Retained Products of Conception or Choriocarcinoma: A Diagnostic Dilemma

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Abstract
The following case report demonstrates a rare case where a patient presents with vaginal bleeding following a first trimester abortion creating an impression of retained products of conception. However, her Beta HCG and Ultrasonography reports were debatable. Despite of falling Beta HCG levels, USG reports and CT scan and MRI findings persistently reported an invasive lesion most likely a choriocarcinoma. These findings caused a dilemma regarding the diagnosis - choriocarcinoma or retained products of conception.

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I. Introduction

Retained products of conception are intrauterine tissue of trophoblastic origin that develops after conception and persists after delivery. RPOC’s can present with intermenstrual bleeding/spotting. Presence of chorionic villi on microscopy confirms RPOC’S.

Retained products of conception and gestational trophoblastic disease can pose a diagnostic dilemma as both present with bleeding and both are due to hyperinvasion of the trophoblast. Major risk factors of invasive placenta are increased rates of cesarean section, uterine evacuation procedures, advanced maternal age, and multiparity. While for gestational trophoblastic disease, risk factors are prior molar pregnancy, prior miscarriage, age, family history etc. Early diagnosis of these conditions is important to prevent future complications of bleeding and infection and also to decide appropriate management. This report deals with a case of post abortal bleeding with raised beta HCG levels and the various differential diagnosis which ultimately turned out to be an invasive placenta.

II. Case Report

32 years old lady presented with bleeding per vagina since 15 days, difficulty in voiding urine. She had undergone a medical abortion one month back with tablet mifepristone and tablet misoprostol followed by spotting with soakage of 1-2 pads per day. PI had a previous LSCS 8 yrs back followed by a spontaneous abortion with no history of suction evacuation. Menstrual history as narrated was regular with last menstrual period around 3 months back. She underwent an ultrasound suggesting heterogenous hypoechoic lesion invading the anterior wall of uterus with myometrial invasion and bladder invasion.

Examination revealed normal BP and pulse rate with no history of fever, altered or foul smelling vaginal discharge. Abdominal examination revealed uterus of size 14 wk with no organomegaly. Per speculum revealed altered coloured bleeding coming form the cavity and on per vaginal examination the uterus was 14 week size, without any evidence of adnexal mass. Keeping the provisional diagnosis of abnormal uterine bleeding following abortion; CHORIOCARCINOMA we proceeded with our first step of a repeat USG examination and a Beta HCG report.

USG was indicative of ill defined hypoechoic lesion invading anterior wall of uterus including myometrial surface, serosa and bladder wall. BHCG was 1195. Meanwhile her urinary complaints were tackled by antibiotics. After 48 hr the BHCG value had fallen to half of the initial value. USG suggesting bulky uterus of size 9.4*6.6*3.9cm with ET -6mm with no e/o any endometrial collection. It read as ill defined hypoechoic lesion in the lower uterine segment and upper cervical region at the site of previous scar, thus giving an impression that possibility of scar pregnancy and retained products of conception should be considered.

With a wider spectrum of differential diagnosis to rule out, decision of MRI was taken. MRI revealed a uterine size of 6.7*4.7*11.3cm with heterogeneously enhancing lesion of size 7.8*7.2*7.1cm expanding into the lower part of uterus and upper third of cervix with multiple ill defined hyperdense components that was anteriorly indenting the posterior bladder wall with loss of fat planes. invasion Dilated tortuous vessels in the anterior myometrium and left adnexa. Few dilated right internal iliac nodes. Concluding it to be of malignant origin - choriocarcinoma

Further a repeat beta HCG after 1 week further reported a fall to about 60% from the 48 hr value. To reach final conclusion final settlement of taking tissue sample by hysteroscopy was adopted.

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Hysteroscopic findings included normal cervical canal with intrauterine adhesions making the possibility to visualise the cornual part difficult.

Polyploid growth on anterior wall of uterus was noted that was biopsied and sent for histopathological examination. The curettage sample with naked eyes were more likely diagnostic of placental membranes and bits, retained placenta. However, the whole placenta could not be removed possibly due to invasion / adherent placenta. Repeat scan suggested a decrease in the size of the lesion with areas of multiple necrosis with potential diagnosis of neoplastic aetiology.

The histopathology report showed retained products of conception and no evidence of any proliferating trophoblast. However, after 7 days of suction evacuation, repeat USG again reported similar findings of enlarged uterus with ET 7mm, with decreased size of lesion showing invasion into endometrium and taking minimal internal vascularity- gestational trophoblastic neoplasia. Hence, a repeat evacuation procedure was scheduled to remove the residual mass present in the endometrium. And once again the tissue diagnosis reported retained products of conception. Finally keeping the diagnosis as retained products, invasive placenta decision of administration of methotrexate was taken. 5 doses of inj methotrexate alternating with inj folinic acid were given and a repeat ultrasound after 15 days was done that showed a significant reduction in size of invasive lesion to 2.3*2.3cm thus confirming the diagnosis of invasive placenta.

First image of MRI showing a hemorrhagic mass of size 7.8*7.2*7.1cm
Image after the evacuation procedure after 15 days, showing lesion decreased from 7*7 cm to 6*5.5cm.

Following the cycles of methotrexate the MRI report showed a significant reduction in the size of the lesion. This shows a size of 2.2*2.3cm mass.
III. Discussion

Human placenta is made of two components the fetal part called the chorionic frondosum and the maternal part called the decidua basalis. Interstitial implantation is completed by day 11. It’s the zona pellucida which forms the line of cleavage during placentation. Endometrial invasion occurs maximally in early pregnancy in the presence of low oxygen tension and low estradiol content while this invasion gets limited in the later pregnancy due to increase in estradiol concentration. The placental development and spiral arteries invasion into the myometrium is completed by 16 weeks. Hyper-invasiveness of the trophoblastic cells and defective decidua basalis due to uterine procedures can result in invasive and morbidly adherent placenta. And this condition can be recognized by 12-16 weeks in ultrasonography.

Morbidly adherent placenta describes an aberrant condition characterised by abnormally invasive or adhered placenta. These disorders are collectively termed as placenta Accreta syndromes. Abnormal adherence is due to partial or total absence of decidua basalis layer and imperfect development of the fibrinoid nitabuchs layer due to which the physiological line of cleavage is lacking and few cotyledons remain densely adhered to the smooth muscles rather than the decidual cells. Caesarean and uterine trauma like evacuation, curettage form the major risk factors. USG findings that can predict invasive placenta are loss of normal hypoechoic retroplacental zone between the placenta and uterus, placental vascular lacunae and bulging into the posterior bladder wall. Colour Doppler findings of less than 1 mm thickness between the uterine serosa and retroplacental vessels and presence of large intraplacental lacunae have highest positive predictive values of invasion. MRI imaging like uterine bulging, heterogenous signal intensity within the placenta indicative of lacunae and dark intraplacental bands on T2 image favour invasion. Such placenta will not separate completely and will result in bleeding following first trimester and early second trimester abortion.

A frequent condition that mimics incomplete abortion can be partial mole showing thickened multicystic placenta on USG. Choriocarcinoma or GTN follows one fourth of Incomplete abortions and are characterised by aggressive invasion into the myometrium and propensity to metastasise. Presenting with irregular bleeding and uterine subinvolution, and as bluish vascular masses on uterine surface intraoperatively. However persistently elevated B-hcg forms the mainstay of diagnosis as tissue is infrequently available.

However, during spontaneous abortion the chorionic villi are lost early. So, absence of chorionic villi is not reliable to distinguish between RPOC’S and GTN. But RPOC’S are present inside the cavity while GTN are intramyometrial. For HPE report to be reliable it should be sent from the implantation site as this site is the last to loose chorionic villi. Also recent studies have shown that abnormal trophoblast are a diagnostic of trophoblastic disease and called choriocarcinoma in situ.

RPOC’S form the most common cause of bleeding following abortions. Others include AVM and subinvolution of placental site. It is a type of retained invasive placenta. USG is the primary modality in diagnosis. Hyperechoic areas of collection within the uterus with slightly increased vascularity with normal ovary and vascular channels extending from placenta to myometria in parallel fashion help in diagnosing RPOC’S. Histopathology report will show decidual necrosis and prescience of chorionic villi.

Gestational trophoblastic neoplasia is abnormal proliferation of trophoblastic cells. These include placental site trophoblastic tumor, choriocarcinoma, epithelioid trophoblastic tumor and invasive mole. Together all these are persistent or malignant trophoblastic tumor. They can be distinguished based on the type of trophoblast they contain.

Choriocarcinoma comprising malignant trimorphic proliferation of syncitio and cytotrophoblast with absence of chorionic villi. It is rapidly invasive and can be diagnosed following completed pregnancy in 50%, in one fourth following abortions and following a complete hydatiform mole in one fourth. The most common symptom is vaginal bleeding. These have great propensity to metastasise. Risk factors include history of prior mole, advanced maternal age, long term contraceptive use and specific blood group. USG findings can resemble retained products. USG shows presence of infiltrative heterogenous mass invading the myometrium, areas of necrosis and hemorrhagewith enlarged uterus and cystic ovaries. Also presence of central and peripheral vascularity with calcification in contrast to parallel vessels seen in retained tissues. Raised beta HCG forms the mainstay of diagnosis. However, cases of choriocarcinoma with low levels of beta HCG have also been reported.

Epithelioid trophoblastic tumor and placental site trophoblastic tumor fall under group of intermediate trophoblastic tumor. GTN are characterized by myometrial invasion with raised beta -HCG levels. PSTT and ETT are types of malignant trophoblastic tumors with low or only moderately increased beta hCG levels. Hence form the major differentials in our case with low beta hCG.

Epithelioid trophoblastic tumors arise in the lower uterine segment and cervix. These remain confined to the uterus and are seen as focally infiltrative, discrete nodules with calcification. They stain positive for inhibin, GATA3, hPL while negative for hCG.
In contrast to ETT, placental site trophoblastic tumors do not exhibit calcification and seen as single cord of tumor cells invading the myometrium. The positive stains include hPL, CD146, focal expression of hCG and negative for PLAP.

Placental site nodules are benign lesions of intermediate trophoblast which is thought to represent incomplete involution of placental implantation site. Patient here can present as menorrhagia, intermenstrual bleeding or abnormal PAP.

HPE shows abundant inflammatory cells with decidual cells and intermediate trophoblast with or without chorionic villi. However, it does not have any proliferative activity as compared to PSTT and ETT that have low proliferative activity. As per the cases published placental site nodule can be seen as areas of increased vascularity and red nodules or as intrauterine adhesions with small yellow white necrotic nodules. Treatment consists of DNC with progestrone releasing intrauterine system.

Subinvolution of placental site can also cause abnormal bleeding but here clinically evident subinvolved uterus with occluded vessels with microthrombi can help in diagnosis.

Another differential could be a scar pregnancy as we cannot deny the fact that cesarean scar pregnancy and Accreta lie in the same spectrum with scar pregnancy as the precursor of morbidity adhered placenta having common histopathological findings.

Low beta hCG levels with presence of chorionic villi can rule out choriocarcinoma as diagnosis however due to hyper invasion with the mass infiltrating and reaching up to serosa, USG and MRI persistently diagnosed it as choriocarcinoma.

As it was a large lobulated lesion we rule out PSTT as PSTT are cords of cells or individual cells. Also absence of any trophoblastic proliferation and abnormal trophoblast rules out PSTT and ETT.

Now we are left with the diagnosis of invasive placenta, partial mole, retained products, ?Scar pregnancy with morbidity adherent placenta.

Histopathology findings of ghost/abnormal villi rules out partial mole/invasive mole. Now left with two, due to early loss of pregnancy and based on declining levels of beta HCG and Histopathology report we conclude this to be invasive placenta presenting as retained tissue.

Post abortion bleeding can be due to many conditions and possibility of malignancy should never be ignored. Hence complete evaluation and cure must be attempted.

IV. Conclusion

The clinical picture, biochemical parameters and imaging are inconsistent in this case forming a diagnostic dilemma. But ruling out other possible diagnosis and considering tissue diagnosis as golds standard I would call it invasive placenta as it invaded the myometrium that caused the dilemma to the radiologist to call it a choriocarcinoma as other findings could be shared by both invasive placenta as well as trophoblastic tumor. Also management with inj. Methotrexate reduced the size of the lesion significantly and also the bleeding episodes. Hence we can safely conclude it as a case of invasive placenta

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