Case Report

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A case report of nonpuerperal uterine inversion from embryonal rhabdomyosarcoma of the corpus in an adolescent: A dilemma on diagnosis and management

Bernadette Mayumi Telan Mortel[1], Irene Mag-Iba Tagayuna[1]

Abstract:

Embryonal rhabdomyosarcoma of the uterus is a rare condition with only a few cases documented. Exceedingly rare, however, is its concomitant incidence with uterine inversion. The infrequency with which genital tract sarcoma with uterine inversion is encountered makes the diagnosis and management a formidable challenge. The present case reports a 12-year-old nulligravida who complained of a rapidly growing introital mass of 3-month duration. Suspicion of nonpuerperal uterine inversion was confirmed by imaging, and malignancy was proven through adequate tissue sampling. While there is no unified protocol in the management of prolapsed genital tract sarcomas, the complete inversion of the corpus necessitated surgery. In the case presented, exploratory laparotomy and total hysterectomy through a double setup, abdomino-vaginal approach was done. The case illustrates the diagnostic, therapeutic, and ethical dilemmas in handling an aggressive tumor in an adolescent. Early recognition and a multidisciplinary approach are extremely crucial in ensuring improved prognosis and holistic treatment.

Keywords:

Embryonal rhabdomyosarcoma, nonpuerperal uterine inversion, pediatric uterine sarcoma, uterine prolapse

Introduction

Uterine inversion is a condition wherein the uterine fundus collapses through the cervix presenting itself as a vaginal or introital mass.[1,2] It is further classified as puerperal or nonpuerperal, with the former being an obstetric emergency, associated with postpartum hemorrhage and a high mortality rate.[1,2] Puerperal uterine inversion (PUI), associated with vaginal delivery, is more common, comprising approximately 86% of all uterine inversions.[3] In contrast, non-PUI (NPUI) is associated with both benign and malignant uterine neoplasms often associated with a chronic and insidious onset. The most common cause of NPUI is leiomyoma, accounting for approximately 80%–95% of all cases.[1,3] Leiomyosarcomas and carcinosarcomas, on the other hand, are the most common malignancies instigating the said condition.[3]

Of the sarcomas, embryonal rhabdomyosarcoma of the uterus is rare, represented in a scarce number of case reports.[1] However, exceedingly rare is uterine rhabdomyosarcoma with associated uterine inversion. Following an extensive review of several international search engines such as PubMed, Cochrane, Clinical

[1]*Section of Gynecologic Oncology and Trophoblastic Disease, Department of Obstetrics and Gynecology, Jose R. Reyes Memorial Medical Center, Manila, Philippines*

Address for correspondence:
Dr. Bernadette Mayumi Telan Mortel, Jose R. Reyes Memorial Medical Center, Rizal Avenue, Santa Cruz, Manila, Metro Manila, Philippines.
E-mail: mayumitelanmortel@gmail.com

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Key, Science Direct, in addition to local sources, namely Health Research and Development Information Network, Department of Health Journals, and *Philippine Journal of Obstetrics and Gynecology*, there have only been eight reported cases of embryonal rhabdomyosarcoma with concomitant uterine inversion from 1887 to present.[1,4-9] This is only the ninth reported case worldwide and the first published report and documented case in the Philippines.

Due to the rarity of the condition, the optimal course toward diagnosis and management has yet to be established. The specific dilemmas encountered in the case are as follows: (1) examination of a prolapsed introital mass in a pediatric patient, (2) histologic confirmation of rhabdomyosarcoma, and finally (3) the work-up and surgical approach of uterine inversion with an associated malignancy. While there are recommendations on the approach to non-PUI and embryonal rhabdomyosarcoma, respectively, there is yet to develop an established protocol on the management of prolapsed uterine inversions with associated gynecologic malignancies.[1,4-9] Consequently, the case report not only aims to discuss a stepwise approach in the diagnosis and management of this unfamiliar condition but more importantly contribute to the development of a standardized treatment for prolapsed malignancies of the female genital tract. This is a case of an adolescent nulligravida who developed a prolapsed introital mass eventually proving to be a case of uterine inversion secondary to embryonal rhabdomyosarcoma of the corpus.

Case Report

A 12-year-old nulligravida presented with an introital mass associated with vaginal discharge and occasional spotting of 3-month duration. The patient had her menarche few months prior and still had irregular cycles, lasting 5–7 days with normal flow. She was initially asymptomatic until 3 months prior to consult, and she suddenly experienced heavy vaginal bleeding with associated mild hypogastric pain characterized as pressure and discomfort in the vagina. This was followed by sudden protrusion of a mass beyond the vaginal introitus approximately measuring 4 cm × 4 cm. The event was acute and spontaneous in onset, not triggered by sudden physical activity and exertion. The pain was spontaneously and gradually relieved after the prolapse of the mass without pain medications. Due to the relief, the patient opted to observe her symptoms without disclosing the incident. Interval history reported rapid growth of mass within 2 months, with occasional spotting. There was no associated bowel or urinary changes, weight loss, or generalized body malaise. Pain was infrequent; however, the discomfort from the progression in size limiting her activities prompted disclosure to her parents, leading to a consultation with an obstetrician-gynecologist. Biopsy of the lower portion of the mass was initially inconclusive revealing atypical cells suspicious for malignancy. Due to a high index of suspicion, a repeat biopsy of substantial tissues was done with results favoring embryonal rhabdomyosarcoma. Upon referral, she had stable vital signs, with no pallor and unremarkable chest and cardiac findings. The abdomen was soft, nontender, with no palpable mass. Approximately 4 cm from the vaginal introitus, a large, friable, irregular mass with focal areas of necrosis was visualized. Further manipulation caused extreme discomfort; hence, pelvic examination was completed under anesthesia. The prolapsed mass measured 18 cm × 16 cm × 13 cm, attached to a pedicle that measured 3 cm × 3 cm. The entire length of the vaginal canal was smooth measuring 4 cm, with no discernible cervix. The uterine fundus was neither palpable on bimanual nor rectoabdominal examination. As the findings were highly suspicious for uterine inversion, the prolapsed mass was eventually identified as the completely exteriorized and inverted uterine corpus. The uterus could not be made separate from the mass, and what initially seemed to be the pedicle was the endocervical canal and cervix [Figure 1]. The rectum was smooth, with no tumoral extension. There were no palpable or enlarged lymph nodes during the examination.

Sonographic findings were congruent with the impression of a non-PUI. The uterus was not visualized in its normal anatomic position. Instead, a U-shaped uterus was seen with the fundus concave and its longitudinal groove at the center of inversion. The endometrial cavity was exposed, inverted, and exteriorized. Attached to the mid and fundal region of the corpus was a heterogeneous mass measuring 19.7 cm × 19.9 cm × 17.9 cm, with irregular borders and abundant color flow [Figure 2]. Magnetic resonance imaging (MRI) findings also showed a U-shaped uterine cavity with an inverted fundus on

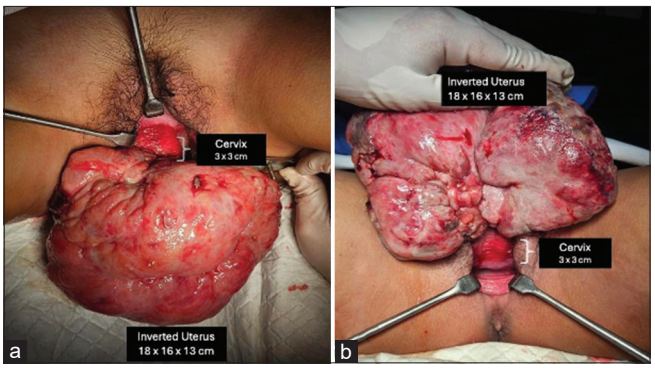

Figure 1: Physical examination findings. (a) Anterior view of the inverted uterus, inseparable from the mass. (b) Posterior view of the inverted uterus and cervix

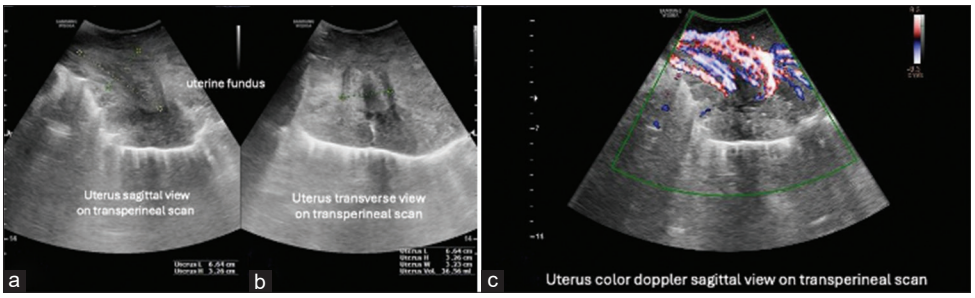

Figure 2: Sonographic findings of transperineal scan of vulvar mass. (a) Sagittal view. (b) Transverse view. (c) Doppler image demonstrating abundant color flow

sagittal view [Figure 3]. On axial view, a bull's eye or target appearance of the uterus was seen, which is pathognomonic of uterine inversion. This was further confirmed in the coronal view as the round ligaments were visualized as pulled medially and downward with the fundus [Figure 4]. Despite the large mass, the lesion was confined to the corpus with no involvement of the other pelvic organs and parametria. Abdominal, pelvic, and inguinal lymph nodes were also not enlarged.

A multidisciplinary team was established, and the patient was co-managed with pediatrics, reproductive medicine, anesthesiology, and behavioral medicine. After thorough counseling, the guardians consented to leave behind the ovaries for future fertility. The surgery was done through an abdomino-vaginal approach. On opening, there was no free peritoneal fluid. The uterus was found to be inverted into the cervix, with the fallopian tubes and ovaries pulled along with it [Figure 5]. Excision of the mass was done vaginally [Figure 6]. The uterus was repositioned and proceeded to do total abdominal hysterectomy with bilateral salpingectomy. Inspection of the bowels, omentum, peritoneal surface, liver, kidneys, stomach, spleen, and paracolic gutters was done with unremarkable findings. There were no palpable pelvic and para-aortic lymph nodes.

Grossly, the huge mass had an irregular border with some rubbery and some soft parts. On cut section, the mass had multiple translucent septa that formed lobulations with areas of hemorrhage and necrosis. In contrast, the endocervical canal and ectocervix were smooth with no gross lesions. The fallopian tubes were grossly normal as well, with no tumor involvement [Figure 7]. There were no intraoperative complications, and the patient tolerated the procedure well with an estimated blood loss of 300 cc. Postoperative course was surgically uneventful as pediatrics and behavioral medicine provided supportive management and counseling. The patient recovered and was thereby discharged on the 4th postoperative day.

Histopathologic findings confirmed the initial reading of embryonal rhabdomyosarcoma. A hypercellular subepithelial zone was visualized and beneath it was a hypocellular myxoid stroma containing round and spindle cells with scant cytoplasm [Figure 8]. Lymphovascular space invasion was not demonstrated within the corpus. Immunohistochemistry staining showed diffuse positivity for desmin, myoD1, and myogenin confirming the diagnosis [Figure 9]. Additionally, the cervix and bilateral fallopian tubes were negative for tumor involvement. Based on the Children's Oncology Group staging for rhabdomyosarcoma, the patient is classified as Stage T1bN0M0 [Table 1].[10] The lesion was confined to the uterus with no nodal and distant metastasis (on imaging), and the mass measured more than 5 cm in the largest diameter. With this, the patient was advised to undergo combination chemotherapy with vincristine-actinomycin-cyclophosphamide for 8 cycles. This will be initiated after the intended ovarian tissue cryopreservation.

Discussion

Rhabdomyosarcoma is an aggressive malignant neoplasm arising from myogenic progenitor cells with various stages of skeletal muscle differentiation.[1,5,7] It is further classified into four subtypes – alveolar, pleomorphic, spindle cell/sclerosing, and embryonal.[1,5] Embryonal rhabdomyosarcoma is the most common classification accounting for nearly 60%–70% of cases.[11,12] However, embryonal rhabdomyosarcoma originating from the uterus is a scarce clinical condition. In a Medline review by Reynolds *et al*., only 12 cases of uterine embryonal rhabdomyosarcoma have been reported from 1972 to 2006.[13] Da Silva *et al*. additionally found only three more cases of the same pathology.[5] In comparison, the rarity of the case presented is further magnified due to its compounding presentation with non-PUI. To date, after extensive review of literature, the patient presented is only the ninth reported case of such exceptionally rare condition [Table 2].

Evident in our case, patients with NPUI complain of a prolapsed mass associated with foul-smelling vaginal discharge, vaginal bleeding, and hypogastric pain.[1,6,14] Alternatively, in the absence of an exteriorized mass, NPUI may present with vaginal fullness, dysmenorrhea,

and dyspareunia. In extreme cases, symptoms may include hypovolemic shock secondary to massive blood loss and urinary retention due to obstruction.[1,8]

As mentioned, the first dilemma encountered in the diagnosis of the case was not only due to the scarcity of NPUI sample cases but also the difficulty of examining a prolapsed vulvar mass within the adolescent age group. According to Wang and Wang, delay or misdiagnosis may occur as routine examination methods of speculum and bimanual vaginal examination could not easily be performed in this age group.[2] For pediatric patients with no history of sexual contact, performing routine speculum and pelvic examination while manipulating the prolapsed mass can cause extreme discomfort.[2,15,16] Doing the examination under anesthesia was a necessary step to adequately assess the mass. In the case above, the characteristic features of NPUI only became evident after induction of anesthesia. The crucial findings are as follows: (1) no recognizable cervical ring along the proximal part of the mass, (2) no recognizable cervical os or probe leading to endometrial cavity, and (3) inability to palpate the fundus in the presence of a vaginal or introital mass. These specific and distinct descriptors first reported by Lascarides and Cohen in 1968 were consistently evident in other cases of NPUI.[2,14,17]

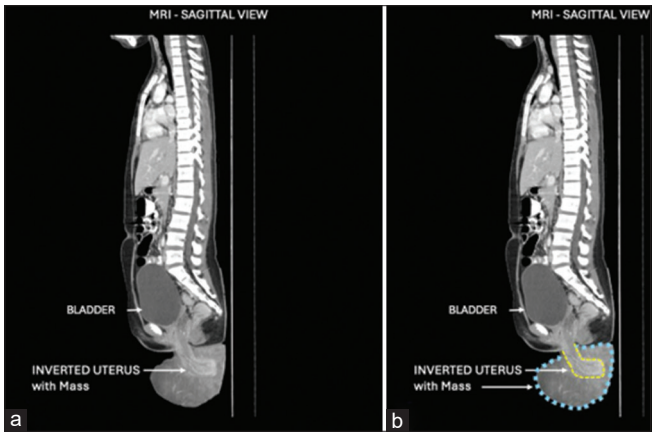

Figure 3: Magnetic resonance imaging images. (a) Sagittal view demonstrating an inverted uterus. (b) Yellow dotted lines delineate the uterine corpus, and blue dotted lines delineate the irregular mass

Non-PUI is staged depending on the degree of the prolapse. Stage 1 pertains to an incomplete inversion

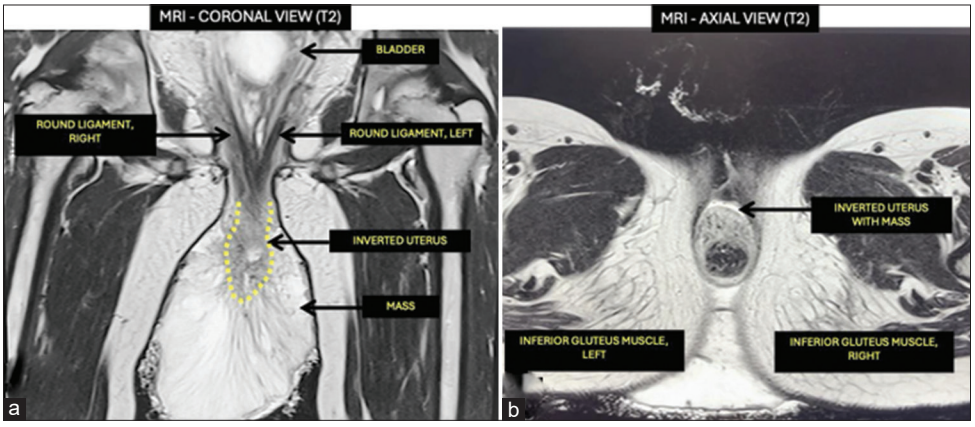

Figure 4: Magnetic resonance imaging images. (a) Coronal view showing an inverted uterus with prolapsed mass. Superior to the uterus are the round ligaments pulled medially toward the inverted uterus. (b) Axial view showing an inverted uterus with bull's eye or target appearance which is pathognomonic of uterine inversion

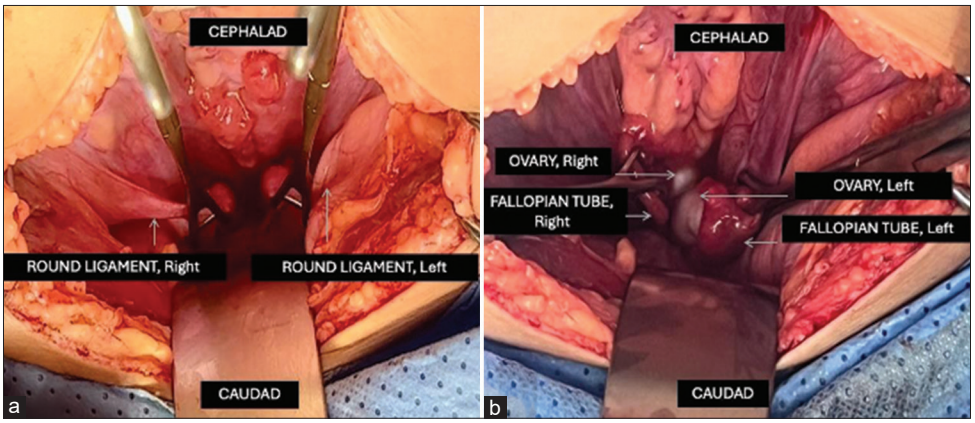

Figure 5: Intraoperative findings. (a) Corpus not visualized in its normal anatomic position, with round ligaments pulled medially and downward. (b) Fallopian tubes and ovaries identified being pulled medially and downward

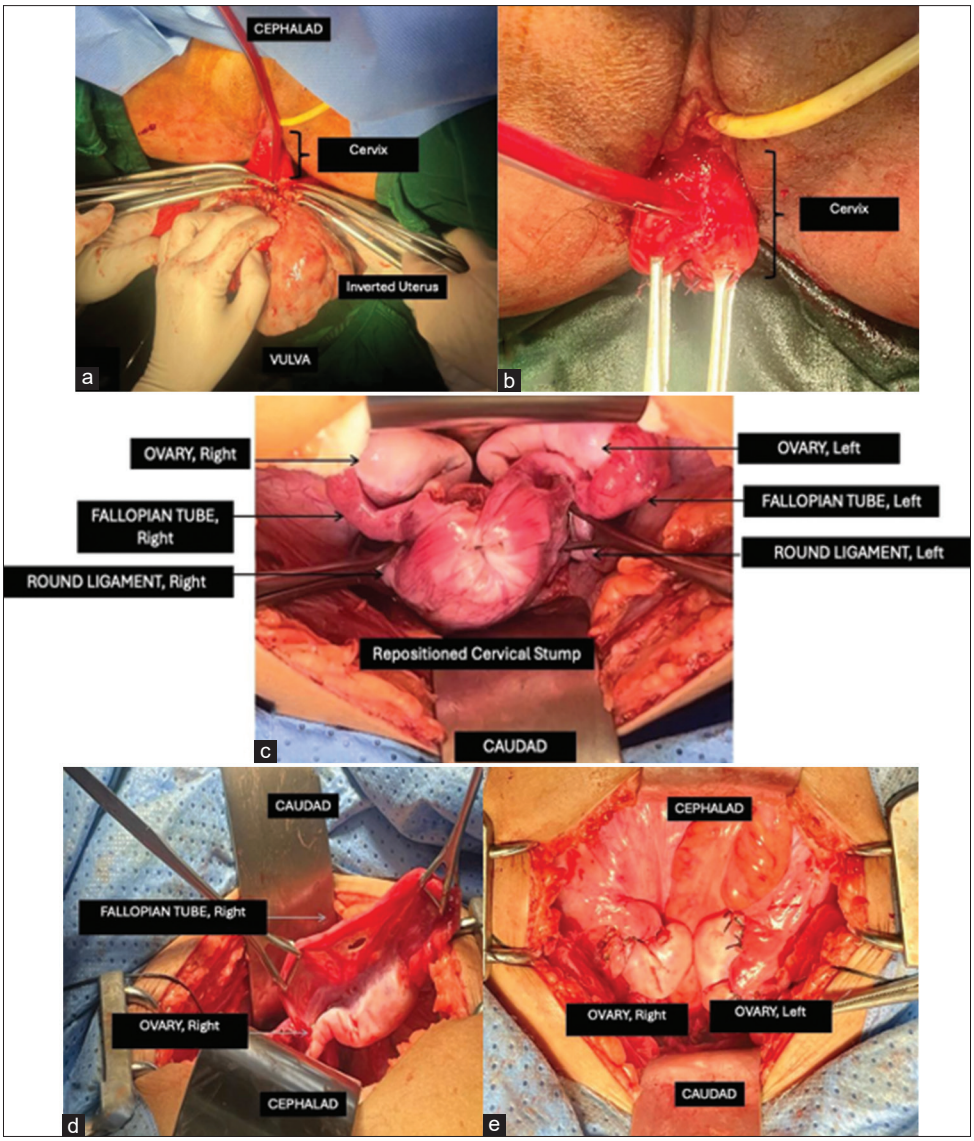

Figure 6: Surgical approach. (a) Vaginal excision of the tumor. (b) Inverted cervical stump. (c) Repositioned inverted cervical stump with remnants of fallopian tube and round ligaments. (d) Proceeded with bilateral salpingectomy. (e) Ovaries *in situ* after abdominal hysterectomy with bilateral salpingectomy

as the fundus remains in the uterine cavity; Stage 2 is the complete inversion of the fundus through the ring of the cervix; Stage 3 is the total inversion of the fundus protruding out the vulva; and Stage 4 is complete uterine inversion with exteriorization of the vagina.[1,2,15,18] The case above was identified as Stage III due to the complete inversion of the uterus and cervix beyond the vulva, without the involvement of the vagina. The pathophysiology behind uterine inversion is multifactorial. The rapid growth of sarcomas induces pressure atrophy on the implantation site resulting in thinned out uterine walls. Additionally, the tumor irritates the myometrium leading to contractions which dilate the cervix. These expulsive forces, in addition to the tumor's traction on weakened myometrial walls, lead to inversion of the fundus into the vaginal canal and occasionally, beyond the vulva[1,2,5,8,19] [Figure 10]. This was observed in our patient as she experienced worsening hypogastric pain attributable to progressive uterine contractions prior to expulsion of the vulvar mass. The compounding effect of the following factors: (1) heft of the tumor, (2) thinned out walls that anchor the mass, and (3) a nulliparous uterus may have provided sufficient traction to pull in the fundus leading to uterine inversion. Other risk factors in the development of NPUI include menopausal status, tumor size, and if present, thickness of the pedicle.[1,2,14]

The second dilemma involves the histologic confirmation of rhabdomyosarcoma. Such confirmation is crucial for the definitive management of the condition. Reported cases of the said condition experienced difficulty in verifying the malignancy due to extensive necrosis, often requiring multiple biopsies.[4,6,9] In the index case

mentioned above, the same difficulty was experienced as the initial biopsy was inconclusive. According to Li *et al*., biopsies from the superficial tumor may not depict the true nature of the disease due to extensive inflammation and necrosis.[1] There have even been negative results when sampling lower portions of the mass, further causing delay in treatment. As such, larger excisional biopsies may be needed to obtain adequate tissues representative of malignancy. Conducting biopsies under general anesthesia may even be necessary for diagnostic procedure.[4,6,9]

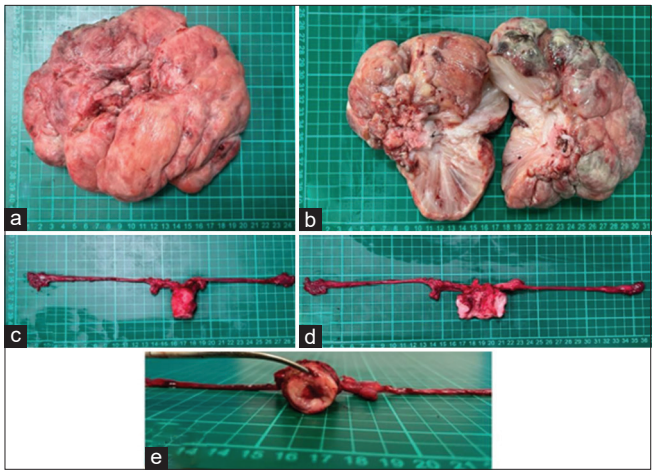

Figure 7: Gross findings. (a) Uterine mass, poorly circumscribed, cream, soft. (b) Cut section of uterine mass showing areas of necrosis and hemorrhage. (c) Cervix showing with no gross involvement. (d) Endocervical canal showing no gross involvement, hemorrhage, and necrosis (e) Ectocervix, no gross involvement

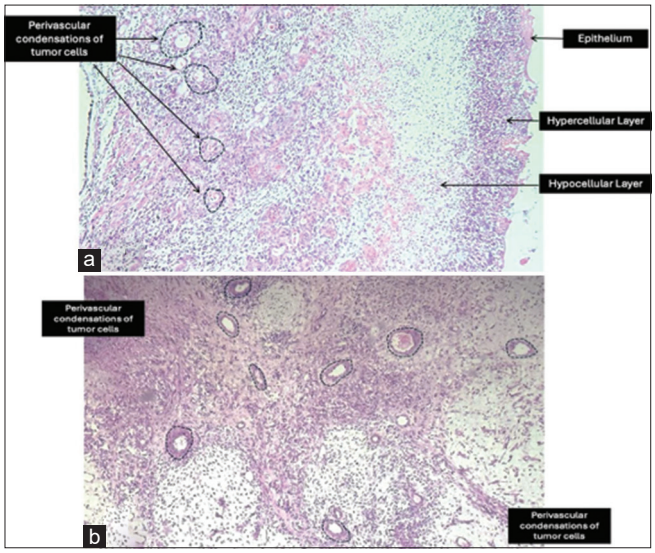

Figure 8: Histologic findings of embryonal rhabdomyosarcoma. (a) Scanner view demonstrating hypercellular layer, also known as cambium layer, beneath epithelium and the hypocellular beneath the cambium. Also visualized are perivascular condensations of tumor cells in dotted lines. (b) LPO view demonstrating perivascular condensations surrounded by tumor cells in dotted lines. LPO: Lower Power Objective

The third dilemma encountered involves the work-up and management of genital tract sarcoma with associated uterine inversion. With NPUI alone, there is no known standardized approach for the work-up and management. As such, Herath *et al*. proposed a treatment algorithm in 2020, after a comprehensive

Table 1: Updated Children's Oncology Group Rhabdomyosarcoma Modified TNM Pre-Treatment Staging Classification

Stage	Sites	Size	N	M
1	Orbit Head and neck (excluding parameningeal) GU – non-bladder/non-prostate	a or b	N0, N1, or Nx	M0
2	Parameningeal Bladder/Prostate Extremity Other (includes trunk, retroperitoneum)	a	N0 or Nx	M0
3	Parameningeal	a	N1	M0
	Bladder/Prostate Extremity Other (includes trunk, retroperitoneum)	b	N0, N1 or Nx	M0
4	All	a or b	N0, N1 or Nx	M1

Tumor
- T (site)$_1$: confined to anatomic site of origin
- T (site)$_2$: extension and/or fixative to surrounding tissue
- a: ≤ 5 cm in longest diameter
- b: > 5 cm in longest diameter

Regional Nodes
- N0: regional nodes not clinically involved
- N1: regional nodes clinically involved as defined as ≥1 cm measured in short axis on CT or MRI
- Nx: clinical status of regional nodes unknown (especially sites that preclude lymph node evaluation)

M: Metastases
- M$_0$: No distant metastases
- M$_1$: Distant metastases present
- Note: The presence of positive cytology in pleural fluid, abdominal fluid, or CSF and the presence of pleural or peritoneal implants are considered evidence of metastases

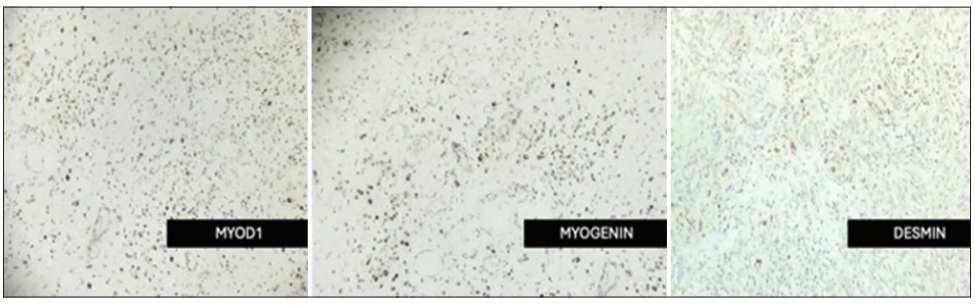

Figure 9: Immunohistochemistry. Positive stain for MyoD1, myogenin, and desmin

Table 2: Summary of literature with ERMS induced uterine inversions[1,4,5,6,7,8,9,24]

Authors (year)	Age/ Gravidity	Presentation	Physical Exam Size of Mass	TNM staging	Surgical Approach	Neoadjuvant/ Adjuvant Treatment	Outcome
Giacolone *et al*. (2004)	14, Nulligravid	3-month history of postcoital bleeding, intermittent pelvic pain, abnormal vaginal discharge, and dyspareunia	Necrotic mass in the upper vagina Hgb 8.5 g/dL	T1, N0, M0	Abdominal (laparoscopic) Mass excision and uterine repair Tumor arterial embolization (femoral)	Unknown	Disease free 2 months later with normal uterus and on chemotherapy
Ojwang *et al*. (2006)	Unknown	Unknown	10.5 x 9 cm mass	Unknown	Unknown	Unknown	Unknown
Da Silva (2008)	15, Nulligravid	3-month history of AUB with 6 days of necrotic tissue discharge	Necrotic mass in the vaginal introitus Hgb 8.3 g/dL	T1, N0, M0	Abdominal (laparotomy) Total hysterectomy following Haultain method	Adjuvant Regimen 1: Vincristine, Doxorubicin, cyclophosphamide actinomycin D Alternating Regimen 2: Ifosfamide, cisplatin, etoposide 3 weekly intervals + Pelvic Radiotherapy	Died 9 months after surgery due to recurrence and dissemination of disease
Ambreen *et al*. (2019)	22, Nulligravid	4-month history of lower abdominal pain and abnormal uterine bleeding	Necrotic mass 4 x 5 cm Hgb 6 g/dL	Unknown	Abdominal (laparotomy) Total hysterectomy following Haultain method	Adjuvant VAC regimen	18cm recurrence after the 3rd cycle. Liver metastasis death 14 months later.
Suneja *et al*. (2020)	14, Nulligravid	Vaginal bleeding and polypoid mass in vagina (unknown duration)	Necrotic introital mass 9 x 5.8 x 8 cm	T1, N0, M0	Abdominal (laparotomy) Total hysterectomy following Haultain method	Neoadjuvant VAC regimen	No recurrence Free of disease at 5-year follow-up
Peng *et al*. (2021)	19, Nulligravid	6- month history of AUB Seizures and aphasia	Necrotic and infected mass 17×15 x 10cm Hgb drop from 10.8 to 6.3 g/dL over 3 hrs	Unknown	Vaginal tumor excision followed by laparoscopic total hysterectomy with bilateral salpingectomy	Adjuvant VAC regimen after 43 days since surgery	Recurrence of 5cm mass in the pelvis Death in 6 months after recurrence of mass and rapid growth (16 cm) despite the 4th cycle of chemotherapy
Li *et al*. (2022)	27, Nulligravid	Presented with 4-month history of AUB and 2 weeks of worsening bleeding. Right lower abdominal pain (sharp) Worsening 3-month history of cramping Foul smelling vaginal discharge	Initial visit to ER, negative HCG, elevated WBC at 15,600, positive urine nitrites and leukocyte esterase with increased neutrophils to 12, 540.	T1, N0, M0	Vaginal tumor excision followed by laparotomy for repair. After confirming histology, separate OR, underwent Abdominal (laparoscopic) total hysterectomy with bilateral salpingooophorectomy	Adjuvant VAC regimen	No recurrence Free of disease for unknown duration
Wright (2022)	22, Nulligravid	6-month history of AUB with intermitted abdominal pain	Necrotic introital mass 6 x 6 6 cm Hgb 3.8 g/dL	Unknown	Abdominal (laparoscopic converted to laparotomy) Modified radical hysterectomy	Adjuvant VAC regimen followed by 4 cycles of VA	Unknown
Current Case (2024)	12, Nulligravid	3-month history of AUB with intermitted abdominal pain	Necrotic introital mass 18 x 16 x 13 cm	T1, N0, M0	Vaginal tumor excision followed by Abdominal (laparotomy) total hysterectomy with bilateral salpingectomy	Adjuvant VAC regimen (to start)	No recurrence

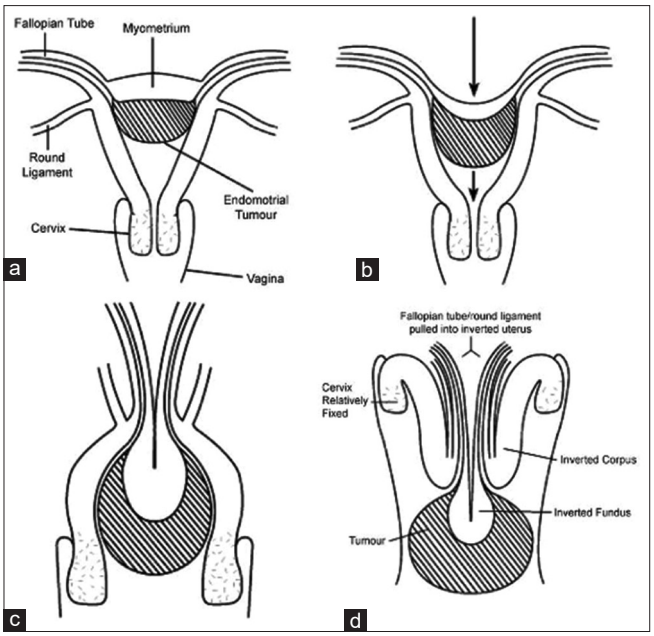

Figure 10: Illustration of uterine inversion (directly lifted from Moulding *et al.*).[20] (a) Growth of tumor at the fundus. (b) Several factors leading to inversion of the fundus with endometrial mass. (c) Prolapse of mass at the level of the cervix. (d) Prolapse of mass into the vagina

literature review and analysis[18] [Figure 11]. According to Herath *et al*., if with clinical suspicion of uterine inversion, imaging modalities in the form of ultrasound or MRI should be done to verify the impression. Supported by several reports, ultrasonography should be considered the first line of investigation due to its wide availability and simplicity.[1,2,5,8,18] Incomplete uterine inversions have sonographic features that show a "Y"-shaped uterine cavity in the longitudinal plane, wherein the base of the "Y" is the nonprolapsed endometrial lining.[1,2,8,18,20] Complete uterine inversion, on the other hand, presents with a "U"-shaped uterus that shows a completely inverted endometrial lining and uterine walls. Furthermore, a bull's eye or target sign is visualized in the transverse plane showing a hyperechoic fundus surrounded by a hypoechoic rim.[1,2,8,18,20] In relation to our case, both the U-shaped uterus and target sign were identified in the patient's ultrasound findings, confirming Stage III uterine inversion. Additionally, other ultrasonographic findings consistent with sarcomas were also reported, as the lesion was described as a heterogeneous mass, with abundant color flow.

Pelvic MRI remains superior to ultrasound due to its higher sensitivity in detecting NPUI.[1,5,9,8,18] The Y-shaped and U-shaped uterine configurations for incomplete and complete inversions are enhanced and appreciated.[1,2,8,18,20] The bull's eye sign is also seen on the transverse view of complete inversion due to the infolding of the fundus toward the cavity.[1,2,18,20] Specific to MRI, however, is its ability to visualize the round ligaments and fallopian tubes protruding centrally from the top of the uterus, indicating that it is being pulled downward and medially with the fundus. This was evident in our patient as both the round ligaments were visualized as being pulled medially toward the inverted fundus. Another advantage of MRI over ultrasound is that it can also provide information on the extent of the disease, whether disseminated, locally advanced, or confined to the lesion.[18,20,21] This was crucial in treatment planning as it allowed the surgical team to develop a less radical approach for a confined disease.

Previously, the Intergroup Rhabdomyosarcoma Study Group recommended a combination therapy comprising surgery, followed by radiotherapy (RT) and chemotherapy. However, the Intergroup Rhabdomyosarcoma Study-IV (IRS I-IV) studies recently concluded that chemotherapy alone had excellent survival rates with much lower morbidity.[22] Arndt *et al*. determined the optimal management for Female genital tract rhabdomyosarcomas (FGU-RMS) and demonstrated a 5-year failure-free and overall survival of 72% and 87%, respectively, amongst those with nonmetastatic tumors using a chemotherapeutic regimen alone.[23] However, the application of this conservative principle to cases of uterine embryonal RMS (eRMS) with uterine inversion remains unclear. As mentioned, to date, there is no standardized protocol or treatment approach for malignant uterine inversions. According to Strahl *et al*., a conservative approach is not a reasonable option for tumor control.[16] On review of the other eight known cases of uterine eRMS with uterine inversion, seven proceeded with surgery followed by neoadjuvant chemotherapy with or without RT.[1,4-9] One involved localized resection of the mass to conserve the uterus, two involved vaginal excision followed by abdominal laparoscopy, while four proceeded with an abdominal approach alone, repositioning the uterus followed by total hysterectomy. Three of the abdominal approaches were through laparotomy, while the last was minimally invasive.[4,5,8,9] The initial step across all laparotomies centered on uterine repositioning using the Haultain method. The posterior constriction ring was cut, and gentle traction of the fundus and round ligaments was applied.[4,5,8] After reinversion, the respective surgical teams proceeded to doing hysterectomies. This is in contrast to the combined abdomino-vaginal laparoscopic approach, wherein the tumor was first excised vaginally prior to reinversion and proceeding with laparoscopic hysterectomy.[1,6] The index case presented above is the first reported to do a double setup through an abdomino-vaginal laparotomy approach with total abdominal hysterectomy and bilateral salpingectomy for prolapsed embryonal rhabdomyosarcoma of the uterus. The tumor was excised vaginally followed by repositioning of the remaining endocervical canal,

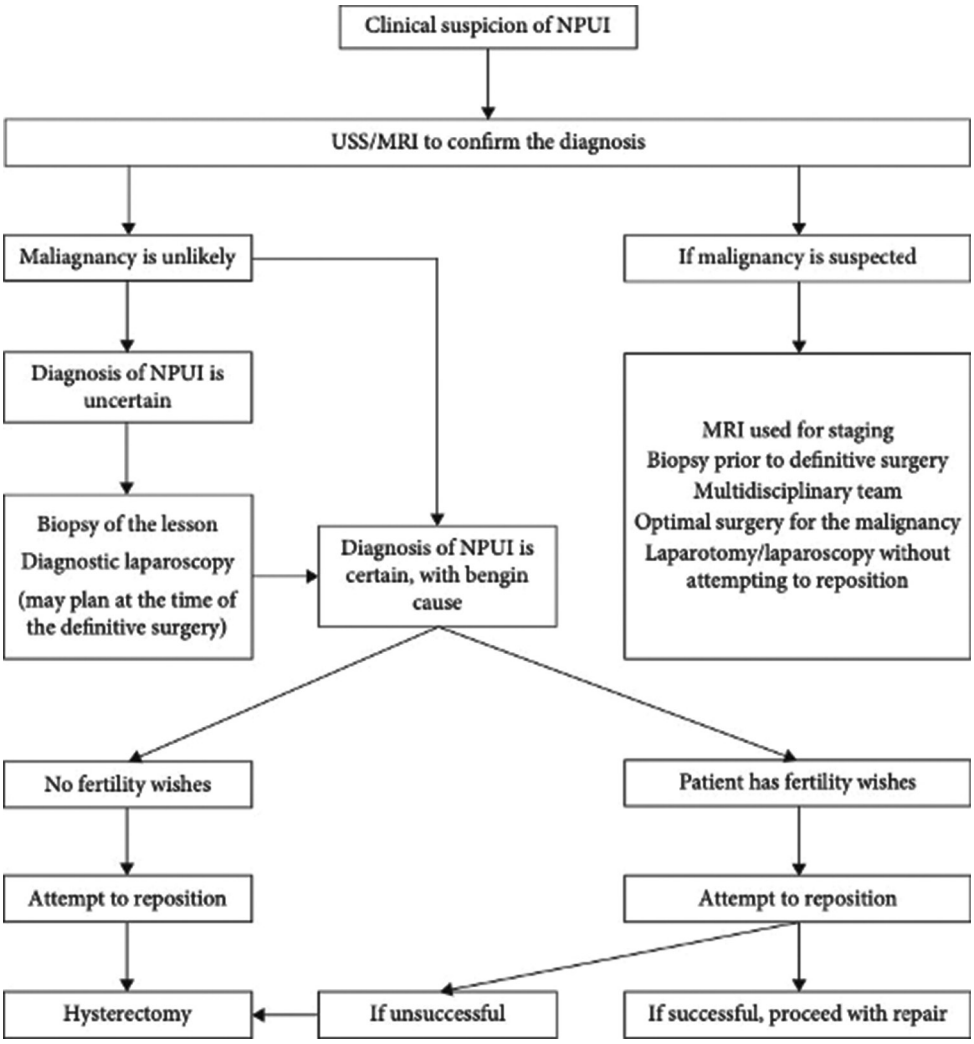

Figure 11: Algorithm for management of nonpuerperal uterine inversion (NPUI) (directly lifted from Herath *et al.*).[18] The above diagram shows the appropriate treatment algorithm for NPUI. NPUI: Nonpuerperal uterine inversion, MRI: Magnetic resonance imaging, USS: Ultrasound

completion of hysterectomy, and bilateral salpingectomy thereafter. Herath *et al*. reviewed 153 cases of NPUI that received surgery since 1940 until September 2018, inclusive of 50 cases of malignancies. Of these, 18% selected the vaginal approach, 48.8% preferred an abdominal laparotomy, while 27.1% proceeded with the abdomino-vaginal approach.[18] The management for our patient would fall under the latter group wherein the tumor was excised vaginally and the rest of the procedure was completed through laparotomy. Vaginal hysterectomy is not recommended in these cases, as according to Lautz *et al*.,[22] intraoperative visualization is very limited. Furthermore, the surgery did not include repositioning of the malignant uterus for two reasons: first, the size of the mass prevented the feasibility of this option, and more importantly, repositioning increases the risk of tumor seeding in the peritoneal cavity.[1,15] While there are other factors to consider, of the 4 cases that underwent uterine repositioning, 2 had tumor recurrence within months after surgery. Finally, the ovaries were left *in situ* as guidelines recommend refraining from oophorectomy if there is no gross involvement of the ovaries, as in our case. Lymphadenectomy was also not done as this was optional for low-risk patients and mainly recommended for those with high-risk disease.[11] Given that the malignancy was limited to the corpus with negative nodes on MRI, lymphadenectomy was reserved.

Histopathology of rhabdomyosarcoma contains both hypercellular and hypocellular areas amidst loose and myxoid stroma.[5,7,11] The hypercellular zone, also known as the cambium layer, is found immediately beneath the epithelium. Perivascular condensations of tumor cells are commonly visualized as well. These are evident in our patient, as shown in Figure 7. Marked pleomorphism, atypical mitosis, and rhabdomyoblasts with cross-striations were also identified, however may be absent in up to 50% of cases.[5] As such, immunohistochemistry to confirm the diagnosis is recommended, particularly

myogenic differentiation (MyoD1),[1] myogenin, and desmin. Positivity for desmin pointed toward rhabdomyosarcoma or leiomyosarcoma. However, positivity for MyoD1 and myogenin, which are skeletal muscle markers, was confirmatory for the diagnosis of rhabdomyosarcoma alone. As seen in the case above, the patient demonstrated diffuse positivity for all three – desmin, myogenin, and myoD1.

Chemotherapy, the gold standard treatment of RMS, is comprised of vincristine, actinomycin, and cyclophosphamide.[22,23] According to the International Soft Tissue Sarcoma Consortium, otherwise known as INSTRuCT, salvage surgery and RT are reserved for disease persistence, recurrence, and those with poorer histology. In a study done by the International Society of Pediatric Oncology on patients with FGU-RMS, 33% responded to the sole treatment of chemotherapy, demonstrating a 5-year overall survival of 91%.[23] In a similar study determining the optimal therapy for FGU-RMS, 20% received chemotherapy alone, with a 5-year overall survival of 87%.[22] Despite the reported favorable response to chemotherapy, uterine rhabdomyosarcoma was identified to have the poorest overall survival rate at 53% among all gynecologic tumor sites.[23] This outcome may be explained by other factors such as the toxicity from different chemotherapeutic trial regimens and the higher propensity of Stage IV disease among patients in this population. Equally important to note, the recurrence rate of uterine RMS is also high at 20%. Other prognostic factors include tumor size, depth of invasion, lymph node involvement, treatment modality (single versus combined), and age.[22,23] Patients aged 1–9 years had a 5-year survival rate of 94%, whereas adolescents and those <1 year old have a poorer survival rate of 76%.[23] Consequently, due to the poor prognosis associated with rhabdomyosarcomas of the uterus and her adolescent age, the patient was still advised to complete chemotherapy despite early-stage disease.

RT was excluded in her postoperative counseling, because according to the latest INSTRuCT guidelines, it is not recommended for those with negative tumor margins. Additionally, it has been shown that despite its protective effect on recurrence with only an 8% relapse after treatment, its impact on 5-year survival has not been proven.[6,23]

To maintain the patient's fertility options, fertility preservation consult was initiated prior to the patient's surgery. Ovarian tissue cryopreservation or oocyte harvest before the start of chemotherapy therapy is an option for her case. Another fertility-sparing method includes the administration of GnRh agonists prior to chemotherapy. This aims to lessen gonadotoxicity by inducing a hypogonadotropic state making the ovaries less vulnerable to chemotherapy. Finally, ovarian transposition may be offered among patients who will receive RT to prevent radiation-induced gonadotoxicity.[22]

Conclusion

Non-PUI is an exceedingly rare presentation of uterine rhabdomyosarcoma. Key findings include a vulvar mass with no visualized cervix and a nonpalpable fundus during internal examination. Histologic confirmation prior to definitive surgery may be achieved through adequate and substantial tissue sampling. Despite the lack of a standardized protocol for embryonal rhabdomyosarcoma with associated uterine inversion, vaginal excision of the tumor followed by total abdominal hysterectomy is an acceptable approach. This is often followed by chemotherapy, the cornerstone treatment, in the form of vincristine-actinomycin-cyclophosphamide regimen. Equally important, patients must be counseled on fertility-sparing options given that the disease commonly affects the pediatric age group. Finally, the case underscores the importance of maintaining a high index of clinical suspicion among pediatric patients presenting with a vulvar mass. Prompt work-up and management are crucial to ensure improved prognosis and quality of life.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

Authorship contributions

Bernadette Mayumi T. Mortel - Conceptualization, resources, data curation, writing (original and revised drafts), visualization.

Irene M. Tagayuna - Conceptualization, resources, data curation, writing (original and revised drafts), visualization.

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Conflicts of interest

There are no conflicts of interest.

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