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Title: Prenatal ultrasound imaging for placenta accreta spectrum (PAS): a practical guide

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Abstract

Purpose of review:

The incidence of placenta accreta spectrum (PAS) is increasing, but it is still a rare pregnancy complication. If undiagnosed, PAS can cause serious maternal morbidity and even mortality at delivery. Ultrasound (US) is an excellent imaging modality for the diagnosis of PAS, but it must be used correctly and there is little training in placental imaging available. The aim of this paper is to review US screening for PAS and provide practical advice on its use for antenatal diagnosis.

Recent findings:

Screening for PAS in a high-risk population (history of previous caesarean delivery (CD) and an anterior low lying/previa placenta) is feasible in well-trained hands with a high sensitivity and specificity from the first trimester but usually occurs around 24-28 weeks. A detailed examination of the placental bed using the US signs defined by EW-AIP with an adequately filled bladder enables the operator to produce a detailed report fully outlining the anticipated findings at delivery. This facilitates a real multi-disciplinary team (MDT) approach which is the goal for optimal PAS management.

Summary:

Women with a history of previous CD and an anterior low lying/previa placenta need a detailed examination of the placenta by an experienced operator. The US examination should be undertaken systematically, and the risk factors and US signs reported in a way which is useful to the MDT.

Keywords:

Placenta accreta spectrum (PAS); abnormally adherent and invasive placenta (AAIP); abnormally invasive placenta (AIP); caesarean scar pregnancy (CSP); ultrasound; screening

Introduction

Placenta accreta spectrum (PAS) or abnormally adherent and invasive placenta (AAIP) defines the clinical conditions where the placenta abnormally adheres to or invades the uterine wall. The Nitabuch layer of the decidua is missing and therefore spontaneous placental separation is not possible. This can affect the whole placental surface or only a part of it (focal PAS). If the placenta is forcibly removed, severe sometimes life-threatening, haemorrhage can ensue.

The pathologist differentiates PAS into 3 subgroups based on the macroscopic and microscopic findings of the relationship between the placenta and the myometrium. Placenta accreta is defined by abnormal attachment to the myometrium with an absent decidua; Increta represents invasion of the trophoblast into the myometrium; Percreta has trophoblast which completely invades the myometrium up to the serosa or even beyond.(1) If clinicians only employ a histopathologically-based system to classify prenatal imaging, they are not fully utilising the available signs to inform clinical management and delivery. Therefore, prenatal imaging should not only attempt to diagnose presence of PAS but should also aim to predict clinically relevant findings, such as neovascularity, posterior bladder wall involvement or cervical invasion, so that management (surgical or conservative) can be appropriately formulated in advance thereby reducing maternal morbidity at delivery.(2) The aim of this paper is to discuss techniques for ultrasound (US) screening for PAS and provide practical advice on the antenatal diagnosis and classification.

Screening for PAS:

The prevalence of PAS in the general population of pregnant women is highly variable at between 1.7 and 16 per 10,000 pregnancies.(3, 4) As previous caesarean delivery (CD) is the single greatest risk factor for PAS, this variation may be partly related to the local CD rate. Also, the location of the scar on the uterus determines the inherent risks of any resulting PAS. PAS invading a previous lower segment caesarean scar provides a particularly 'toxic' combination as the risks are significantly increased due to factors related to the anatomical location including; potential for transecting the placenta with a lower segment incision; the poor contractility of the lower segment and the potential for invasion into the bladder, cervix and/or parametrium. Therefore, identifying women antenatally with a placenta

previa complicated by PAS has the greatest potential for reducing maternal mortality and morbidity, consequently most current guidance, including that from FIGO and the RCOG, focusses screening on the subset of women with previous CD.

Fortunately, robust prenatal diagnosis of PAS is possible using US as long as the operator is experienced.(5) A systematic review and meta-analysis of US studies involving 3707 pregnancies at risk for PAS (history of caesarean section combined with anterior low-lying or previa placenta) found that the overall performance of US is excellent, with a sensitivity of 90.72% (95% CI 87.2-93.6), specificity of 96.94% (95% CI 96.3-97.5), and diagnostic odds ratio of 98.59 (95% CI 48.8-199.0).(6) Therefore, the placental location should be assessed in all women presenting for a mid-trimester US scan. If the placenta is low (<2cm from the internal os) or a previa (covering the internal os) she should be asked if she has had a previous CD.(5, 7) If she has, she should be referred to the most experienced operator available for a more detailed US examination of the placenta. If the diagnosis is unclear, a second opinion should be organized by an operator with sufficient experience in the prenatal assessment of PAS.(5, 7, 8)

Preferably all sonographers should be aware of the signs of PAS however, this is not yet a standard part of US training courses and there is no prospective data on the efficacy of screening for PAS at the routine midtrimester US examination by non-expert operators.(9) Introducing a population based screening program would require careful consideration, planning and assessment for clinical utility, but the current pragmatic strategy is becoming increasingly necessary owing to the constant rise in the number of CDs.(8)

First trimester screening for PAS

Under the right conditions, PAS can be screened for at the 11-13 week US scan. Panaiotova et al (10) screened 22,604 singleton pregnancies by recording the placental location and asking about history of uterine surgery. 1298 (6%) were considered at high risk for PAS due to a low lying placenta and a history of uterine surgery. These were all referred to a specialist clinic and re-assessed at 12-16 weeks for the presence of the following signs: non-visible caesarean scar, bladder wall interruption, thin retroplacental myometrium, presence of intraplacental lacunar spaces, presence of retroplacental arterial-trophoblastic blood flow and irregular placental vascularization demonstrated by three-dimensional power doppler. (Figure

3). Fourteen women were diagnosed with PAS at 12-16 weeks' gestation. At delivery 13 of these women were confirmed to have PAS with one false positive. No false negatives were reported.(10)

Caesarean scar pregnancy and PAS

Recent evidence suggests that caesarean scar pregnancy (CSP: Figure 1) is the precursor of PAS. (10, 11). In 2003, Jurkovic et al proposed the diagnosis of CSP by transvaginal US should be made if the following criteria were satisfied: 1. Empty uterine cavity; 2. Gestational sac located anteriorly at the level of the internal os covering the visible or presumed site of the previous lower uterine segment caesarean section scar; 3. Evidence of functional trophoblastic/placental circulation in colour and/or pulsed Doppler examination; 4. Negative "sliding organs sign" (inability to displace the gestational sac from the level of the internal os using gentle pressure on the transvaginal probe).(12) (Figure 2)

More recently reported is the 'crossover sign' (COS) which aims to define the location of the CSP more precisely in an attempt to assess the risk of adverse pregnancy outcomes including development of PAS.(13) Authors recommend the following technique: in a sagittal view of the uterus, a straight line is drawn connecting the internal cervical os and the uterine fundus through the endometrium (endometrium line). The gestational sac is identified and its superior-inferior diameter (S-I), perpendicular to the endometrial line, is traced. Patients are categorized according to the relationship between the endometrial line and the S-I diameter of the gestational sac into two groups. (Figure 3) A subsequent retrospective study with 68 pregnancies concluded that the COS may identify women who will go on to develop clinically significant PAS(14) but further confirmatory research is needed to confirm clinical utility.

The current issue with diagnosis of CSP is that many women do not have an US scan before 11 weeks' gestation unless they experience complications such as vaginal bleeding. This can make the diagnosis difficult due to the size of the sac by this gestation. The smaller the gestational sac is, the easier it is to define whether it is within the caesarean niche, surrounded by myometrium or "just" close to the internal os and in limited contact with the caesarean scar.(12) Another issue limiting introduction of screening for CSP is how to manage it when it is diagnosed. A recent systematic review and meta-analysis showed that CSP with fetal heart activity

managed expectantly is associated with a high rate of maternal morbidities including haemorrhage, early uterine rupture, hysterectomy and severe PAS.(15) A second systematic review of different treatment strategies on CSP report a hysterectomy rate of 1.5-7% in 3 randomized controlled trials and of 41% in case of expectant management.(16) Out of the 41 pregnancies managed expectantly, 31 live birth occurred (74%). The only prospective case series to describe the natural evolution of CSP was reported by Zosmer et al.(17) In 10 cases, five women needed a hysterectomy at delivery for PAS but no fetal nor neonatal complication was described. Therefore, the woman should be informed about the high risk of pregnancy complications from severe haemorrhage (PAS included) and interruption of pregnancy can be offered. However, clear evidence to support systematic pregnancy interruption in all cases of CSP does not exist.

It has recently been proposed that an early (6-9 weeks) first trimester scan should be mandatory in pregnancies following a caesarean delivery.(18) The evidence for such a statement is weak but the hypothesis is logical. Further investigation with prospective studies including a detailed description of the type of CSP, pregnancy follow-up and the outcome for mother and child are required to support this.

Practical advice for ultrasound examination for PAS

- *Transabdominal or transvaginal?*

The examination is classically started by a transabdominal approach with a standard convex ultrasound probe (3-5 MHz). Improvement in image quality can be obtained by using a higher frequency (5-9MHz) probe or where possible, a linear transducer. Indeed, in the case of an anterior placenta, depth of penetration is usually less important and better resolution close to the probe is required. This is possible with a high frequency probe. The placenta has to be explored systematically, from one border to the other, in order to examine the entire placental bed. The transabdominal scan generally provides a good overview and many clinicians are happy to rely on just this modality although it can be limited in women with a high body mass index (BMI). This is often overcome however, by asking the woman to lift her panus and scanning underneath it. Some clinicians prefer the transvaginal approach which generally also employs a high frequency probe. The advantage is closer proximity to the lower segment, cervix and praevia or low-lying placenta, but the field of view is

narrow. It also provides the most accurate assessment of the relationship of the placenta to the internal os of the cervix to define if it is a previa. If the rationale is explained, the transvaginal approach is usually well accepted by the women. Most clinicians employ a combination of transabdominal and transvaginal US according to the individual woman's circumstances.

- *Machine settings*

The appropriated setting of the US machine is important for correct 2D grayscale imaging (depth, focus and gain), but it is even more essential when using colour flow mapping and power Doppler. Excessive vascularity of the lower uterine segment is associated with abnormal placental invasion but is an extremely subjective sign. It is even challenging for highly experienced operators to correctly assess blood flow. Appropriate machine setting includes the correct power Doppler gain setting for the individual woman, often referred to as the sub-noise gain. This is the gain value where any bloom artefact just disappears on reducing the level. This individual setting allows for optimal visualization of the flow despite differences in tissue attenuation. Likewise, the correct velocity scale for colour flow is crucial to appropriate visualization of the vasculature: if it is set too high, low flow will not be seen; if too low, an "aliasing" artefact will appear.(8)

Many modern US machines also offer compound imaging (CRI, CrossXBeam, sonoCT etc). This sends signals at multiple angles, allowing it to "see" tissue from multiple angles with the intention of eliminating artefact. This effectively 'smooths' the image seen and tends to blur the interface between the placenta and the myometrium, making many of the US signs difficult to interpret. It should be turned off when examining for the grayscale signs of PAS.

- *Gestation for USS*

Although Panaiotova et al (10) demonstrated that PAS can be diagnosed between 12 and 16 weeks, they relied on placental localisation at 11-13 weeks to assign risk and determine who should be referred to the specialist clinic. Until sonographers are adequately trained to reliably identify placental location in the first trimester the majority of screening will occur at the mid-pregnancy anomaly scan. The timing of the diagnostic US by an experienced operator will depend on the resources available but should preferably be as soon as possible in women with any risks for preterm

delivery or vaginal bleeding to enable a risk assessment to be made in the event of an emergency delivery. Asymptomatic women with no risks for pre-term delivery can usually wait until after 24 weeks (when the trophoblast invasion should be complete) but should be seen by 28 weeks at the latest.

- *Requirement for bladder filling*

The US scan must be performed with a filled bladder (between 200-300ml). This is vital because the bladder outline enables identification of the lower uterine segment, presumed location of the previous caesarean scar, and allows assessment of placental position relative to it. Also, without a full bladder, important signs such as bladder wall interruption, placental bulge and utero-vesical hypervascularity cannot be appropriately assessed.(8, 19, 20) (Figure 4)

- *Probe pressure*

If too much pressure is exerted on the transabdominal US probe the “retroplacental clear zone” can be obliterated and the myometrium appear falsely thinned leading to anomalous results. (Supplementary video 1)

- *Insonation angle*

It is important to ensure that the probe remains as perpendicular to the placental bed as possible to facilitate appropriate examination of the placental-myometrial interface. Failing to do so can lead to significant ‘drop-out’ artefact preventing robust assessment particularly of the lower aspect of the lower segment (Figure 5).

Standardised ultrasound descriptors

In 2016, the European Working Group on abnormally invasive placenta (EW-AIP) published a proposal to standardize US descriptors of PAS produced by Delphi consensus (21). The aim was to produce a clear definition for each commonly cited US sign based on the published descriptors. US images with examples of the presence and absence of each descriptor are published in this paper (21).

The EW-AIP standardised ultrasound signs and their physio-pathology

- *Loss of the “clear zone”*

This term is used when the hypoechoic line normally seen in the myometrium under the placental basal plate (the “clear zone”) is not visible on ultrasound. The echolucent area under the placenta is thought to be caused by the thinning of the decidual basalis and development of the fibrinoid layer (Nitabuch’s layer).(19) It’s absence is thought to be caused by an abnormal extension of the placental villi through the decidua basalis into the myometrium. This sign has been reported in around 70% of cases in series that include information on the depth of invasion.(22) It has been noted that the appearance of this sign changes with advancing gestational age and can be more easily seen in an anterior high, placenta. Care must be taken with the US probe pressure as it can be easily obliterated by pressing on the surrounding tissues. It is more readily visualised with a filled bladder.(20)

- *Myometrial thinning*

This sign is reported as prenatal diagnostic sign for PAS but is only reported in 50% of cohort studies.(22) In abnormally invasive placenta the myometrium appears to be vanishingly thin as it cannot be seen (or measured) separately to the placenta. Differential diagnosis includes a “uterine window”, here a normal placenta covers a dehiscence in the myometrium. Therefore, the pathology of a uterine window is that of a scar defect rather than a placental abnormality.(19)

- *Placental lacunae*

This is the presence of numerous lacunae including some that are large and irregular, often containing turbulent flow visible in greyscale imaging. This descriptor is visible on transabdominal and transvaginal US and is the most common US sign described in PAS with around 80% of the authors reporting it prenatally, independently of the depth of invasion.(19) The differential diagnosis has to be made with placental lakes (echolucent areas in the centre of a cotyledon) which have nothing to do with PAS.

Placental lacunae develop secondary to the distortion of the anatomy of 1 or more cotyledons including in interlobular septa due to the arrival of high-velocity (peak systolic velocity often >10cm/sec) maternal blood from a radial or arcuate artery.(23) The blood flow inside the lacunae can be detected and observed also in colour and/or pulsed-wave Doppler.

- *Placental lacunae feeder vessels*

These are seen as vessels with high velocity blood flow arising from the deep arterial vasculature of the myometrium which feed the lacunae. An study found that the total area occupied by vessels in normal and placenta increta placenta beds is similar, but that vessels are significantly sparser and larger in an invasive placenta.(24) This could explain the abnormal hemodynamics underlying the development of the lacunae in invasive placentation.

- *Bladder wall interruption*

This is the loss of, or interruption to, the bright line representing the bladder wall (the hyperechoic line between uterine serosa and the bladder lumen). This is potentially caused by villous invasion into the muscle of the posterior wall of the bladder, thereby changing the echogenicity, but is most often an US artefact arising from the massive neovascularity found between the posterior bladder wall and the anterior aspect of the uterus.(19) Care must be taken with the angle of insonation which can cause artefactual drop-out if the probe is not kept in the correct axis to the placental bed.

- *Placental bulge*

This is defined as the deviation of the uterine serosa away from the expected plane, caused by an abnormal bulge of placental tissue into a neighbouring organ, typically the bladder. The uterine serosa appears intact, but the outline shape is distorted.(21) It's most likely represents villous invasion deep into and/or through the myometrium resulting in loss of structural integrity of the surrounding uterine muscle. The placenta will then bulge outward into surrounding structures.(19) This phenomenon is also described at MRI and laparotomy (the "snowman" sign).(25)

- *Focal exophytic mass*

Placental tissue seen breaking through the uterine serosa and extending beyond it usually into a filled urinary bladder. This finding is extremely rare.

- *Subplacental and/or utero-vesical hypervascularity*

This is the observation of a 'striking' or abnormally large amount of colour Doppler signal seen in the placental bed or between the myometrium and the posterior wall of

the bladder. It is a subjective decision by the operator and therefore requires experience with normal placental beds which are very vascular. This sign probably indicates numerous, closely packed, tortuous vessels in that region (demonstrating multi-directional flow and aliasing artefact). It results from excessive dilatation of the uteroplacental circulation beyond the spiral arteries, including the radial and arcuate arteries as well as the myometrial arterio-venous anastomoses (26), and it's a prominent feature of PAS on prenatal US.(19) This can indicate the finding of extensive neo-vascularisation within the peritoneum, especially between the anterior wall of the uterus and the posterior wall of the bladder at laparotomy.

- *Bridging vessels*

These vessels appear to 'bridge' from the placenta, across the myometrium and beyond the serosa into the bladder or other organs. Often running perpendicular to the myometrium.(21) This 'bridging' is an US artefact as these vessels do not traverse between the myometrium and bladder but are actually the contorted vessels of the neovascularity within the peritoneum caught in cross-section in a 2-dimensional image.(19)

Reporting an ultrasound scan for PAS

An international consortium of experts published a pro forma for US reporting in suspected PAS-cases (27). Following this document ensures that the operator has considered many of the risk factors associated with PAS then examined the woman in a systematic manner, reporting on all of the standardized descriptors. This should ensure that all potential diagnostic factors have been considered and help the operator to come to a decision on the risk of PAS for that particular woman. However, an US report needs to be useful for the other healthcare providers involved including the surgeons preparing for delivery. Difficult decisions need to be made in advance of starting the surgery such as whether partial surgical resection or conservative management may be appropriate.(28) To decide this, the surgical team need detailed information regarding the invasion and vascularity they will find when they start to reflect the bladder downwards e.g. into the cervix or parametrium. The US operator is in the perfect position to provide this information and so should consider what clinically relevant information is required.

The US report should therefore contain detailed information on the exact location of the placenta and its relationship to the surrounding structures, the degree of vascularity seen between the bladder and anterior uterus and in the cervix/parametrium, and the thickness of the myometrium. US reports should no longer just report the signs and state “possible percreta on the left” but should give a detailed, clinically useful report e.g. “there is an antero-left lateral placenta previa covering the internal os and extending posteriorly for approximately 5cm. This is seen to be bulging into the bladder and possibly the broad ligament on the left. The myometrium is vanishingly thin and cannot be identified on the left where there is suspicion of invasion into the posterior bladder wall. There is significant hypervascularity anteriorly and extending into the cervix on the left side”. This will enable to surgical team to plan appropriately and ensure that the correct decision on management strategy is taken before the surgery is started. To ensure that this occurs it is vital that the US operators understand the complexity of surgery and the surgeons understand the difficulties and potential limitations of the US. A truly well-functioning multi-disciplinary team (MDT) will have the US operators who have been present in theatre and surgeons who are familiar with the US room.

Clinical grading at delivery

Comparison of US description with clinical observation at delivery and with the pathological report if available is of great importance. FIGO has recently produced a clinical classification for PAS determined by the findings at delivery .(29) This should be reported for all cases of PAS and the exact intrapartum findings fed back to the sonographer and compared to the report and images to ensure ongoing continual professional education. An MDT debriefing after delivery should be considered to improve the understanding of PAS by each team-member.

Conclusion

Whilst PAS remains relatively rare the incidence is increasing significantly with the rising rate of caesarean delivery. Women with a history of previous CD and an anterior low lying/previa need a detailed examination of the placenta by an experienced operator. The US examination should be undertaken systematically and the risk factors and US signs reported as per the recommended proforma. The sonographer should also endeavor to report the clinically relevant findings which will

enable the surgical team to plan the delivery. If the examination is inconclusive or PAS is suspected, the patient should be referred to a center of excellence(28) in PAS-management to get second opinion and/or best clinical management for delivery.

Figures

Figure 1

35 years G3P2 history of one caesarean section, referred at 15 weeks.

- A. Sagittal view of the uterus demonstrating the location of the pregnancy in the lower uterine segment (solid line: empty uterine cavity, arrow: urine in the bladder)
- B. Transverse view with colour Doppler showing the important blood flow around the gestational sac.

Figure 2

- A. Caesarean scar pregnancy (CSP) at 7 weeks with positive embryonic/fetal heart activity. Retroverted uterus. (Supplementary video 2A)
- B. CSP at 6 weeks, no fetal heart activity and not viable with low progesterone and decreasing HCG. Anteverted uterus.
- C. Same CSP as image B with colour Doppler. This highlights the extent of blood flow around the gestational sac even in a non-viable pregnancy.

Figure 3

- A. Caesarean scar pregnancy (CSP) at 5+ weeks as example for the “crossover sign” (solid line: endometrium line, dotted line: superior-inferior line)
- B. CSP at 6+ weeks: “crossover sign” (solid line: endometrium line, dotted line: superior-inferior line)

Figure 4

Sagittal view of the lower segment of the uterus in the third trimester (A. empty bladder, B. full bladder, C. full bladder with colour doppler)

(Supplementary videos 4A, 4B and 4C)

Figure 5

Case of PAS in the lower uterine segment: A. Incorrect angle of insonation (artefacts at the bladder-placental interface); B. More appropriate angle of insonation better (any artefacts at the bladder-placental interface)

Supplementary Videos:

- Example of excessive probe pressure (Supplementary video 1)
- To accompany Figure 2 – Supplementary video 2A
- To accompany Figure 4 - Supplementary videos 4A, 4B and 4C

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