (7 %)	0.86
Number of previous caesarean deliveries			
0	42 (84 %)	4 (27 %)	0.67
1	8 (16 %)	6 (40 %)	0.66
2 or more	0 (0 %)	5 (33 %)	0.01
Other previous uterine surgery or procedure[#]			
No	46 (92 %)	12 (80 %)	
Yes	4 (8 %)	3 (20 %)	0.52
IVF pregnancy			
No	38 (76 %)	12 (80 %)	
Yes	12 (24 %)	3 (20 %)	0.43

Data in parentheses are percentages of individuals with complete data

[#] Includes myomectomy, dilation and curettage, surgical termination of pregnancy, uterine artery embolisation

Using Fisher's two-sided exact test, we found that the presence of an intraplacental T2 dark band, intraplacental abnormal vascularity, uterine bulging, heterogeneous placenta and placental protrusion into the internal os was significantly associated with invasive placenta praevia (Table 4).

Discussion

Our study showed a history of two or more caesarean deliveries with placenta praevia is a significant risk factor for invasive placenta, as did previous reports [1,9,10,18,19]. Furthermore, our results show that our new MRI finding of the placental protrusion sign is a useful addition to the established MRI findings for the diagnosis of invasive placenta praevia.

Placental invasion is defined as the condition in which anchoring villi implant onto uterine smooth muscle without intervening decidua. Matrix molecules, local growth factors and large granular leukocytes present in the decidualised endometrium are believed to play a role in regulating trophoblast invasiveness and the formation of a normal basal plate. It has been suggested that placental invasion is the consequence of the failure of the endometrium and decidua basalis to reconstitute after repair of a caesarean incision or other uterine surgery [26]. Placenta praevia, which is a risk factor for invasive placenta, reportedly occurs in approximately 0.3–0.5 % of pregnancies [20]. The cause of placenta praevia is still unknown, but it is reported to occur more commonly among women who are older, those who smoke, have had children before, have had a caesarean section or other uterine surgery, or who have scars inside the uterus [18,19]. However, the exact details of the pathological correlation between placenta praevia and placental invasion have remained unclear; uterine scarring may predispose women to placental implantation in the lower segment. Furthermore, the placenta overlying the less well-vascularised cervix following caesarean section may be subject to dysfunction of the factors regulating trophoblast invasiveness and/or a formation of the normal basal plates. Given these theories, it is understandable that a

Table 3 Frequency of and inter-observer reliability for MR imaging features for subjects with normal and with invasive placenta

	Non-invasive placenta praevia ($n=50$)		Invasive placenta praevia ($n=15$)		
MR imaging feature	Reader 1	Reader 2	Reader 1	Reader 2	Kappa value
Intraplacental T2 dark band	3 (6 %)	1 (2 %)	11 (73.3 %)	8 (53.3 %)	0.67
Intraplacental abnormal vascularity	0 (0 %)	1 (2 %)	13 (86.7 %)	11 (73.3 %)	0.82
Uterine bulging	1 (2 %)	4 (8 %)	10 (66.7 %)	8 (53.3 %)	0.52
Heterogeneous placenta	1 (2 %)	9 (18 %)	12 (80 %)	9 (60 %)	0.48
Myometrial thinning	44 (88 %)	30 (60 %)	15 (100 %)	15 (100 %)	0.24
Placental protrusion into internal os	0 (0 %)	0 (0 %)	11 (73.3 %)	10 (66.7 %)	0.85

Data in parentheses are percentages of individuals with complete data

Table 4 Fisher's two-sided exact test of MRI features for invasive placenta praevia

MR imaging feature	*P* value	
	Reader1	Reader2
Intraplacental T2 dark band	<0.0001	<0.0001
Intraplacental abnormal vascularity	<0.0001	<0.0001
Uterine bulging	0.0083	<0.0001
Heterogeneous placenta	0.0063	<0.0001
Placental protrusion into internal os	<0.0001	<0.0001

history of many caesarean sections leads to a high probability of invasive placenta praevia. This is compatible with the results of our sociodemographic data analysis.

Determining the presence or absence of an adherent placenta before delivery is essential for effective perinatal planning and management. Antenatal imaging techniques consisting of ultrasound and MRI can help establish the diagnosis of adherent placenta. As mentioned earlier, since many authors recommend MRI for women with inconclusive ultrasound findings [10–15], further clarification of MR findings for placental invasion is important for overall improvement of diagnostic performance.

Our new finding related to placental invasion, that is, the presence of placental protrusion into the internal os (placental protrusion sign), proved to be associated with invasive placenta praevia. In theory, however, basal plates may also play a role in regulating the development of villi. In the absence of a normal basal plate, proliferation of villi cannot be controlled, and they may thus protrude into the internal os. Normal patients were assumed not to show any protrusion signs by both reader 1 and reader 2. In the absence of a placental protrusion sign, the placenta is thus overwhelmingly likely to be normal. In cases in our study with positive protrusion signs, adhesion of the placenta to the cervix was proved pathologically. Moreover, no normal endocervical epithelium was observed in the adhering segment (Fig. 2). In one case, where the internal os was ill defined and the boundary between the internal os and the cervix was unclear on MRI, pathological analysis revealed that the placenta had infiltrated into the cervix (Fig. 3). Thus, normal but unclear internal os and cervix on MRI may also suggest the occurrence of

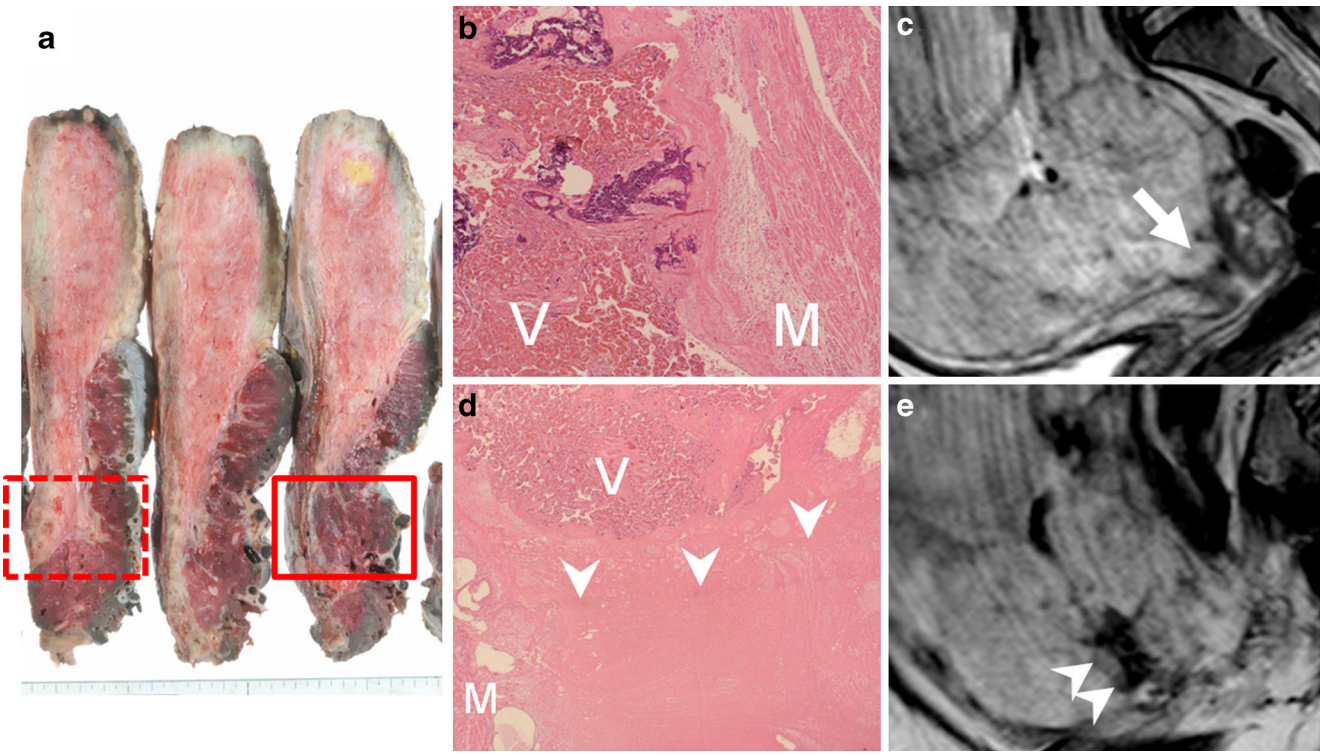

Fig. 2 A 36-year-old woman with placenta praevia and placenta accreta. (**a**) Hysterectomy specimen shows placental adhesion to the lower uterine segment and a portion of the cervix. The sections outlined with *solid* and *dashed lines* correspond to the uterine cervix and placental adhesion, respectively. (**b**) High-power field of view of the section outlined with a *solid line* in (**a**). Anchoring villi (*V*) have implanted directly onto the uterine smooth muscle (*M*) without intervening decidual cells. No normal endocervical epithelium was observed in the adhering segment. (**c**) Sagittal T2-weighted turbo spin-echo (*T2W-TSE*) image shows the placenta projecting into the internal os (*arrow*). (**d**) High-power field of view of the section outlined with the *dashed line* in (**a**). Thrombus is observed in the placenta (*arrowheads*). Anchoring villi (*V*) have implanted directly onto the uterine smooth muscle (*M*) without intervening decidual cells. (**e**) Sagittal T2W-TSE image shows intraplacental T2 dark band (*arrowheads*), corresponding to (**d**)

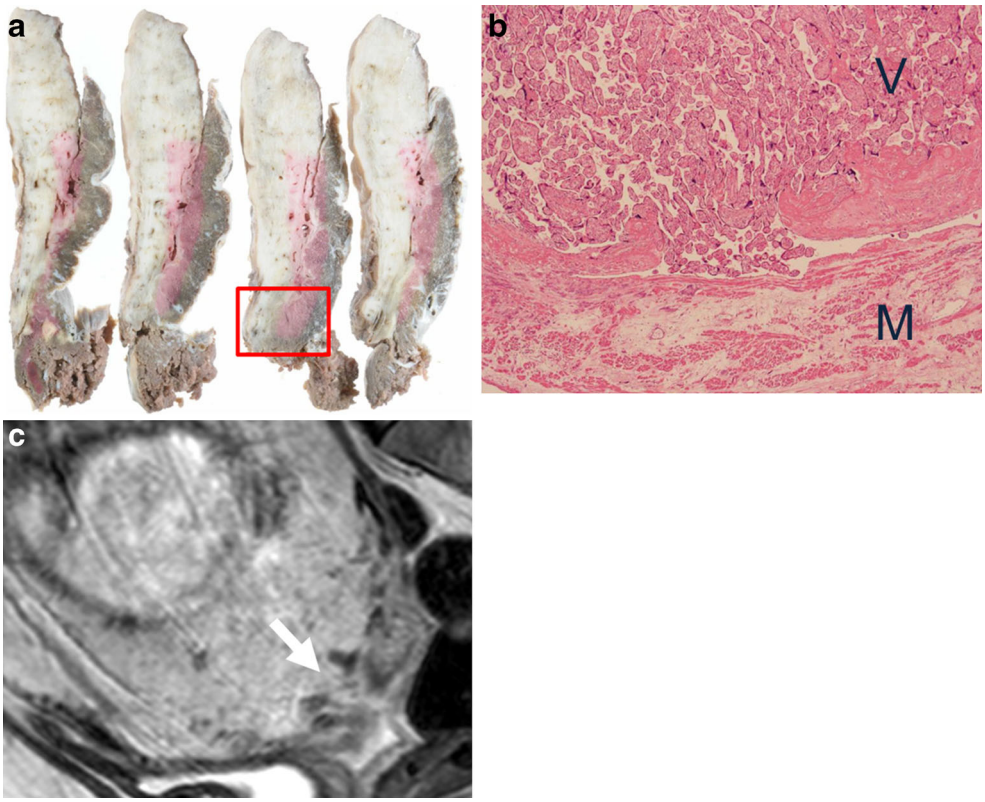

Fig. 3 A 34-year-old woman with placenta praevia and placenta increta. (**a**) Hysterectomy specimen shows placental adhesion to the lower uterine segment and a portion of the cervix. (**b**) The section in the *square* in (**a**) corresponds to the uterine cervix with placental adhesion. Anchoring villi (*V*) have implanted directly on the uterine smooth muscle (*M*) without intervening decidual cells. (**c**) Sagittal T2W-TSE image shows the placenta projecting into the internal os (*arrow*) and indistinct boundary between the internal os and cervix

placental invasion. One of the limitations of this study is that these MRI findings were unfortunately not compared with ultrasound findings. Signs of placental protrusion into the internal os can be evaluated by ultrasound, so that in this case a correlation between MRI and ultrasound findings of this sign should have been examined to confirm its clinical utility and reliability. Future studies should therefore include such correlation studies.

An early criterion for the identification of placenta accreta focussed on the evaluation of direct invasion of the placenta

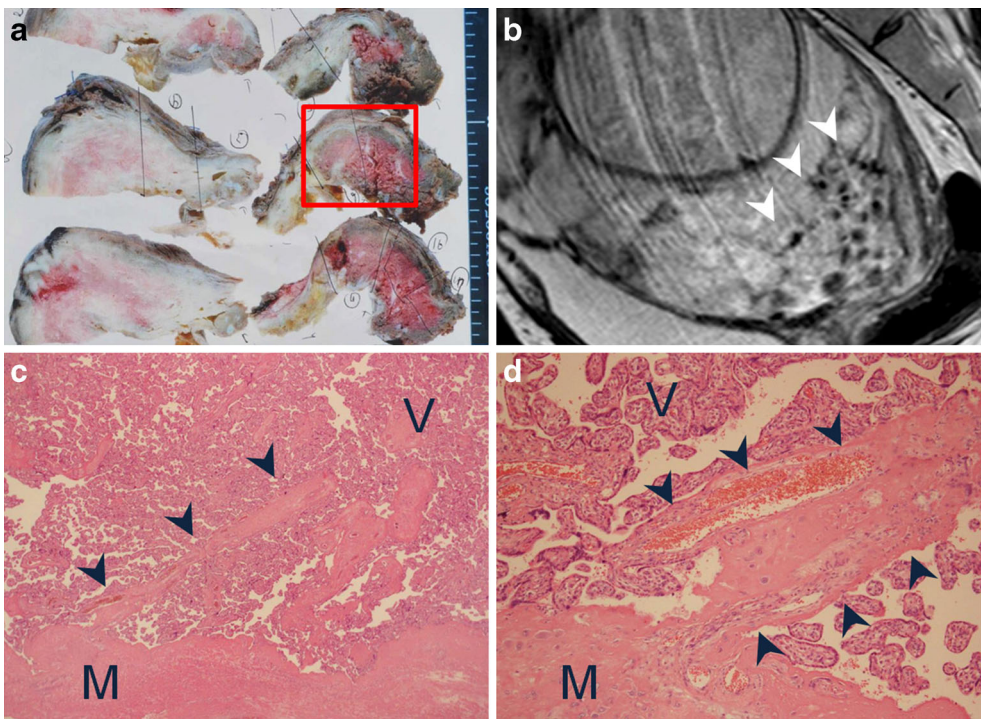

Fig. 4 A 34-year-old woman with placenta praevia and placenta accreta. (**a**) Hysterectomy specimen shows placental adhesion to the lower uterine segment and a portion of the cervix. (**b**) Sagittal T2W-TSE image shows abnormal intraplacental vascularity in the lower uterine segment. (**c**, **d**) High-power fields of view of the section in the *square* in (**a**). Anchoring villi (*V*) have implanted directly onto the uterine smooth muscle (*M*), without intervening decidual cells. Vascular structures that seem to originate from the maternal uterine myometrium were observed in the villi

into the uterus, as indicated by thinning or indistinctness of the myometrium [21]. However, several recent studies have reported that this MRI finding is non-specific because even in normal cases the myometrium becomes thin during pregnancy, especially in the third trimester. In our study, too, interrater reliability for the finding of myometrial thinning proved to be poor; thus, we regarded this MR finding to be unsuitable for the diagnosis of placenta accreta and it was excluded from the subsequent Fisher's two-sided exact test.

In 2007, Lax et al described three new secondary signs of invasive placenta on MRI [24]: an irregular, thick interplacental T2 dark band, marked placental heterogeneity and bulging of the lower uterine segment. Our study also showed that these three MRI findings were significantly associated with invasive placenta. A previous study found that an interplacental T2 dark band consisted of fibrin deposition histopathologically [27]. We also found that the T2 dark band on MRI corresponded to intraplacental fibrin deposition and that it was surrounded by placental adhesion (Fig. 2). Fibrin deposition can also occur in non-invasive placenta, but it is usually no more than 1–2 cm in size [24]. It can be assumed that there is a correlation between extensive fibrin deposition and placental adhesion and that the former can be a cause of placental heterogeneity. Lax et al. hypothesised that uterus bulging may be related to an abnormally tense myometrium that results from placental invasion into the normal myometrium. In this study, interrater reliability for the finding of an interplacental T2 dark band was substantial, but it was moderate for the findings of heterogeneous placenta and uterine bulging. It should be kept in mind, however, that the latter two findings may be relatively easily influenced by the readers' subjective interpretation.

In 2011, Derman et al. identified an additional MR criterion, abnormal placental vascularity [25]. It is defined as tortuous enlarged flow voids on T2-TSE or ssh-TSE sequences deep within the placenta measuring at least 6 mm in diameter. Several authors using 2D colour Doppler or 3D power Doppler ultrasound also reported that abnormal placental vascularity was detected in invasive placenta [28,29]. Moreover, both reader 1 and reader 2 in our study confirmed that there was a significant correlation between abnormal placental vascularity and placental invasion. Furthermore, MRI findings confirmed the pathological findings of dilated vascular structures that seemed to originate from the uterine myometrium (Fig. 4). Normal maternal spiral arteries at the myometrium-placenta interface are positioned parallel to the villous branches of the chorionic arteries and perpendicular to the surface of decidual cells. One hypothesis is that the maternal artery may develop where the placenta adheres closely to the myometrium and subsequently infiltrates the placenta.

There are several limitations to this study besides the omission of correlation analysis of MRI and ultrasound findings mentioned earlier. First, the size of the invasive placenta sample was small because of the rare occurrence of this condition. This may have affected the results of statistical analyses. Furthermore, because the correlation between each of the MRI features was strong, multivariate analysis was considered unsuitable and therefore omitted. Second, this was a retrospective study, but the results reported here can be helpful for the initiation of a new, prospective study to evaluate the diagnostic capability of MRI for placental invasion. Finally, comparing MRI and pathological findings is problematic in that the pathological cutaway view does not necessarily correspond to the MRI slice section. In addition, we could not perform correlation analysis of the imaging and pathological findings of the case, which was proven by surgical assessment to have an invasive placenta. In spite of these limitations and the need for further studies, we suggest that the new MRI finding of protrusion of the placenta into the internal os is as good an indicator of invasive placenta praevia as other previously reported MRI findings.

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