Yolk Sac Tumour of Uterine Cervix in a Two-Year-old Girl: A Case Report.

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ABSTRACT

Background: Germ cell tumour (GCT) of malignant origin is a rare and heterogeneous group of tumours in the paediatric population. It could be seminomatous and non-seminomatous. The non-seminomatous group is less commonly seen. The most commonly seen type under the non-seminomatous group under the age of three years is the yolk sac tumour. The majority of yolk sac tumours is seen in the gonad while very few develop in extra gonadal sites such as the sacrococcygeal region, retroperitoneum, mediastinum, pelvis and stomach among others. Extra gonadal germ cell tumour is extremely rare in the cervix and when it occurs there may be challenges in the management. We report this case due to its rarity and the possibility of cure by chemotherapy, thus preserving fertility. **Case Presentation**: A 2-year-old female toddler presented with a 9-month history of persistent bleeding and discharge per vagina. At first, the bleeding was once a month and progressively worsened to once a day. There was no change in bowel and urinary habits. There was a pooling of blood in the vaginal vault on pelvic examination, otherwise unremarkable. Abdominopelvic ultrasound scan and magnetic resonance imaging were suggestive of a tumour of the uterine cervix. The mass was excised and sent for histopathological analysis. The histology of the mass showed a yolk sac tumour. Other laboratory investigations including tumour markers were essentially normal. She had treatment with bleomycin, etoposide, and cisplatin regimen (BEP) of chemotherapy as against radical surgery for potential preservation of fertility. She is five years on follow–up at the time of this report. There was no clinical, laboratory, or radiological evidence of recurrence. **Conclusion:** The 2-year-old female toddler responded well to chemotherapy. This obviated the need for radical surgery. There was preservation of potential for future fertility.

Keywords: Yolk sac, tumour, chemotherapy, uterine cervix.

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Introduction

Germ cell tumours (GCT) are rare malignant tumours with heterogeneous origins accounting for about 3% of all cancers in the paediatric population.[1] It could be seminomatous and non-seminomatous which is less commonly seen.[2] The most commonly seen type under the non-seminomatous group under the age of three years is the yolk sac tumour.[3] This is otherwise known as an endodermal sinus tumour. The majority of yolk sac tumour is seen in the gonad while very few develop in extragonadal sites such as the sacrococcygeal region, retroperitoneum, mediastinum, pelvis, pineal gland, liver, omentum, and stomach among others.[4] The most common extragonadal site is the mediastinum.[5] Germ cell tumours predominate in female subjects (boy: girl ratio=0.8:1).[6] The commonly involved extragonadal site in the genital system in females is the uterus, vaginal, and cervix in that order of sequence.[5] The yolk sac tumour accounts for 5-10% of all germ cell tumours in the USA.[7] The aetiology of the yolk sac

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tumour is largely unknown while the risk factors for germ cell tumours are undescended testes, radiation exposure, a disorder of sex development, family history, infertility, and Klinefelter syndrome among others, the only consistent risk factor for yolk sac tumour in the medical literature is Klinefelter syndrome.[8] The pathophysiology of the extragonadal yolk sac tumour is unclear. The classic theory explains the local transformation of misplaced primordial germ cells while the alternative theory suggests reverse migration of occult carcinoma in situ from the gonad.[9] The clinical presentation of patient with yolk sac tumour depends on the site of the tumour, the patient with ovarian yolk sac tumour may present with abdominal distension and pain and other constitutional symptoms of malignancy, the patients with yolk sac tumour of the cervix may present with persistent vaginal bleeding with or without attendant symptoms of anaemia. Pelvic examination may reveal a palpable pelvic mass which may be obvious on either speculum examination or vagino-uteroscopy. The diagnosis of a yolk sac tumour of the cervix is suspected following abnormal tumour markers such as Alpha fetoprotein, Lactate Dehydrogenase, and Beta Human Chorionic Gonadotrophin. The diagnosis is confirmed with a biopsy for histology which is the goal standard. Cross-sectional imaging such as computed tomography, magnetic resonance imaging, and positron emission tomography scan of the chest, abdomen and pelvis are done to determine the extent of the disease for adequate staging.[10] The modality of treatment of the yolk sac tumour of the uterine cervix can be chemotherapy, surgery and radiotherapy or a combination of them depending on the stage of the disease.[11] Extragonadal yolk sac tumour staging is based on some prognostic factors such as the organ of involvement, involvement of the lung, and the extent of tumour markers, unlike the gonadal counterpart where tumour node and metastasis staging is used.[12] There may be treatment dilemmas of patients with yolk sac tumour of the reproductive tract, especially in patients that are yet to complete their family size or in female child with great concern for future fertility. The options available for the preservation of fertility as well as the possibility of cure are primary chemotherapy and fertility-sparing surgery as against radical surgeries. The chemotherapy regimen of choice is bleomycin, etoposide and cisplatin.[13] Follow-up was done to monitor relapse by periodic general physical examination, assay of tumour markers, and imaging investigations. Extra gonadal germ cell tumours are extremely rare in the cervix and when it occurs there may be challenges in the management. We report this case due to its rarity and the possibility of cure by combination of chemotherapy (bleomycin, etoposide and cisplatin), thus the potential for preserving fertility.

Case Presentation and Management

A 2-year-old female toddler presented with a 9-month history of persistent bleeding and discharge per vaginum. At first, the bleeding was once a month and progressively worsened to daily occurrence basis. There was associated passage of clots. There was no history of change in urinary and bowel habits. No associated bleeding in any other part of the body. There was no history of trauma, abuse, weight loss, or difficulty in breathing.

On examination, she was healthy-looking, not in distress, not pale, anicteric, afebrile, not cyanotic, and well hydrated. The abdomen was soft with no palpable mass. A vaginal examination revealed the pooling of blood in the vault. Every other system was clinically unremarkable.

Pelvic ultrasound showed a bulky cervix containing a well-defined oval-shaped heterogeneously isoechoic mass measuring 46 x 35 x 44mm involving partly the uterus. A significant flow signal was seen within it on colour/power Doppler interrogation (**Fig. 1**).

Magnetic resonance Imaging (**Fig. 2**) of the pelvis revealed a large (43 x 33 x38mm), well-circumscribed cervical mass displacing the uterus superiorly and rectum inferiorly. The mass was iso- and hyperintense on T1 and T2/STIR weighted sequences and demonstrated heterogeneous enhancement. No blooming is seen on Gradient recalled echo. There was no fluid in the endometrial cavity. Minimal fluid was seen in the vagina

Both ovaries were normal. There was no pelvic lymphadenopathy. Chest radiogram did not reveal any suspicious findings. Laboratory investigations: alpha-fetoprotein of 3.92ng/ml. The haematological and biochemical results were essentially normal.

A core biopsy for histology during assessments under anaesthesia confirmed a yolk sac tumour. Figure 3. The diagnosis was explained to the patient's relatives including options of treatment. There was a management dilemma as the patient was prepared for radical resection of the mass including total abdominal hysterectomy and bilateral salpingo-

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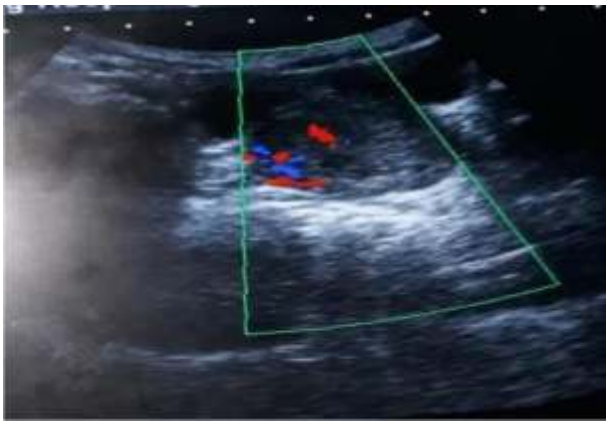
oophrectomy with or without adjuvant chemotherapy to guarantee cure. The patient's relatives were not forthcoming with the procedure due to no chance of future reproduction. The patient was offered three cycles of cisplatin etoposide and bleomycin. Post-chemotherapy surveillance with ultrasound revealed no residual mass and alpha-fetoprotein was negative as shown in Figure 4. She is five years on follow-up. No clinical, laboratory, or radiological evidence of relapse.

Figure 1A: Transabdominal pelvic ultrasound Longi--tudinal duplex sonogram



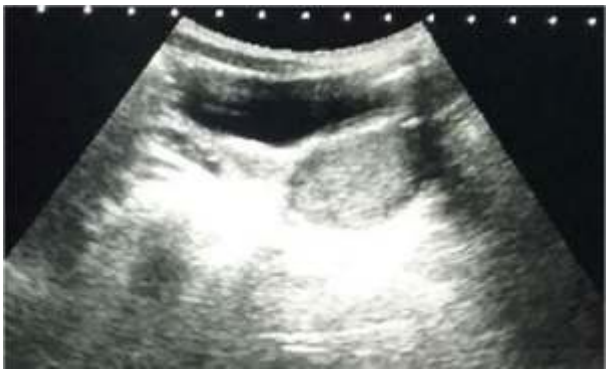


Figure 1B. transverse views how a heterogeneous solid isoechoic mass with well–defined regular margins (arrow) at the cervix, posterior to the urinary bladder. The significant flow was demonstrated within the mass on-power Doppler interrogation

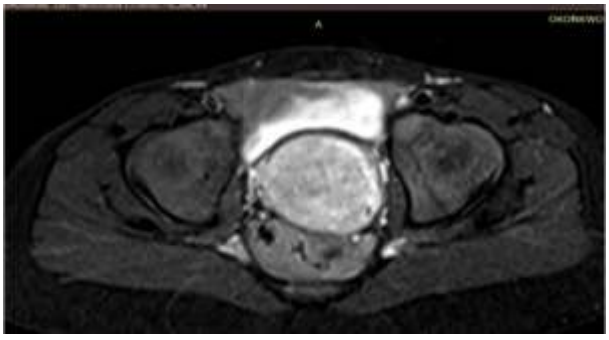


Fig 2A.

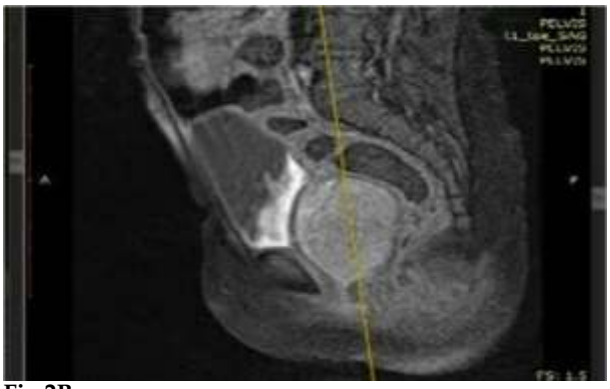


Fig 2B.

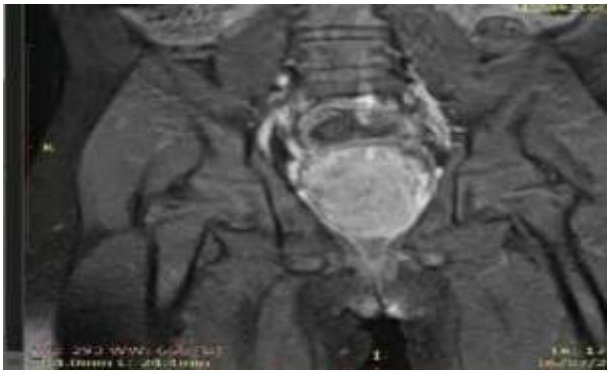


Fig 2C.

Figure 2A-C: A: Axial, B. coronal and C. sagittal contrast-enhanced fat-suppressed MRI images of the pelvis demonstrate an enhancing cervical mass, involving the uterine body superiorly and indenting the rectum. The fat planes around the cervix are preserved.

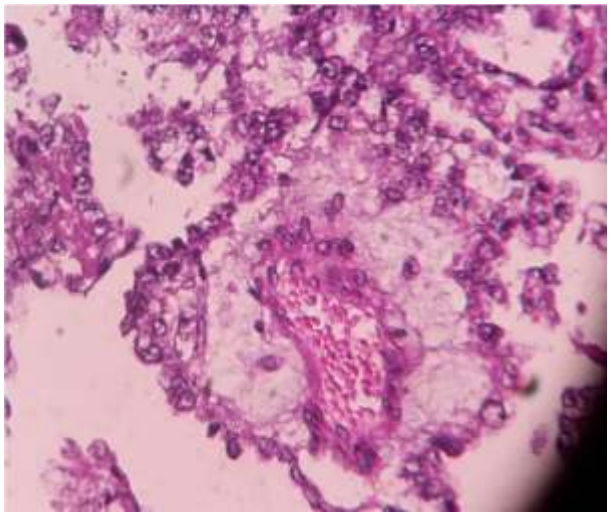


Figure 3: Section shows tumour tissue composed of malignant epithelial cells arranged in metacystic and nest patterns. The cells are round to oval with increased nuclear-cytoplasmic ratio, prominent nucleoli and scanty cytoplasm. A few of the cells are arranged radially around blood vessels reminiscent of Shiller Duval's body.

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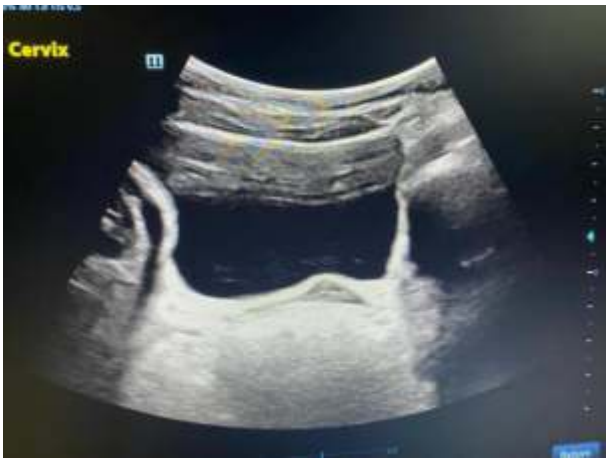

Figure 4: Trans-abdominal Pelvic ultrasound with longitudinal and transverse view show complete resolution of the tumour.

Discussion

Extra gonadal yolk sac tumour is an extremely rare clinical condition. The management might be laden with challenges especially when fertility is at stake. The index case of yolk sac tumour of the cervix partly involving the uterus. We shared our experience on the management dilemma concerning the case. The cervix is an uncommon site for rarely seen extra gonadal yolk sac tumour.[14] This case is one of the few that has been reported in the medical literature. In a study in Zaria that examined 189 malignant childhood tumours only 15 children had germ cell tumours.[15] Williams also reported only one case of yolk sac tumour (endodermal sinus tumour) in a study spanning over 13 years period which examined 1325 cases of childhood tumours in Ibadan, Nigeria.[14] Some of the other genital sites that have been reported are vaginal, uterus, and penile shaft in male patients.

Although the most common germ cell tumour under the age of three years is the yolk sac tumour. It has been reported that it has a bimodal age distribution in which the first peak is seen before the age of one and the second peak at adolescence. This index case report did not differ from this age distribution.

The clinical features of extra gonadal yolk sac tumour depend on the site of the body that is involved hence the development of persistent vaginal bleeding in this case as it involved the cervix and partly the uterus. The diagnosis is usually suspected following raised tumour markers and advanced cross-section imaging as done in this case. A positron emission topography-computed tomography scan is an ideal investigation of choice for metastatic workup.[16] This was not done in this case because information from abdomino-pelvic magnetic resonance imaging was sufficient. Elevation of alpha-fetoprotein has been consistently linked with yolk sac tumour as against other tumour markers. This case was not an exception as the only detected tumour marker was alpha-fetoprotein although it was normal. Other similar case series have reported raised alpha-fetoprotein. This may be perhaps due to the degree of differentiation of the tumour. The well-differentiated tumour may not elaborate high tumour marker. The diagnosis of a yolk sac tumour of the uterine cervix is confirmed with histopathological examination of the mass resected following vagino-uteroscopy.

The primary treatment option for the yolk sac tumour of the uterine cervix is controversial due to its rarity however, surgical resection of the mass with or without chemotherapy or radiotherapy is well known in the literature. The patient's relative declined due to desirous for future fertility.

This was a big challenge considering the overall survival of the patient. A trial of chemotherapy not only potentially cured the disease but also enhanced the chance for future fertility.

The follow-up of the patient has been unremarkable. This may not be unconnected with the good prognostic factors at presentation with normal alpha-fetoprotein and no distant metastasis.

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Conclusion

The 2-year-old female toddler responded well to chemotherapy. This obviated the need for surgery. There was preservation of potential for future fertility. There was a significant challenge considering the overall survival of the patient. A trial of chemotherapy not only potentially cured the disease but also enhanced the chance for future fertility. The follow-up of the patient has been unremarkable. This may not be unconnected with the good prognostic factors at presentation.

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