CASE REPORT

Perivascular epithelioid cell tumour and mesonephric adenocarcinoma of the uterine cervix: an unknown co-existence

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Abstract

A 67-year-old woman with post-menopausal bleeding and a suspicious endocervical mass was referred to gynaecology outpatients’ for diagnosis and management. Cervical punch biopsies taken showed a benign cervical perivascular epithelioid cell tumour (PEComa), with MRI imaging and PET-CT scan indicating a 3–4 cm endocervical tumour with malignant features. The patient underwent radical hysterectomy with lymph node dissection and the surgical specimen histopathology demonstrated a residual benign PEComa and a stage IIB mesonephric adenocarcinoma (MNA) of the cervix. There is no disease recurrence 12 months after surgery. Cervical PEComas are extremely rare tumours of mesenchymal origin deriving from the perivascular epithelioid cells with only 14 cases described so far. Cervical MNAs are rare tumours originating from the remnants of the mesonephric duct of Wolff with only 40 cases reported. Our case adds to the existing literature and highlights the challenges with regard to preoperative diagnosis, treatment and prognosis.

INTRODUCTION

The existence of a perivascular epithelioid cell tumour (PEComa) with a mesonephric adenocarcinoma (MNA) of the cervix is extremely exceptional. The first case of cervical PEComa was reported in 2004 and to the best of our knowledge there are only 15 cases of this tumour described in the published literature including the present case [1–6]. A recent literature review has reported that since 1962 there have been only 40 cases of MNA of the cervix described to date [7]. We report the clinical presentation, diagnostic approach and treatment of such a unique co-existence.

CASE PRESENTATION

A 67-year-old woman was referred from primary care to gynaecology outpatients’ due to post-menopausal bleeding and a clinically suspicious cervix. The patient reported no history of...
post-coital bleeding or abdominal pain and had a normal smear history. She had two normal vaginal deliveries and had received hormone-replacement therapy following her menopause for a brief time period. There was no significant past medical or family history.

On clinical examination, a 2 cm friable mass that bled on contact was found protruding through the uterine cervix. Cervical punch biopsies and an endometrial sampling biopsy were taken. Imaging investigations of the uterine cervix were arranged and the case was referred to the local tumour board for further management.

The cervical punch biopsies showed flat sheets of an epithelioid tumour with minimal pleomorphism, cytoplasmic pigmentation, scattered mitoses (A and B: hematoxylin–eosin staining, 10×, 40×). The tumour was strongly positive for HMB-45 (C), showed weaker patchy positivity for Melan-A (D) and was negative for S100 (E). No stromal component was identified. The final surgical specimen histology from the hysterectomy showed PEComa (large arrow) and mesonephric adenocarcinoma (small arrow) immediately adjacent to each other (short arrows) (F: hematoxylin–eosin staining, 10×).

Figure 1: The cervical punch biopsies showed flat sheets of an epithelioid tumour with minimal pleomorphism, cytoplasmic pigmentation, scattered mitoses (A and B: hematoxylin–eosin staining, 10×, 40×). The tumour was strongly positive for HMB-45 (C), showed weaker patchy positivity for Melan-A (D) and was negative for S100 (E). No stromal component was identified. The final surgical specimen histology from the hysterectomy showed PEComa (large arrow) and mesonephric adenocarcinoma (small arrow) immediately adjacent to each other (short arrows) (F: hematoxylin–eosin staining, 10×).
indicative of a malignant tumour. The mass was in close proximity to the posterior wall of the bladder but there was no definite direct invasion. No evidence of metastatic disease or abnormal lymph nodes was shown (Fig. 2).

The patient underwent radical hysterectomy with bilateral salpingo-oophorectomy and pelvic lymphadenectomy. Histopathology showed a residual benign PEComa and a moderately differentiated MNA. The MNA was composed of small glands with mild nuclear pleomorphism, scanty mitoses and no cytoplasmic vacuolation. Many of the glands contained dense eosinophilic luminal material. The MNA of the cervix was 4 cm in size, and was extending into the isthmic region and the myometrium of the uterine corpus. The vaginal resection margins and the paracervical fat were also involved (R1 resection). The 17 lymph nodes in total from the pelvis were identified and they were all free of the malignant tumour.

The patient was finally diagnosed with a tumour of the uterine cervix comprising a completely excised residual benign PEComa and a moderately differentiated MNA of the cervix FIGO stage IIB with positive excision margins and positive parametrial involvement. After radical surgery, the patient received chemo-radiotherapy and brachytherapy treatment. There is no disease recurrence 12 months after the surgery. The patient is being monitored closely.

**DISCUSSION**

Cervical PEComa is an extremely rare tumour of mesenchymal origin deriving from the perivascular epithelioid cells. The mean age of women presenting with cervical PEComas in the literature is 41 years (range: 24–67) [1–6]. This is much younger than the mean age of those with uterine PEComas [3] which
has been reported to be 51 years [2]. Patients usually present with a pelvic mass or abnormal vaginal bleeding [8]. Two of the cases of cervical PEComas were related to tuberous sclerosis complex, which is a genetic disorder characterized by mental retardation, seizures and the presence of tumours such as cutaneous angiofibromas [6]. Because clinical presentation is non-specific and imaging tests such as ultrasound, MRI and PET-CT scanning are totally inconclusive as to the nature of the tumour, a tissue specimen with immunohistochemistry is needed to establish the diagnosis [5].

MNA is a rare tumour that derives from the remnants of the mesonephric duct of Wolff in the lateral regions of the cervix [7]. In the recent literature review of 40 cases of MNA of the cervix described so far, the mean age of women was 52 years (range: 24–73) [7]. Most women present with abnormal vaginal bleeding and/or with a cervical mass [7, 8]. The patient’s cervical screening cytology tests are usually negative and diagnosis is established by the histopathological examination of tissue specimens taken from the cervix [7]. MNA of the cervix is one of the few histological types of cervical cancer that is not related to the human papilloma virus (HPV) [9].

According to the 2014 World Health Organization classification of tumours of the female reproductive organs, PEComas are tumours of mesenchymal origin with distinct morphological and immunohistochemical features that aid their diagnostic [9]. They typically contain epithelioid cells with clear to eosinophilic, granular cytoplasm demonstrating melanocytic and smooth muscle differentiation, thought to be derived from the so-called perivascular epithelioid cell [9]. PEComas frequently express the markers of HMB-45 (92%) and Melan-A (72%) [2]. In addition, up to 80% stain positive for smooth muscle actin, whereas desmin and h-caldesmon expression is less common [8]. In one case report, a subset of PEComas was identified with positive staining for TFE3 and a molecularly confirmed TFE3 gene rearrangement [4].

Cervical PEComas are rare and their biological behaviour is unknown. For this reason, there are two classification systems described in the literature in the attempt to classify them as ‘benign’, ‘malignant’ or of ‘uncertain malignancy potential’ and to allow for prognostication. The first classification was developed by Folpe et al. [3] and the proposed criteria for malignancy were: tumour size ≥5 cm, mitotic count >1/50 HPF, necrosis, high nuclear grade and infiltrating growth pattern. The second classification was suggested by Schoolmeester et al. [10] and involved the following criteria: size ≥5 cm, mitotic index ≥1/50 HPF, significant nuclear atypia, necrosis and lymphovascular invasion. If no criteria are met then the cervical PEComa is classified as benign. If the tumour has 1–3 of the criteria, then it is considered of uncertain malignancy potential, and if there are 4 or more criteria then it is malignant. The PEComa tumour in our case was benign according to the criteria described above.

Treatment for cervical PEComas usually involves hysterectomy, with only two cases being reported of local excision only [6]. Due to the rarity of the disease, it cannot be confirmed whether a cervical PEComa has a better prognosis when compared to a uterine corpus PEComa. In the cases of cervical PEComa described so far, only one woman who received local excision had disease recurrence (8.3%), whereas in a case series of 42 uterine corpus PEComas there were nine women with disease recurrence (21.5%) [3].

Cervical MNAs present with a mixture of morphological and immunohistochemical features that assist in the diagnosis [7]. They usually present with florid mesonephric hyperplasia and with a densely eosinophilic luminal secretion [7]. It has been reported that there is no lobular architecture, the nuclei have malignant features and the Ki-67 proliferation index is 15–20% [7]. Cervical MNAs have positive immunostaining for CD10, CK7, calretinin, EMA, vimentin, Pax8 and CA125, but negative immunostaining for CEA [7, 9].

Due to the rarity of cervical MNA the biological behaviour and prognosis of these tumours is not known. It has been reported that MNA carries a worse prognosis than the other histological types. It has been described that women with stage I MNA had a recurrence rate of 32% as compared to a recurrence rate of 16 and 11% for adenocarcinomas and squamous cell carcinomas of the cervix in early stage cancer [7, 11].

Treatment for cervical MNA depends on the stage of the cervical malignancy and involves radical hysterectomy with bilateral salpingo-oophorectomy, pelvic lymphadenectomy and adjuvant chemotherapy or radiotherapy [7]. In our case, the patient underwent radical hysterectomy with pelvic lymph node dissection and the final histopathology of the surgical specimen demonstrated residual benign PEComa and a stage IIB MNA of the cervix. The patient is being followed up by the gynaecologic oncology team and there is no disease recurrence 12 months after the surgery.

In conclusion, we report the first case of a tumour of the cervix with the component of a benign cervical PEComa and that of a stage IIB MNA. This case adds to the current body of literature and highlights the challenges that are imposed on the management in terms of preoperative diagnosis, treatment and prognosis.

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CONFLICT OF INTEREST STATEMENT
There is no conflict of interest.

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ETHICAL APPROVAL
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CONSENT
Informed consent was obtained from the patient.

GUARANTOR
Dimitrios Papoutsis is the guarantor of this case report.

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