Delayed and successful manual removal of abnormally adherent placenta necessitated by uterine sepsis following conservative management with adjuvant methotrexate – a rewarding clinical experience

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Abnormally adherent placenta is characterised by direct attachment of chorionic villi to the uterine wall, often resulting in life-threatening postpartum haemorrhage. Traditionally this complication has been managed by peripartum hysterectomy, which is associated with massive blood loss, injuries to the urinary tract and, importantly, permanent loss of fertility. Encouraging results reported in recent years have led to a gradual shift towards conservative management of select cases of placenta accreta, with the primary aim of conservation of the uterus and fertility. This strategy also avoids the surgical morbidity of peripartum hysterectomy. We report a case of placenta accreta in which delayed manual removal necessitated by uterine sepsis following conservative management with methotrexate was completely successful.

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Obstetric haemorrhage results in a significant proportion of maternal deaths worldwide, and abnormally adherent placenta (AAP), comprising placenta accreta, increta and percreta, is a rare but important cause of haemorrhage.[1] The incidence of AAP is on the rise owing to increasing caesarean delivery rates, and obstetricians are likely to see this unusual complication more frequently. The established method of treatment in postpartum haemorrhage due to AAP remains peripartum hysterectomy,[2] which is associated with high surgical morbidity and is a difficult choice when the patient wants to preserve her fertility. We report a case of AAP managed conservatively with adjuvant methotrexate (MTX) followed by delayed but successful complete manual removal of the placenta, necessitated by uterine sepsis. There have been numerous reports[3] of spontaneous explusion of placental tissue after MTX therapy for AAP, but to the best of our knowledge this is the first case in which manual removal necessitated by uterine sepsis was complete and successful.

Case report

A 26-year-old primipara was referred to our institute with retained placenta, 48 hours after giving birth vaginally at home. Manual removal of the AAP had been attempted and abandoned at the referring institute. The patient said that she had not had uterine surgery or curettage of any kind in the past. She was markedly pale (haemoglobin concentration 5.1 g/dl) but haemodynamically stable. The uterus was non-tender and well retracted, with the fundus palpable at the umbilicus. There was no active vaginal bleeding. Manual removal was attempted, but was unsuccessful because the placenta was adherent to the anterior uterine wall and no plane of cleavage could be found between them. On grey-scale ultrasound imaging, 10×7 cm placental tissue was visualised with loss of the retroplacental sonolucent zone. On magnetic resonance imaging (MRI), placental tissue was seen to be invading the myometrium with consequent myometrial thinning in the left parasagittal plane anteriorly (Figs. 1 and 2).

The young woman expressed a strong desire to preserve her fertility, and opted for conservative management. A septic screen was negative and prophylactic broad-spectrum antibiotics were initiated. A single dose of 60 mg (1 mg/kg) MTX was administered intramuscularly. The patient had a spike of fever on day 7 of the conservative management. At this time the uterus was non-tender, blood, urine and endocervical swab cultures were sterile, and the white cell count was within normal limits. Parenteral ampicillin, clindamycin and gentamycin were initiated. The patient remained afebrile for 3 more days, but then developed a high-grade fever with chills and rigors. The white cell count rose slightly. Abdominal examination revealed a surprising 3 cm involution of the uterine fundus. Bimanual examination revealed an open cervical os and the new finding of a plane of cleavage between the placenta and the myometrium. Complete manual removal of the placenta was done in theatre and confirmed by ultrasound during

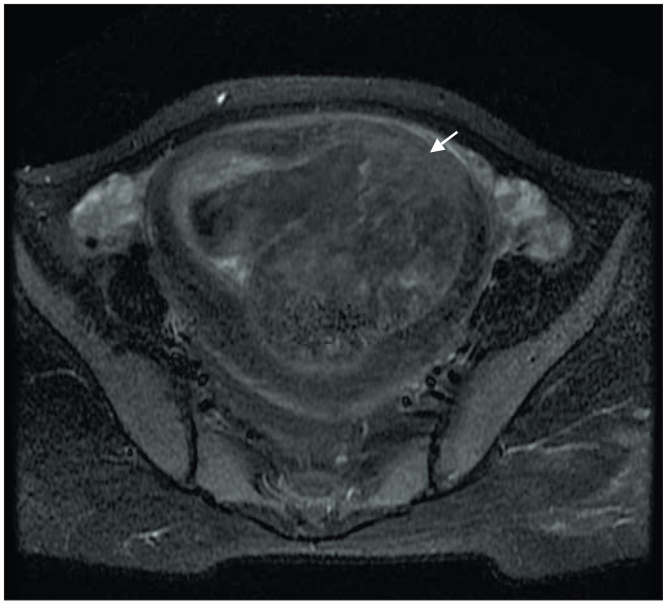

Fig. 1. Fat-saturated T2W axial magnetic resonance image showing hyperintense signalling in the anterior uterine wall to the left of the midline (arrow), thinning of the myometrium, and disruption of the normal placental myometrial interface.

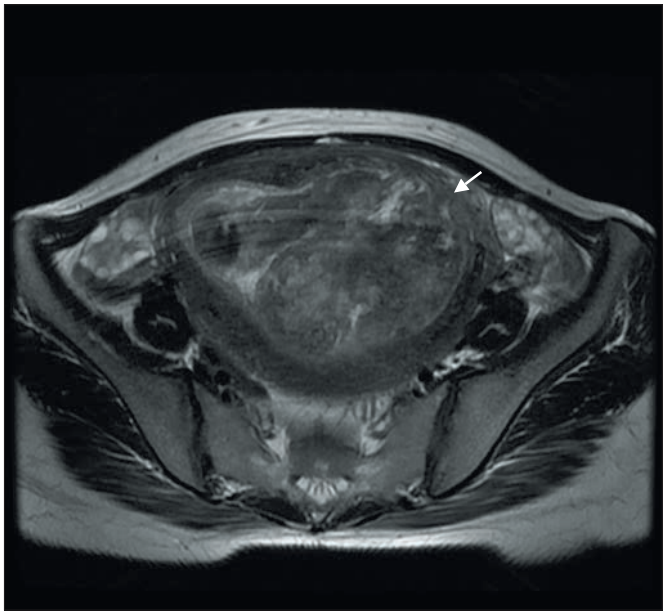

Fig. 2. T2W fast spin echo image showing hyperintense signalling of the anterior uterine wall to the left of the midline (arrow).

the procedure. The placenta was necrotic and foul smelling, and was sent for histopathological examination. The patient's condition improved dramatically after its removal, and she was discharged 5 days later.

Discussion

AAP is a rare condition, characterised by attachment of chorionic villi directly to the myometrium and is likely to be seen more frequently in the near future owing to rising caesarean section rates. Although the reported incidence ranges widely from 1 in 540 to 1 in 2 500 because of the varying clinicopathological criteria used to define the condition,[4] there is universal agreement with regard to its dramatic rise in the past 3 - 4 decades.[1,2]

The major risk factor for AAP is prior caesarean section. Minor factors include prior uterine curettage, endometrial ablation, myomectomy, hysteroscopic surgery and uterine artery embolisation – curiously, our patient had none of these. Despite the risk factors being well established, the underlying cause of AAP is not fully understood. Current aetiological concepts include abnormal decidualisation (with an absent normal plane of cleavage above the decidual basalis) and a primary defect of trophoblast function leading to abnormal invasiveness.[5] AAP can be diagnosed antenatally in patients at risk with grey-scale ultrasound, aided by colour Doppler and MRI. Postnatally the diagnosis is made clinically, when placenta is retained and attempts at manual removal reveal an AAP leading to profuse uterine bleeding. Although there are a number of imaging (ultrasound, Doppler and MRI) features characteristic of AAP in the antenatal period,[5] there is not much clarity with regard to whether the same features apply in postnatal detection of AAP.

The established method of management of AAP is peripartum hysterectomy,[2] which is associated with significant surgical morbidity, massive haemorrhage and, importantly, loss of fertility.[6,7] When a case is diagnosed before delivery, the outcome is likely to be best if the patient is managed in a tertiary-level setting by a multidisciplinary surgical and supportive team.[8] Every detail from skin incision and type of uterine incision to uterine conservation or radical management can be planned in advance. The management of postnatally diagnosed placenta accreta is more challenging, as the diagnosis is usually made in an emergency situation with little or no time for planning. The obstetrician's task is challenged further if the patient wants to preserve her fertility, because experience with conservative management is anecdotal, narrow and still evolving. The primary aim of conservative management is preservation of the uterus and fertility. An additional benefit is avoidance of the surgical morbidity associated with peripartum hysterectomy.

Conservative management of AAP includes leaving the placenta completely or partially *in situ* with or without adjuvant MTX and/or proximal vascular occlusion.[3] Prophylactic antibiotics have been recommended for prevention of uterine infection, but their efficacy remains to be proven. Placental involution is assessed by serial ultrasound scans and/or MRI. Serial serum human chorionic gonadotrophin measurements as a marker of placental involution have not been found to be reliable.[3,9] Complications of conservative management include profuse vaginal bleeding, uterine sepsis, fever, placental polyp formation and vesico-uterine fistula formation (in placenta percreta involving the urinary bladder). Vaginal bleeding and sepsis are the two main complications resulting in treatment failure, and require long-term follow-up.[3]

Use of MTX for the conservative management of AAP was first described by Arulkumaran *et al.*,[10] and since then more than 20 cases have been described. It is assumed that MTX hastens absorption of the placenta by reducing its vascularity rather than affecting cellular multiplication, since trophoblast proliferation is absent at term. Insight into the role of MTX in improving the outcome of conservative management is largely based on case reports and experimental evidence is lacking. Timmermans *et al.*[3] have comprehensively reviewed the literature on the

conservative management of AAP with MTX alone. Among the 19 cases reported, there were only 3 treatment failures requiring hysterectomy; 6 patients had spontaneous expulsion of the placenta, aided by manual removal in 1 case.

Conclusion

On the basis of our experience and a review of the literature, we believe that conservative management should be offered to carefully selected women with AAP who are haemodynamically stable and free of any co-morbid conditions and have a strong desire to retain their fertility. Whether adjuvant MTX is beneficial or not is debatable, as a similar success rate has been reported for patients managed with conservative treatment alone.[4] However, as has aptly been said, 'absence of proof is not proof of absence'. Adjuvant MTX therapy, particularly when the whole placenta is left *in situ* (a trend seen in the literature), might be beneficial, but more evidence is required. Our endeavours to conserve our patient's uterus were successful and satisfying, but we have yet to see whether she will be able to have a viable pregnancy in the future.

Conflict of interest. We hereby declare that there is no conflict of interest.

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