Uterine inversion associated with malignancy – A challenge in surgical management: A case report*

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ABSTRACT

Uterine inversion is a rare clinical problem. Most cases of uterine inversions are puerperal inversions wherein it is encountered as an obstetric emergency, and sometimes a diagnostic challenge in gynecology. Uterine inversions associated with malignancies such as endometrial carcinoma and sarcoma are even rare. We report 2 cases of this rare condition. A 55 year old diagnosed with endometrial carcinoma and a 60-year-old woman diagnosed with sarcoma (malignant mixed mullerian tumor) presented with mass protruding from the vaginal introitus. The diagnosis of complete uterine inversion was confirmed in both cases during laparotomy. Total abdominal and vaginal hysterectomy and bilateral salpingo-oophorectomy, bilateral pelvic lymph node dissection, paraaortic lymph node sampling was done. It required a challenging surgical procedure to remove the tumor along with the review of literature especially of its association with malignancies.

Keywords: Uterine inversion, endometrial adenocarcinoma, malignant mixed mullerian tumor

INTRODUCTION

Non-puerperal uterine inversion is a rare condition. Uterine inversion associated with malignancy is even rare with no exact prevalence estimates available to date. A search of the literature in PubMed revealed only 3 articles and 7 articles on uterine inversions caused by endometrial carcinoma and sarcoma, respectively. Locally there has never been a published paper emphasizing on the rarity of uterine inversion associated with malignancy. This paper describes two cases of this rare condition.

THE CASE

CASE 1

This is a case of H.O. 36-year-old nulligravid from Bicol, who came in due to heavy menstrual bleeding. Past medical history and family history are unremarkable. She is a college graduate, non-smoker and non-alcoholic beverage drinker. Her first coitus was when she was 26 years old, with two sexual partners. She is married to a 38-year old businessman. Fertility work-up was done which revealed normal semen analysis for her husband. Patient had polycystic ovaries by ultrasound and took Althea for three months. She had her menarche when she was 13 years old with subsequent menses coming in at irregular interval occurring every 2-3 months, lasting for 3-4 days consuming 3-4 pads/day, fully soaked, with no associated dysmenorrhea. Her last menstrual period was last August 5, 2015.

One year prior to admission, patient complained of heavy menstrual bleeding consuming 3-4 baby pads per day lasting 2-3 days with no associated signs and symptoms. Patient sought consult at a private OB-Gyn and ultrasound revealed cervical mass and was referred to Bicol Regional Training and Teaching Hospital wherein speculum and cervical punch biopsy done revealed negative for cancer and suggest repeat biopsy. However, patient was lost to follow up until 7 months prior to admission, persistence of symptoms associated with dizziness prompted the patient to seek consult at Bicol Medical Center wherein she was subsequently admitted. A total of 5 units of PRBC were transfused. Transvaginal ultrasound done revealed enlarged uterus, markedly thickened endometrium (3.33 cm), hyperechogenic, with irregular endomyometrial junction, no normal cervical tissue identified, both ovaries not visualized. Repeat cervical punch biopsy revealed endocervical adenocarcinoma (cannot rule out if cervical or endometrial in origin) (Figure 1).

Patient was then referred to our institution wherein patient was admitted for BT of 3 units PRBC. Transvaginal ultrasound revealed prolapsed endometrial mass consistent with malignancy with more than 50% myometrial invasion. Immunohistochemistry done

*Third Place, PGH Department of Obstetrics and Gynecology 2016 Fellow's Interesting Case Contest

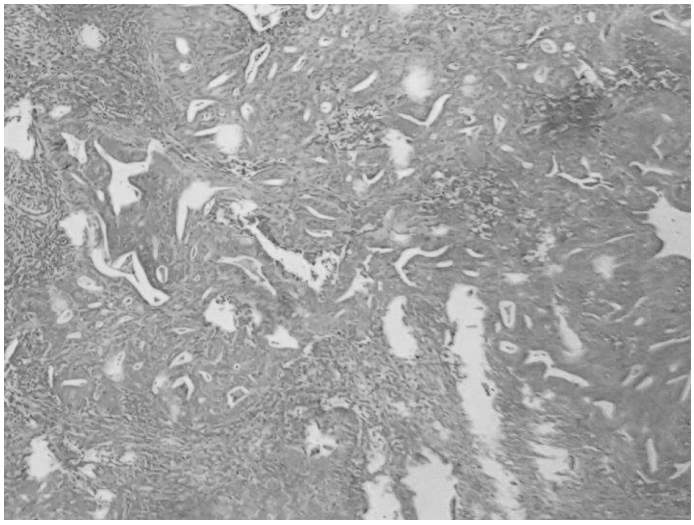

Figure 1. Cervical punch biopsy

revealed positive for vimentin and negative for CEA, which favored a primary endometrial carcinoma (Figure 2). Patient was scheduled for surgery, hence was admitted.

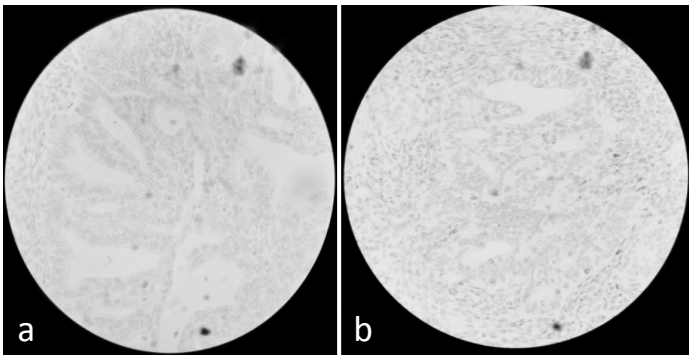

Figure 2. Immunohistochemistry. a) Vimentin. b) CEA

On physical examination, patient had stable vital signs, BSA of 1.4, BMI 21.79 and ECOG O. On pelvic examination, patient had normal external genitalia, (+) 10 x 10 cm fungating, friable mass occupying the entire vaginal canal cervix hard to assess, corpus small, no adnexal masses nor tenderness, bilateral parametria smooth and pliable. Transvaginal/Transabdominal ultrasound revealed that the urethra, urinary bladder mucosa and rectum are intact. The uterus measures 11 x 9.8 x 9.8 cm with smooth contour and homogenous echopattern. The cervix is effaced measures 2.4 cm in length with homogenous stroma (Figure 3). Prolapsing out of the endometrial cavity and occupying the vaginal canal is a heterogenous mass measuring 9.9 x 8.8 x 8.9cm. It is contiguous with the endometrial mass (Figure 4).

Color flow mapping shows abundant peripheral vascularity, which on Doppler interrogation reveals low resistance indices. Within the endometrial cavity is a heteregenous mass measuring 7.6 x 5.4 x 5.1 cm with more than 50% myometrial invasion at the fundal

Figure 3. Transvaginal Ultrasound of the efface cervix

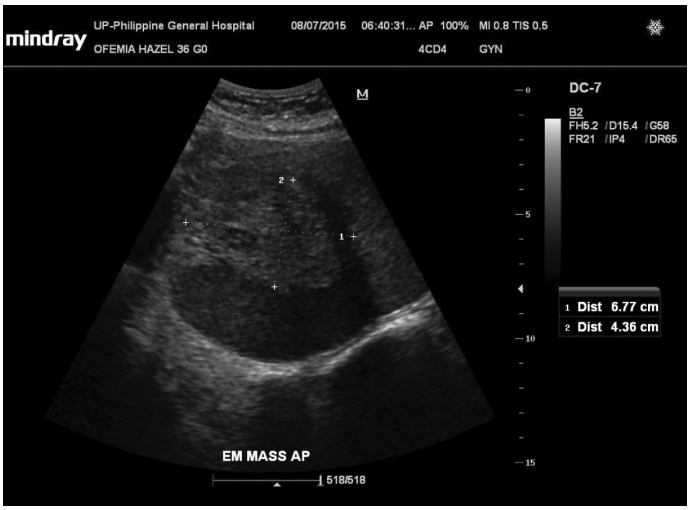

Figure 4. Transvaginal Ultrasound of the prolapsed endometrial mass

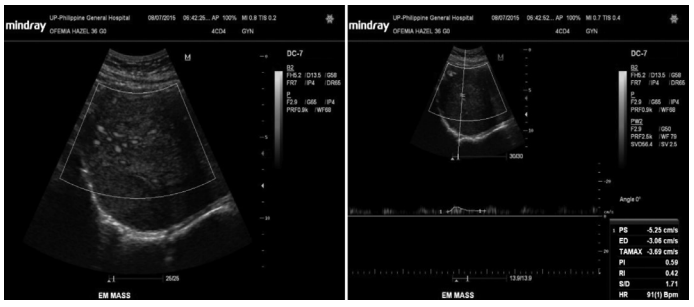

Figure 5. Doppler studies of the endometrial mass

area. The mass seems to originate at the fundal area. The subendometrial halo at the anterior and posterior regions is intact. The uterine serosa is intact. Color flow mapping shows abundant central and peripheral vascularity, which on Doppler interrogation reveals low resistance indices (Figure 5). There is a well-circumscribed hypoechoic mass measuring 2.7 x 2.5 x 2.1 cm at the posterior myometrium, intramural. Both ovaries cannot be visualized. There are no adnexal masses seen. There

are no bilateral pelvic or para-aortic lymph nodes. The liver parenchyma is homogenous. The bilateral renal calyces are not dilated. There is no free fluid in the cul de sac.

Patient underwent exploratory laparotomy, peritoneal fluid cytology, Haulltain maneuver, extrafascial hysterectomy, bilateral pelvic lymph node dissection, para-aortic lymph node sampling. Intraoperatively, there was no ascites. The liver, gallbladder, subdiaphragmatic surface, spleen, kidneys, stomach, intestines and appendix were all smooth and grossly normal. There were no palpable pelvic or para-aortic lymph nodes noted. The uterus was completely inverted with round ligaments and some part of the fallopian tubes embedded in the concavity of the pelvic cavity and measured 7 x 5 x 4 cm with smooth, tan serosal surface (Figure 6).

The cervix measured 3 x 8 x 6.5 cm and was dilated by a 10 x 10 cm prolapsing friable endometrial mass. On cut section, the endometrial canal measured 5 cm, 3 cm of which was the endocervical canal. The myometrium measured 1.4 cm anteriorly and posteriorly. Occupying the entire endometrial cavity and prolapsing out of the cervix, is a friable and necrotic mass measuring 12 x 12 x 5 cm. It was attached at the fundal area with more than 50% myometrial invasion (Figure 7). The vaginal cuff measured 0.5 cm circumferentially. The left ovary measured 5 x 4 x 3 cm while the left fallopian tube measured 9 x 0.8 x 0.5 cm. The right ovary measured 4 x 2 x 1 cm while the right fallopian tube measured 11 x 0.7 x 0.5 cm. The bilateral adnexae were grossly normal. The harvested lymph nodes were not suspicious for malignancy. Estimated blood loss was 1000 ml.

No intraoperative complications were noted. Pathological examination revealed a tan, rubbery, polypoid, solid, friable mass measuring 9 x 8 x 7 cm. Microscopic examination of the said mass revealed Endometrial adenocarcinoma, endometrioid type (FIGO grade 2), with >50% myometrial invasion and invasion of < 1/3 of endocervical canal (tumor is 2 cm from the external cervical os). Positive for lymphovascular space invasion (Figure 8). Negative for perineural space invasion. Negative for tumor: All lymph nodes in specimens labeled “left obturator lymph nodes” (6), “ right obturator lymph nodes “ (4), “left external iliac lymph nodes” (4), “right external iliac lymph nodes” (7). Fibrofatty tissues labeled “A1 lymph node”, Left and right parametrial margins, proliferative endometrium, unremarkable left and right ovaries and bilateral fallopian tubes.

The postoperative course was uneventful and the patient was discharged on the third postoperative day. The patient was for systemic chemotherapy with Carboplatin-Paclitaxel every 3 weeks x 6 cycles followed by pelvic EBRT.

Figure 6. Uterine inversion

Figure 7. The inverted uterus with an exophytic mass covered with necrotic tissue after Haultain procedure

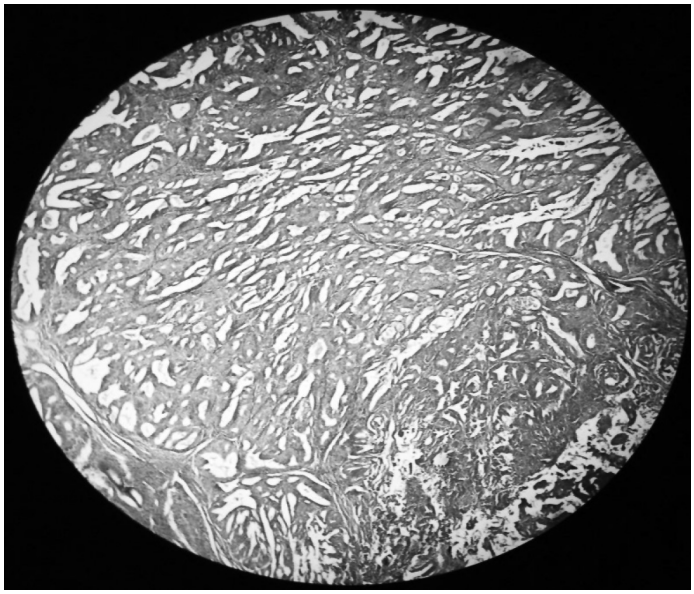

Figure 8. Endometrial adenocarcinoma, endometrioid type, FIGO grade 2

CASE 2

The patient was a 60-year-old G5P5 (5005) from Nueva Ecija who complained of introital mass. Past medical history, personal and social history were unremarkable. Patient had her first coitus when she was 20 years old with a total of 2 sexual partners, promiscuity unknown. She denies any contraceptive pill intake or IUD use. She also had no regular Pap smear done. All her pregnancies were delivered to term by spontaneous vaginal delivery at home assisted by midwife with no associated feto-maternal complications.

Three months prior to admission, the patient had foul-smelling vaginal discharge. No other symptoms. No consult done. Two months prior to admission, the patient had profuse vaginal bleeding lasting for 5 days using 3-4 pads per day. She consulted at a local hospital where assessment was cervical mass. Cervical punch biopsy done showed squamous cell carcinoma, non-keratinizing. She was then referred to Philippine General Hospital (PGH). The patient was advised concurrent chemoradiation, However, the patient refused to undergo further treatment due to financial constraints. In the interim, the patient continued to have foul-smelling vaginal discharge with intermittent vaginal bleeding. Few hours prior to admission, the patient had profuse vaginal bleeding using 2 baby diapers then noted prolapse of an introital mass. This prompted consult at the PGH OB Admitting Section.

On physical examination, there was a 10 x 10 cm hypogastric mass, solid, movable but non-tender, no fluid wave noted. Pelvic examination revealed a 12 x 10 cm irregular, necrotic, friable mass prolapsing out of the introitus (with superior portion seems to be the corpus and inferior portion seems to be the cervical mass), bilateral parametria smooth and pliable, inferior pole of the AP mass palpable at the cul de sac (Figure 9).

Transvaginal ultrasound revealed that the urethra, urinary bladder mucosa and rectum are smooth and intact. The prolapsed mass consists of the normal appearing corpus measuring 5.4 x 3.8 x 2.7 cm with smooth contour and homogeneous echopattern. The endometrium is heterogeneous measuring 1.9 cm with intact subendometrial halo. Inferior to the corpus is an irregular, heterogeneous cervical mass measuring 11.0 x 8.7 x 6.5 cm extending up to the isthmic area. Color flow mapping of the cervical mass shows scant central vascularity, which on Doppler interrogation revealed low resistance indices (PI=0.77, RI=0.54) (Figure 10).

Both ovaries are not visualized. Occupying the abdominopelvic cavity, superior to the vaginal stump, is a complex heterogeneous, predominantly solid mass measuring 11.5 x 11.9 x 5.5 cm, with cystic spaces within (Figure 11).

Figure 9. Fungating polypoid mass protruding out of the introitus

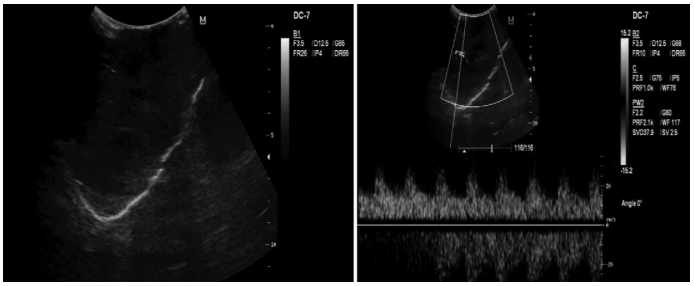

Figure 10. Transperineal ultrasound and Doppler studies of the introital mas

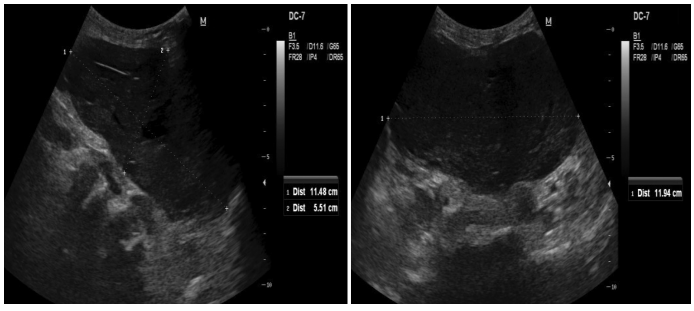

Figure 11. Abdominopelvic mass

Color flow mapping of the abdominopelvic mass shows scant vascularity which on Doppler interrogation revealed low resistance indices (PI=0.37, RI=0.30) (Figure 12).

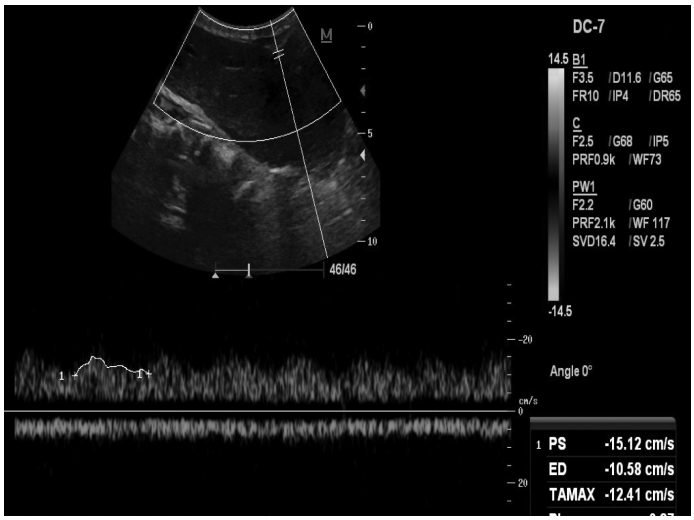

Figure 12. Doppler studies of the abdominopelvic mass

There are hypoechoic masses seen along the right iliac vessels ranging from 0.4 – 0.9 cm. There are atleast 3 hypoechoic masses seen along the left iliac vessels measuring 2.3 x 3.0 cm. There are hypoechoic masses seen along the left iliac vessels measuring 2.3 x 3.0 cm. There are hypoechoic masses seen along the aorta measuring 0.9 cm each. The liver parenchyma is homogeneous. The bilateral renal calyces are not dilated. There is no free fluid in the abdominopelvic cavity.

The patient underwent exploratory laparotomy, peritoneal fluid cytology, adhesiolysis, bilateral salpingo-oophorectomy, vaginal hysterectomy, infracolic omentectomy, para-aortic lymph node sampling, biopsy of adhesions.

Intraoperatively, there was a necrotic mass measuring 11 x 8 x 6 cm prolapsing out of the introitus and seems to be attached to a reddish tubular structure which seems to be the uterus. The vagina was smooth, and measured 6 to 7cm. On laparotomy, there was minimal ascites noted. The omentum was firmly adherent to the left ovarian mass. The other abdominal organs were grossly normal on inspection and palpation. There were multiple palpable pelvic and para-aorti lymph nodes. The left adnexa was converted to a solid, necrotic, friable and hemorrhagic mass measuring 15 x 10 x 10 cm occupying the cul de sac area (Figure 13). On cut section, it revealed areas of hemorrhages and necrosis (Figure 14).

The uterus was inverted with note of the necrotic prolapsing mass attached at the fundal area with more than 50% myometrial invasion. The remaining normal uterus measured 4 x 4 x 2 cm. The cervix seemed effaced. On cut section of the uterus, it revealed the right adnexa wherein the right ovary measured 3 x 1.5 x 1 cm and the right fallopian tube measured 6 x 0.5 cm and grossly free of tumor. This confirmed the diagnosis of the uterine inversion (Figure 15). There were multiple palpable fixed

Figure 13. Left Adnexal mass

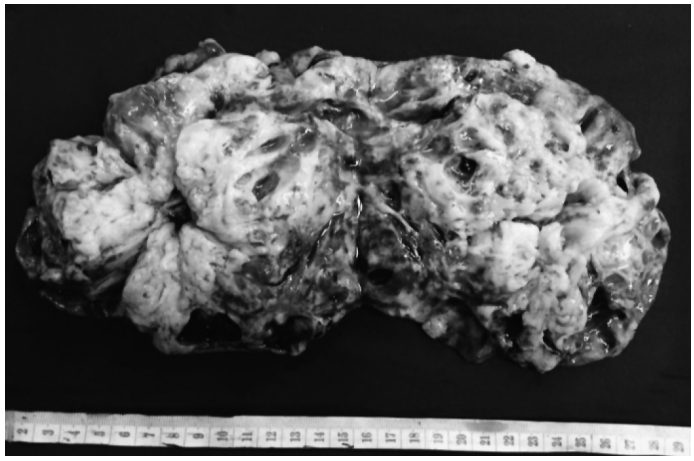

Figure 14. Cut section of the left adnexal mas showing areas of necrosis and hemorrhage

Figure 15. Cut section of the inverted uterus with the right adnexa

pelvic lymph nodes and para-aortic lymph nodes were suspicious for malignancy. Estimated blood loss was 800 ml. There were no intraoperative complications noted (Figure16).

Microscopic examination revealed a malignant mixed mullerian tumor involving more than 50% of the myometrial thickness with lymphovascular space invasion observed. The left ovary and para-aortic lymph nodes were positive for malignancy (Figure 17).

The patient was discharged on the fourth postoperative day. She was advised adjuvant chemotherapy but due to geographic and financial constraints, patient refused.

Figure 16. Final image after vaginal hysterectomy

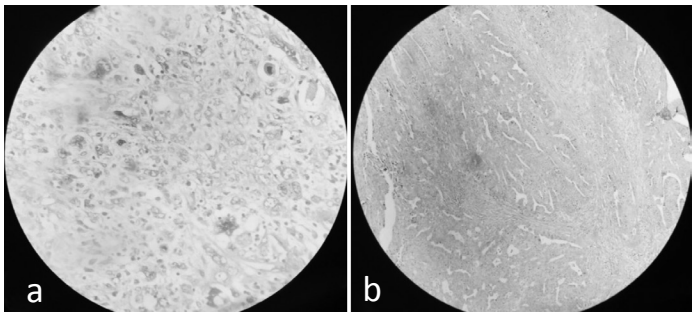

Figure 17. Malignant mixed mullerian tumor. Both a) sarcomatous and b) carcinomatous component have malignant cytologic features (nuclear morphism and mitotic activity)

DISCUSSION

Uterine inversion refers to a decline of the uterine fundus to or through the cervix, resulting to the uterus being turned inside out. As to our knowledge, there has never been an accurate figure in literature available for the frequency and incidence of uterine inversion. Moreover, we are unaware of local studies published on uterine inversions associated with malignancy.

Uterine inversion is classified into puerperal inversion and non-puerperal inversion.[1] Puerperal inversion is not in itself a common condition and is usually presents as an obstetric emergency. This is usually due to strong umbilical cord traction during the third stage of labor[2]. Non-puerperal uterine inversion, on the other hand, is extremely rare with 88 reported cases (Table 1); 81 (92%) of these are associated with uterine tumors, of which 20% were malignant.[3] An online PubMed search documents only 3 articles on uterine inversion associated with endometrial carcinoma[4-6] and 6 articles on uterine inversion associated with sarcoma.[7-12]

Table 1. Frequency of primary disease of non-puerperal uterine inversion in published reports.

Primary Disease	Frequency
Leiomyoma	63/88 (71.6%)
Sarcoma	12/88 (13.6%)
Endometrial carcinoma	6/88 (6.8%)
Idiopathic	7/88 (8.0%)

Based on the onset and evolution of the condition, uterine inversion can be acute and chronic. Acute uterine inversion is more histrionic and characterized by severe pain and bleeding and sometimes presents with shock. Chronic uterine inversion on the other hand is classified when 4 weeks have passed before the condition.[13] It is usually insidious and usually presents with vaginal discharge, pelvic discomfort and irregular vaginal bleeding and sometimes anemia. Our patients presented with chronic vaginal bleeding and introital mass.

Uterine inversion can also be classified based on degree of inversion.[15] Stage 1 – Inversion of the uterus is intrauterine or incomplete. The fundus remains within the cavity. Stage 2 – Complete inversion of the uterine fundus through the cervix. Stage 3 – Total inversion, whereby the fundus protrudes through the vulva. Stage 4 – The vagina is also involved with complete inversion through the vulva along the inverted uterus. Our patient who was diagnosed with endometrial carcinoma and sarcoma presented with stage 2 and stage 4 uterine inversions, respectively.

Etiology

The cause of uterine inversion is sometimes unclear. According to Lascarides et al[16], the etiologic factors include (a) sudden extrusion of tumor from the uterus, (b) thin uterine wall, (c) dilatation of the cervix (d) tumor size (e) thickness of the tumor pedicle and (f) tumor attachment site. Our first case had a tumor attached to the uterine fundus, which increased in size in time distending the myometrium, irritating the wall and develops expulsive contractions making the uterine muscle progressively relaxed, then the cervix is dilated expediting inversion. However, in our second case, who was diagnosed with sarcoma, the mechanism is believed to be different. A sarcoma generally induces softening of the uterine wall, often forming tumors, which project into the uterine cavity, and are brought under the influence of the active musculature. Such a condition may predispose to uterine inversion.[1, 14]

Diagnosis

The diagnosis of uterine inversion is made by a complete history and physical examination. It is suspected when tumor is palpable in the vagina but the uterine fundus is not palpable by a pelvic examination. In the case we presented, extruded tumors were observed in the vagina, but a pelvic examination failed to identify uterine inversion. Uterine inversion was not suspected. We also misdiagnosed the second case as prolapse cervical carcinoma. Therefore, a high index of suspicion should be kept in mind especially when the inversion is partial.[17]

Imaging studies can help facilitate diagnosis of uterine inversion. Several articles were published regarding the diagnostic modality of choice in uterine inversion. Kowan et al[17] and Lewin et al[18] discussed the use of ultrasound in diagnosing uterine inversion. In transabdominal ultrasound, the uterus may appear as "target sign" with a hyperechoic fundus surrounded by a hypoechoic rim, representing fluid within the space between the inverted fundus and the vaginal wall. In Transvaginal ultrasound, the uterus appeared as a mirror image normally situated uterus. The uterine fundus is in the vagina with fluid in the vaginal fornices. The two opposed serosal surfaces simulated the appearance of and endometrial stripe or "pseudostripe". Compared to sonographic imaging, MRI findings are much more evident. Lewin et al[18] recommend the use of T2-weighted MRI to confirm the diagnosis. Signs indicative of uterine inversions include U-shaped uterine fundus on sagittal image and a "bulls-eye" configuration on axial image. Although available, this was not done in our 2 patients.

Differential Diagnosis

The following are the differential diagnosis for non-peuerperal uterine inversions:

1. Prolapsed, pedunculated uterine fibroid
2. Prolapsed, endometrial polyp
3. Carcinoma of the cervix

Management

The appropriate treatment depends on preoperative diagnosis. For benign uterine inversions, repositioning the uterus is usually done after the tumor has been removed. Johnson et al[19] described manual repositioning through the vagina in managing acute uterine inversion. Saline hydrostatic pressure positioning was also described by O'Sullivan and modified by Oguey and Ayida[20]. Spinell and Kustner techniques are similar trans-vaginal surgical reposition techniques. Spinell's approach is anterior and requires dissection of the bladder and an anterior uterine wall incision, Kustner's is a posterior approach with incision on the posterior uterine wall, which makes it a bit easier and safer.[21]

More common methods done during laparotomy are the Huntington and Haultain techniques. Huntington procedure is done by locating the cup of the uterine inversion, then dilating the cervical ring, followed by gentle upward traction of the round ligament of the uterus.[22] The Haultain procedure uses a vertical incision in the posterior portion of the constriction ring followed by gentle traction on the round ligaments.[23] This procedure was done in our first case presented.

When a uterine malignancy is associated with uterine inversion, establishment of the nature of malignancy is prudent as well as the stage and associated pathology. For both types of malignancy presented, surgery with appropriate staging biopsies is the mainstay of treatment. Ehrlich et al reported that the abdominal approach is the best and least hazardous treatment for uterine inversion caused by uterine sarcoma.[24]

CONCLUSION

Although uterine inversion associated with malignancy is a rare condition, it should be kept in mind and should be managed immediately. The challenge in our case is that uterine inversion was diagnosed intraoperatively and has to be managed based upon little or no previous experience with the appropriate surgical technique. A High index of suspicion in the proper diagnosis of uterine inversion and sharp and clear knowledge about gynecologic oncology surgery will merit a successful and effective outcome. ■

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