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CASE REPORT PROF-4325

PLACENTA ACCRETA;

MATERNAL OUTCOME AFTER CONSERVATIVE MANAGEMENT IN A WOMAN DESIRING FERTILITY.

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ABSTRACT… Placenta accreta is an obstetrical emergency associated with significant maternal morbidity and mortality. Traditionally, hysterectomy at the time of cesarean section has been the mainstay of therapy especially in cases where diagnosis is made antenatally. In recent years different conservative treatments for partly or totally adherent placental tissue in the uterine cavity have been reported in patients willing to preserve fertility. We report a case of successfully managed placenta accreta with methotrexate in our department. The patient was haemodynamically stable, had desire for future fertility and gave informed consent to all the possible risks of conservative management including repeated episodes of bleeding, multiple blood transfusions, pain, infection, delayed hysterectomy and prolonged follow up. We used a regimen of two doses of methotrexate given a week apart. Further studies are required to study the effectiveness of methotrexate and to establish its dose and schedule in conservative management of placenta accreta.

Key words: Accreta, Beta HCG, Methotrexate.

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INTRODUCTION

Placenta accreta is the abnormal implantation of the chorionic plate in the myometrium, due to the absence or defect in the basal decidua and fibrinious Nitabuch layer. The rising rate of cesarean section and advanced maternal age has resulted in a 10-fold increase in the incidence of placenta accreta: the reported incidence has increased from 1/7000 delivery to 1/2500 delivery.[1]

Following identifiable risk factors are seen among women with placenta accreta: scar from previous uterine surgery, curettage, Asherman's syndrome, uterine ablation, placenta previa, uterine anomalies, uterine leiomyoma, prior intra-uterine infections, advanced maternal age and parity and raised maternal serum alpha-fetoprotein (AFP) levels.[2,3]

Morbidity associated with placenta accreta could be dramatic with massive hemorrhage, blood transfusions, intra-abdominal infections, disseminated intravascular coagulation, multiorgan failure, ureteral damage and fistula formation.[4] Mortality rates as high as 7% are reported to be associated with placenta accreta.[5]

Traditionally, cesarean hysterectomy at the time of delivery, a lifesaving surgery for the mother, has been the preferred management for placenta accreta.[6] This procedure not only results in loss of future fertility but also has associated peri-operative risks.[7] Massive hemorrhage depends upon the attempts to manually remove the placenta which opens up the spiral vessels and sinuses. Conservative management in the cases of placenta accreta is only done in cases where fertility is desired and patients are

haemodynamically stable. The decision is made by the obstetrician at that very moment while doing the surgery, either to leave the placenta partly or totally in situ. Conservative methods include using uterotonic drugs, prophylactic antibiotics, methotrexate, balloon catheter occlusion, devascularization procedures.[8]

Our current knowledge about maternal outcome after conservative management of placenta accreta is very limited and is predominantly based on case reports and case series.[9] Among conservative management methotrexate is the most common and simple approach, based on the fact that it leads to rapid placental involution.

We report a case of placenta accreta managed conservatively by leaving the placenta in situ followed by intramuscular injections of methotrexate.

CASE REPORT

A 27 year old, G4P1+2 at 28+3 weeks of gestation was referred from a district level hospital with ruptured membranes of 30 days. The patient had one uneventful normal vaginal delivery followed by two dilatation and curettages (D&C) done at 8 and 7 weeks of gestation for missed miscarriages. She presented in active phase of labor and was tachycardiac, febrile with a total leucocyte count (TLC) of $26x10^3$/microliters suggestive of chorioamnionitis. High Vaginal swab was taken and broad-spectrum antibiotics were started including metronidazole to cover anaerobes. She delivered vaginally within 2 hours of presentation. Following a spontaneous vaginal delivery placenta was retained for 1 hour. When explored under general anesthesia placenta was found to be adherent to the fundus and left lateral wall of uterus. Procedure was abandoned as patient began to bleed heavily. Intraoperative vaginal bleeding was managed with combination of vigorous uterine massage, uterine packing, uterotonic agents including oxytocin infusion, misoprostol and carboprost. 4 units of blood were transfused and broad-spectrum antibiotics were continued. The bleeding settled over the following 24hours, at which point the packing was removed. Her previous ultrasounds did not suspect placenta accreta. However an ultrasound done (Figure-1), after exploration of uterus revealed a vascularized inhomogeneous area of 9x 6 cm invading the myometrium: *placenta accreta*.

The patient had a strong desire for future fertility and we informed the couple about the possible risks involved in conservative approach. The couple decided for conservative management, accepting all the risks. In order to promote uterine involution injection methotrexate was given ($50mg/m^2$). Her TLC fell to normal range and beta HCG level fell from 2750miu/ml (prior to methotrexate) to 1750miu/ml on day 5 of surgery. A repeat Doppler on day 5 showed a progressive reduction of placental blood flow, without significant decrease in size of non-vascularized inhomogeneous area. A second dose of methotrexate was given on day 5. A repeat beta HCG on day 9 was 1210miu/ml. Patient was discharged on day 11 on a course of cephalexin, in good health for follow-up as outpatient. She presented with secondary PPH on day 16 and passed a small piece of placenta about 4x3cm. She was managed with uterotonic agents and was transfused two units of blood. Repeat ultrasound showed a reduction in the placental surface area from 9x6 cm (on previous scan) to 5x3 cm. She was kept in-patient for another 3 days and was discharged on oral antibiotics.

Outpatient management consisted on twice-weekly visits to monitor for infection and bleeding. Laboratory investigations included full blood count (FBC), beta HCG, C-reactive protein and ultrasound scan. It took in total 12 weeks after delivery for beta HCG to become undetectable and placental size on scan to reduce to 3x2cm. We discussed with the patient the option to remove that tissue under ultrasound guided D&C which patient declined. She complained of vaginal spotting irregularly. She was monitored for another one month and last ultrasound done, in total after 16 weeks of delivery showed an echogenic, nonhomogenous and non-vascular mass of 3x2cm. Since patient had intense desire for future fertility and she had already declined for dilatation and curettage, we started her on oral

progestogens for her irregular vaginal bleeding. She presented after another 2 weeks complaining of passing a tissue of about 3x3 cm vaginally. On repeat scan (Figure-2), there was no placental tissue found.

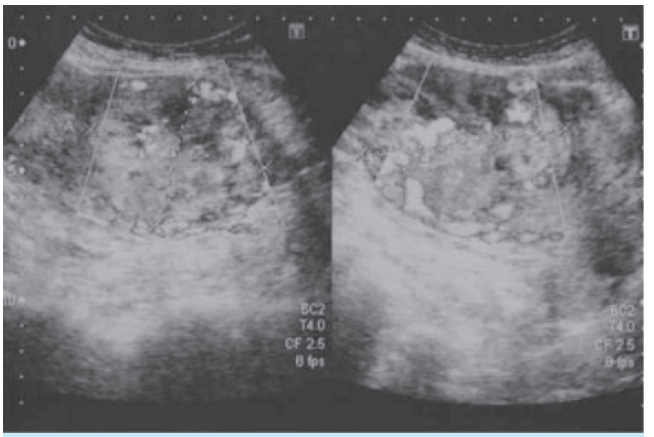

Figure-1. Pelvic ultrasound of patient, before commencement of treatment Large vascular mass of retained placental tissue measuring 9.0x6.0x6.5cm (vol. 160gms) have deeply penetrated into the myometrium.

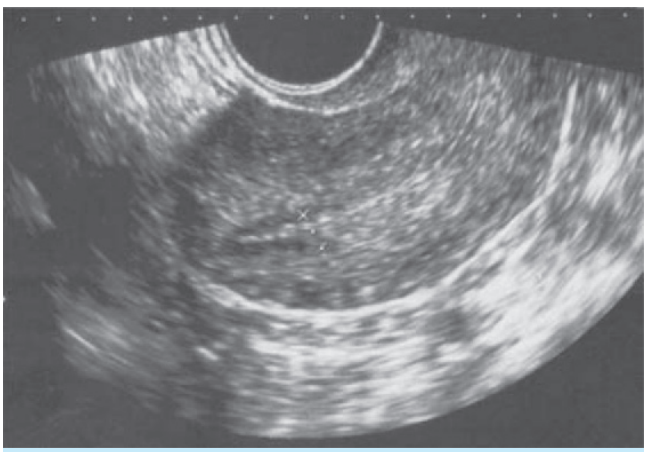

Figure-2. Endovaginal ultrasound of patient. No evidence of retained products of conception. Left anterolateral wall shows calcified lesion measuring 18.5x17.4mm. Endometrial thickness is 5.3 mm.

DISCUSSION

The Optimal management of abnormally adherent placenta remains unclear. Traditionally, hysterectomy is the treatment of choice especially in cases where the diagnosis is made antenatally.[10] According to some recent systematic reviews, emergency postpartum hysterectomy is associated with maternal mortality of 3% and maternal morbidity of 56% and the complications include loss of fertility, damage to adjacent organs, complications including massive haemorrhage and its sequel: DIC and infections.[11,12] However it's also been learned that planned caesarean hysterectomy is associated with less peri-operative complications compared to emergent caesarean hysterectomy.[13]

However, as extirpative management leads to loss of fertility, a conservative approach is required. Different strategies have been adopted with varying success rates, as described in the literature, for conservative management of placenta accreta: including haemostatic sutures,[14] balloon tamponade,[15] pelvic devasularisation,[16] and medical treatment with methotrexate. Yet there is no randomized controlled trial to compare the efficacy of the procedures.

Methotrexate has been used commonly with few published case reports showing that it could lead to rapid placental involution.[17] Methotrexate is an antimetabolite that affects the cell division by interrupting the synthesis of purine nucleotide thymidylate, amino acid serine and methionine. However its role is controversial, as arguments have been raised against its efficacy on the fact that it acts on rapidly dividing cells and there is no active trophoblastic cell division at term. Despite this controversy, still individual case reports have been made on successfully treated cases of placenta accreta with methotrexate.[18] Pre requisites before starting treatment with methotrexate include mild to moderate bleeding, a normal complete blood count (CBC), Renal function tests (RFTs), Liver function tests (LFTs) and counselling of the couple regarding possible failure of treatment and prolonged follow up. However there is no agreed protocol regarding the dose and schedule of methotrexate. We administered two doses of methotrexate one week apart without significant side effects like myelosuppression, gastrointestinal effects, liver toxicity and renal failure.

We followed our patient on twice-weekly visits with Beta HCG levels, c-reactive proteins, CBC, and Doppler scans in order to monitor response to therapy. According to the existing literature, Beta HCG and HPL (Human placental lactogen) are

the two laboratory investigations used to correlate with the decreasing placental perfusion. Zepiridis et al in his study found that HPL levels correlate better with decreasing placental perfusion rather than beta HCG.[19] We in our case relied on beta HCG and pulsatility index of uterine arteries by Doppler scans as a predictor of success of our management. One strong observation noted in our case was that beta HCG level became un detectable 4 weeks before the resolution of placental tissue, hence did not correlate with the placental involution.

There are significant risks of serious morbidity and possible mortality associated with conservative management. Infection, sepsis and persistent vaginal bleeding are the risks associated with leaving the placenta in the uterus.[20] In our case we encountered repeated episodes of moderate to heavy vaginal bleeding, which were managed with medical measures. We did not proceed with devascularisation procedures in our case. Pain was the second most common symptom, managed with analgesics. Our patient did not develop infection, most probably because we started and continued on intravenous broad-spectrum antibiotics for a minimum of 10 days followed by oral cephalexin. We fail to draw any conclusion about the efficacy of methotrexate, as Beta HCG became undetectable after 12 weeks of delivery and 4 weeks before spontaneous expulsion of placenta. As the patient was not willing to proceed with any surgical intervention to remove the placental tissue, despite the fact she bleed irregularly we started her on oral progestogens 30mg/day, from which she benefitted, hence avoiding delayed hysterectomy. Whereas in a study conducted by Stein Bishop, 16% and 18% were the hysterectomy rates after embolization and expectant management.[21]

From our case report we endorse to always think of possibility of placenta accreta among patients with retained placenta after delivery. One should always do assessment for risk factors for accreta before proceeding with attempts at manual removal, as it is associated with increased risk of hemorrhage and maternal morbidity. Retrospectively, we found that dilatation and curettage was the most common identifiable risk factor along with prolonged ruptured membranes in our case.

We lay great emphasis on that all such cases should be only managed in centres, which are adequately equipped and has resources in terms of maternal fetal medicine specialist, anaesthetists, urologist, haematologists and pelvic surgeons and blood bank team. Treatment should be only offered to those patients who strongly adhere to the follow-ups and understands risks of conservative management.

CONCLUSION

- All these patients should only be managed in centres with adequate resources.
- Careful selection of patients is essential, appropriately counselled and motivated patients who agree to adhere to close follow up should be selected only.
- Further studies are required to study the effectiveness of methotrexate in conservative management of placenta accreta.

CONFLICT OF INTEREST

The authors have any conflict of interest to declare.

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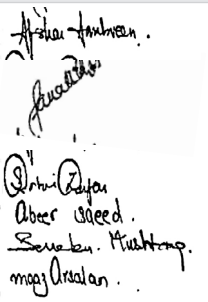
1	Afshan Ambreen	Writing, Case report	
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