CASE REPORT

Mesonephric adenocarcinoma of the vagina masquerading as a suburethral cyst

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Accepted 7 June 2018

SUMMARY

Mesonephric adenocarcinoma (MA) of the vagina is an extremely rare tumour of the female genital tract. There are currently 22 reported cases in the published literature. Consequently, its pathophysiology and disease progression remain poorly understood.

A 63-year-old woman presented with a history of a swelling in her vagina. Two-dimensional pelvic floor ultrasound and MRI demonstrated a multiloculated cyst with no malignant features. Initial workup provided a working diagnosis of a suburethral cyst. The diagnosis of MA was made on histology after excision of the cyst. Subsequent postoperative investigation showed no spread of the disease. The patient completed a course of prophylactic brachytherapy to prevent the possibility of any recurrence of disease. Due to its rarity, it remains difficult to diagnose MA of the vagina even on histological analysis. We would therefore recommend a low threshold to excise or perform tissue biopsy of unspecified vaginal masses.

BACKGROUND

Mesonephric adenocarcinoma (MA) of the vagina is an extremely rare form of female genital tract cancer and accounts for less than 0.1% of all vaginal cancers.^{1–3}

It is more commonly found in the uterus, cervix, urethra and bladder.^{1,3–9} MA of the vagina has a bimodal age pattern and tends to present in the first two decades and between the fifth and sixth decades of life.^{1,4,5,8,9} In the 21st century, newer techniques in immunohistochemistry have been able to aid in the diagnosis of MA due to multiple different architectural arrangements of epithelial and connective tissue present in MA.¹⁰ However, due to its rarity, its pathophysiology and disease progression remain poorly understood and the diagnosis and treatment remain a challenge.¹

Her gynaecological and obstetric history includes uterine fibroids and two children delivered via caesarean section. She had a normal cervical smear history and had not previously used any hormone replacement therapy. Her relevant medical history included mild bronchial asthma and hypertension which were controlled on medications. She had a high body mass index of 37, was a non-smoker and did not drink any alcohol.

Abdominal examination was limited due to her body habitus. On vaginal examination, a 3 cm cystic mass, with no associated discharge from the urethra was seen. The cyst was non-tender and non-compressible. The suburethral mass was identified on the anterior vaginal wall to the left of the midline with an adherent base. There was no associated uterovaginal prolapse.

INVESTIGATIONS

Initial investigations including a midstream urine culture and sensitivity did not demonstrate any signs of infection and a transvaginal scan reported a finding of a multifibroid uterus with an endometrial thickness of 5 mm and normal ovaries. MRI revealed an encapsulated spherical mass measuring 31×27×29 mm in the left lower anterior pelvis to the left aspect of mid-vagina and left posterolateral aspect of the upper urethra (figure 1). The appearance was suggestive of mucinous content. Three-dimensional endovaginal ultrasound scan (BK Medical Type 8838 probe) and two-dimensional transperineal ultrasound (Type 8802 probe) revealed a multiloculated cystic mass located at the left side from midline measuring 48×28×36 mm which was in close proximity to the bladder (figure 2). There was no demonstrable connection between the mass and the urethra, thereby excluding a urethral diverticulum. The conclusions of both the MRI and ultrasound were that the mass was a suburethral vaginal cyst.

CASE PRESENTATION

A 63-year-old Afro-Caribbean woman presented to the Urogynaecological clinic with a gradual onset of a painless swelling in the vagina. This was associated with symptoms of urinary urgency without incontinence. There was no concomitant dysuria, urinary frequency, postmicturition dribble, haematuria, vaginal discharge or bleeding. She denied any history of vaginal trauma, use of vaginal pessaries or any red flag symptoms such as recent weight loss and change of bowel habits.

DIFFERENTIAL DIAGNOSIS

1. Suburethral cyst
2. Urethral diverticulum
3. Urethrocele
4. Inclusion cyst
5. Gartner duct cyst
6. Endometriotic cyst

TREATMENT

Surgical excision of the suburethral cyst was performed by a Consultant Urogynaecologist

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To cite: Shoeir S, Balachandran AA, Wang J, et al. *BMJ Case Rep* Published Online First: [please include Day Month Year]. doi:10.1136/bcr-2018-224758

Figure 1 MRI of 3 cm suburethral cyst on coronal view.

(AHS). Prior to excision of the cyst, a rigid cystoscopy was performed to rule out the presence of a urethral diverticulum. On cystoscopy, the posterior urethral wall was found to be irregular with no evidence of a fistula communication between the cyst and the urethra.

The cyst was demarcated using a surgical marker prior to surgical incision and was found to be 5 cm in diameter distending the anterior vaginal wall. The anterior aspect of the cyst wall was tethered to the posterior urethral surface. Local excision of the cyst was performed. The cyst wall was carefully dissected almost in its entirety but burst at the site of tethering just before completion. Sebaceous-like material and fluid were released. The tiny remnant of the cyst wall was then excised. The vaginal skin was sutured continuously with Vicryl 2/0.

Although a fistula was not identified, the urethral mucosa appeared thin and therefore an indwelling Foley catheter was placed in the bladder on free drainage for 6 days. The patient had an uneventful recovery and a successful voiding trial without the catheter.

Histopathology revealed a fibromuscular cyst wall formed of sheets of epithelioid cells with some areas associated with a spindled appearance. No clear cells were seen. Osseous metaplasia was present, and the tumour was infiltrating skeletal muscle. Immunohistochemistry showed that the epithelial cells were diffusely positive for AE1/3, cytokeratin 7 (CK7), epithelial membrane antigen, paired box gene (PAX)8, Ber-EP4, vimentin and cluster of differentiation (CD)56. There was focal staining for CD10, CK5, p63, p16, CD99, smooth muscle actin, CD117, transducin-like enhancer of split -1 and calretinin. The

Figure 2 Two-dimensional transperineal ultrasound image demonstrating a multiloculated cystic mass measuring 44×28×36 mm.

immunostaining for CK20, Wilms tumour 1, estrogen receptor, progesterone receptor, androgen receptor, glial fibrillary acidic protein, GATA binding protein 3, thyroid transcription factor 1, NapsinA, carcinoembryonic antigen, caudal type homeobox 2, prostate-specific antigen, prostatic acid phosphatase, racemase, thyroglobulin, synaptophysin, S100, desmin, myogenin, myogenic determination 1, D2-40, inhibin, high-mobility group AT-hook 2, hepatocyte nuclear factor 1, CD34 and beta catenin (nuclear) were negative. The K167 index was 1%–3%. The case was also reviewed externally and although not fully specific, the positivity of cytokeratins, vimentin, CD10, calretinin and PAX8 favour the diagnosis of vaginal mesonephric adenocarcinoma with stromal invasion was made. The differential diagnoses, including clear cell adenocarcinoma, endometrioid adenocarcinoma, a Skene's gland type adenocarcinoma or a salivary gland or Bartholin gland type adenocarcinoma were considered but thought unlikely from the morphology and immunoprofile.

OUTCOME AND FOLLOW-UP

The patient was referred to a tertiary cancer unit for disease staging. Positron emission tomography (PET), CT scan, examination under anaesthesia and a diagnostic hysteroscopy plus endometrial biopsy were performed. There was no sign of residual or recurrent disease. The imaging and biopsy results did not reveal any signs of metastases. Based on this, a stage 1 MA was diagnosed. The patient completed a course of prophylactic brachytherapy 30 Gy in six fractions using a multichannel vaginal applicator directed at 5 mm depth from the target area to minimise the risk of recurrence. She tolerated the treatment very well with no side effects at 6 weeks after the treatment. Follow-up is planned every 3 months for the first year with a surveillance MRI at 6 months after the surgery.

DISCUSSION

An electronic search of the literature was performed with no restrictions to either the publication language or the years of search. MEDLINE, EMBASE, NICE database and Google search items included: mesonephric adenocarcinoma, vagina, cervix and/or urethral diverticulum. This search retrieved a total of 43 references. After exclusion of duplications and irrelevant papers, a total of 16 papers were identified and studied.

Vaginal adenocarcinoma is the second most common form of vaginal cancer.¹⁰ The WHO classification of vaginal adenocarcinoma includes endometrioid, clear cell, mucinous and mesonephric subtypes.¹¹ Mesonephric adenocarcinoma is an extremely rare tumour of the vagina affecting less than 10% of the vaginal adenocarcinomas.^{2 12} There have been 22 cases reported in the published literature mainly in the 1960s and 1970s.^{1 2 4–7 12 13} Consequently, there is limited knowledge pertaining to the pathophysiology, treatment and disease and the progression of MA. We have presented a case of MA using MRI and alternative imaging modalities such as 2D and 3D pelvic floor ultrasound. Advanced histopathological analysis and immunochemistry enabled an accurate diagnosis so that the appropriate management strategy can be adopted following discussion in a multidisciplinary meeting.

Mesonephric adenocarcinomas develop from the remnants of mesonephric (Wolffian) ducts and present in up to 20% of adults.^{4 9 12} These ducts run laterally from the broad ligament to the uterus and cervix to reach the vagina.^{1 12} In very rare occasions, the remnants of mesonephric ducts may transform to cancer.¹⁴ The prevalence is highest in the first two decades and between the fifth and sixth decades of life.^{1 2 4 7 13} Unlike

other vaginal malignancies, the majority of mesonephric adenocarcinomas tend to arise from the anterolateral position in the vagina where the remnant of degenerated mesonephric ducts are located.^{2,4}

In most cases of MA of the vagina, patients tend to present with abnormal vaginal bleeding and a vaginal mass that may be polypoidal, plaque like or ulcerated lesions.^{1,15} In our case, the tumour was a well-circumscribed cystic structure without a punctum, which did not communicate with the urethra. Previous case reports showed poor prognosis in multiple cases secondary to incomplete excision of the tissue.² Pelvic floor ultrasound (2D and 3D) and MRI were useful in demarcating the edges of the cyst wall, the proximity to the bladder and providing detailed information of the structure of the cyst which aided in surgical excision. We are not aware of a previous description of imaging using 2D and 3D transperineal and endovaginal ultrasound to image MA. In our case, although ultrasound provided clear images, no malignant features were identified prior to surgical intervention. This could reflect early diagnosis before any infiltration of tumour occurred.

Due to the heterogeneity of the tumour, diagnosis is often difficult. Consequently, advanced immunohistochemical techniques have been found to be helpful in identifying these cases but it is largely based on its morphological appearance.¹⁰ MA is associated with a better prognosis if it is well-circumscribed, not infiltrating into adjacent structures and without lymph node involvement or distant metastasis.^{5,7} Metastasis and positive lymph nodes are associated with aggressive proliferation of the disease.^{8,14} The position of the disease in the vagina does not seem to have any bearing on overall prognosis.²

In the 1960s, the management of MAs involved radical surgery associated with a high mortality due to incomplete excision.^{2,4} More recently, the management strategies included either

a combination of surgical excision and radiotherapy to radiotherapy alone depending on patient comorbidities and operability of the tumour.¹⁶ In a small series of patients with a variable follow-up, the overall outcome of either treatment modalities appear equally effective and little is still understood regarding optimum treatment.⁵

Early diagnosis of mesonephric adenocarcinoma of the female genital tract is associated with a better prognosis.⁶ Due to the small number of reported cases worldwide and lack of knowledge of disease pathophysiology and progression, there is a large variation in the literature regarding long-term follow-up and treatment of patients with MA and therefore management is often left to the discretion of the clinician. Due to the rarity of disease, the low sensitivity of imaging modalities to identify malignant change and the lack of any early 'red-flag' warning signs; it remains difficult to diagnose MA of the vagina. We would therefore recommend a low threshold to excise or perform tissue biopsy to exclude malignant change in unspecified vaginal masses.

Acknowledgements Special acknowledges to Professor Glenn McCluggage at the Royal Victoria Hospital Belfast. He reviewed the histology results and added a wider range of immunohistochemical studies to help favour the diagnosis of the mesonephric adenocarcinoma of the vagina.

Contributors SS wrote the original drafts of the case report, coordinated between the team and contacted the patient to take her consent for publication. She did a provisional literature search on the mesonephric adenocarcinoma of the vagina and followed guidance on corrections, revision and rewriting the case report answering the highlighted questions related to the accuracy of the content of the report. AAB revised the case report draft, corrected layout and rewrote the discussion. JW wrote the histopathology findings and how the diagnosis was made. AHS performed the ultrasound, conducted the surgery, supervised, guided and followed through the whole process of writing the article. He advised on how to perform a thorough literature search. He revised and agreed on the final case report content. All contributors revised the final copy of the case report and agreed on its content.

Funding The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

Competing interests None declared.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

Patient's perspective

I was worried when I had a progressive swelling in the vagina and I thought by undergoing the excision of the vaginal cyst the problem will be solved. I felt at ease in the postoperative consultation even when I was informed about the unexpected diagnosis of cancer. The consultation was detailed, empathetic and constructive. The management I received at the tertiary centre was excellent and I had no side effects from the radiotherapy. My sister was worried that she might develop the tumour. The doctor reassured me that the disease is very rare and does not run in families.

Learning points

- It is important to consider the possibility of primary adenocarcinoma in patients who present with a vaginal mass, particularly a suburethral cyst or a urethral diverticulum.
- To consider a combined oncology radiology and urogynaecology multidisciplinary discussion prior to surgery in order to optimise patient care.
- Three-dimensional ultrasound and MRI, though useful in identifying the lesions are of a low sensitivity and specificity in identifying malignant change.
- Tissue biopsy and cytology should be considered prior to surgical intervention to aid the diagnosis and treatment for unspecified vaginal masses.

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