MALIGNANT CERVICAL PEComA: A CASE REPORT AND REVIEW OF THE LITERATURE

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ABSTRACT:

Background: Perivascular epithelioid cell tumors represent a family of mesenchymal tumours characterised by co-expression of melanocytic and muscle markers. The PEComa family of tumours includes angiomyolipoma, lymphangioleiomyoma, clear cell “sugar” tumour of the lung and rare clear cell tumours of various location. The designation PEComa, not otherwise specified, has been applied to these “unusual clear cell tumours” which are rare and mainly located in the uterine body. Most PEComas follow a benign clinical course, but tumours with aggressive behaviour have been increasingly reported. Folpe first proposed criteria for assessment of malignancy in 2005. To the best of our knowledge, 35 uterine non-benign and only 13 cervical PEComas have been reported in the available medical literature in the English language.

Case description: We report a case of 57-year-old woman with malignant cervical PEComa, emphasising the diagnostic challenges. We have tried to evaluate the malignant potential of uterine PEComas according to Folpe criteria.

Keywords: PEComa, smooth muscle epithelioid tumour, tuberous sclerosis complex

INTRODUCTION

Perivascular epithelioid cell tumors (PEComas) represent a family of mesenchymal tumours defined by their co-expression of melanocytic and muscle markers [1, 2, 3]. The concept of a family of tumours sharing morphologically and immunophenotypically distinctive perivascular epithelioid cells (PECs) was proposed by Bonetti et al. in 1992 [4]. These cells were first described in renal angiomyolipomas by Apitz in 1943 and had no normal anatomic counterpart [5]. The PEComa family of tumours includes angiomyolipoma (AML), lymphangioleiomyoma (LAM), clear cell “sugar” tumour of the lung (CCST) and rare clear cell tumours of various location [1]. The designation PEComa not otherwise specified (PEComa-NOS) has been applied to these “unusual clear cell tumours” which are rare and mainly located in the uterine body [6, 7]. PEComas show marked female predominance, and some are seen in patients with the tuberous sclerosis complex (TSC), especially those located outside the gynaecological tract [1, 2, 3].

Most PEComas are benign, but a subset demonstrates aggressive behaviour. All the cases reported before 2005 were designated as “benign cases” and “non-benign cases” [6]. In 2005, Folpe et al. analysed 26 soft tissue and gynecologic PEComas and defined criteria for their malignancy according to which PEComas could be divided into categories, as benign, with uncertain malignant potential (UMP) and malignant [3]. Folpe criteria are given in Table 1.

<table>
<thead>
<tr>
<th>Category</th>
<th>Folpe criteria 2005</th>
<th>Schoolmeester criteria 2014</th>
<th>Modified-Folpe criteria Conlon 2015</th>
</tr>
</thead>
<tbody>
<tr>
<td>Benign</td>
<td>None of: size ≥5 cm, infiltrative growth pattern, high nuclear grade and cellularity, mitotic rate ≥1MF/50HPF, necrosis, vascular invasion</td>
<td>Less than four: size ≥5 cm, high-grade nuclear features, necrosis, vascular invasion or mitotic rate ≥1MF/50HPF</td>
<td>One or less: invasive edge, size ≥5 cm to &lt; 10 cm, 2-3MF/50HPF, lymphovascular invasion</td>
</tr>
<tr>
<td>UMP</td>
<td>One of: 1. Nuclear pleomorphism/multinucleated giant cells only or 2. Size ≥5 cm</td>
<td></td>
<td>One of: 1. isolated marked atypia 2. size ≥10 cm or 3. ≥4MF/50HPF</td>
</tr>
</tbody>
</table>
PEComas of the gynaecological tract are rare, and most of them are sporadic uterine tumours (not associated with TSC) [8]. PEComas of the uterine cervix are exclusively rare: only 13 cases have been reported so far [9]. The first cervical PEComa was described by Fadare et al. in 2004, together with the term, PEComatosis introduced as an occurrence of benign PECs on the peritoneal surface probably due to de novo proliferation [6]. We present the clinical and morphological features of a malignant cervical PEComa case and emphasise the diagnostic challenges.

**CASE REPORT**

A 57-year-old woman was admitted to St Marina University Hospital for surgical treatment with a histological diagnosis of squamous cell cervical carcinoma performed at another institution. The gynaecological examination revealed a barrel-shaped uterine cervix with a soft, bulky tumour about 11 cm in diameter. The CT scan revealed an enlarged uterus measuring 8x12, 4x9.4 cm. A large nodule was detected in the isthmic cervical region measured 11.1x10.6 cm, compressing the urinary bladder. The results from the general physical examination were unremarkable. Hemogram, urine and blood biochemistry investigations were within normal ranges. Radical hysterectomy with bilateral salpingo-oophorectomy and pelvic lymph node dissection were performed. The patient had no clinical or family history of TSC.

**Gross and Microscopic Evaluation**

Gross and microscopic assessment of the cervical mass showed it to be an 11 cm solid tumour, unencapsulated but deceptively circumscribed, located on the left side of the cervical wall (Fig. 1.) However, the periphery of the tumour showed a significant degree of infiltration. The cut surface was mottled with areas of necrosis and haemorrhages. The tumour was composed of solid nodules of epithelioid cells with eosinophilic-to-pale cytoplasm, well-defined cellular membranes and mild-to-moderate nuclear pleomorphism. Some cells displayed large bizarre nuclei. Prominent thin-walled blood vessels were present, and a perivascular cellular arrangement was seen in some places. A spindle-cell component was identified. The spindle cells were arranged in fascicles with areas of fibrosis, and some of them showed smooth muscle appearance (Fig. 2). The mitotic rate was elevated (>4MF/50HPF), and tumour necrosis was present. Immunohistochemically, the epithelioid cells stained strongly and diffusely with HMB-45, and just focally with muscle markers. Spindle cells conversely stained diffusely with smooth muscle actin and desmin (Fig. 3 and Fig. 4). Both cellular types were negative for Melan A and CKAE 1/3, and were focally positive for CD 10. Vaginal resection margins, both parameters and adnexa, uterine body and all removed lymph nodes (16 in number) were grossly and histologically free of tumour infiltration. The definite diagnosis of malignant cervical PEComa was based on the above morphological and immunohistochemical features. The patient chose to have adjuvant radiotherapy. She is alive, with no evidence of local recurrence or distant metastasis 6 months after the intervention. She was scheduled to have regular CT scans of the abdomen, chest and pelvis at 6-month intervals as part of the follow-up.

**Legend:** MF/HPF-/mitotic figure per high power fields.

<table>
<thead>
<tr>
<th>Malignant</th>
<th>Two or more:</th>
<th>Four or more:</th>
<th>Any necrosis or</th>
</tr>
</thead>
<tbody>
<tr>
<td>Size ≥ 5cm, Infiltrative growth pattern, High nuclear grade and cellularity, mitotic rate ≥ 1MF/50 HPF, necrosis, vascular invasion</td>
<td>size ≥ 5 cm, high-grade nuclear features, necrosis, vascular invasion or mitotic rate ≥ 1MF/50HPF</td>
<td>Any necrosis or Two worrisome features</td>
<td></td>
</tr>
</tbody>
</table>

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**Fig. 1.** Large, well demarcated tumor located in the left wall of cervical canal with mottled cut surface. Uterine body is spared (up left), and tweezers are introduced inside the endocervical canal.
Fig. 2. PEComa Hematoxylin and eosin stain (HE) x10. Atypical spindle cell component (left low) and epithelioid cell component (up right) with brisk pleomorphism (insertion).

Fig. 3. HMB-45 expression in epithelioid cell component (x10).

Fig. 4. Smooth muscle actin expression in spindle-cell component (x10).

DISCUSSION

Only 14 cases of cervical PEComas (including the case herein described) have been reported up to now. Clinical and morphological findings, treatment and follow-up data of these cases are presented in Table 2. Half of the cases have not been specified according to their malignant potential at all. In the other two cases, terms as “with malignant potential” [13] and “low-grade malignancy” were used [15]. Because of limited current data, cervical PEComas should be considered tumours of UMP and should be monitored for a long period because of their potential for local recurrence and metastasis [16, 20]. Another 35 uterine “non-benign” PEComas are presented and evaluated according to Folpe criteria in Table 3. Until February 2019, all these cases have been reported in the available English-language medical literature. Tumours included in both tables were initially reported, or later designated as PEComas.
### Table 2. Cervical PEComas.

<table>
<thead>
<tr>
<th>Reference</th>
<th>age</th>
<th>Size and spread at pres, MP</th>
<th>Folpe criteria of aggressive behavior</th>
<th>TSC</th>
<th>Treatment</th>
<th>Follow-up</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Fadare 2004 [6]</td>
<td>41</td>
<td>Cervix - 2.2 cm. + small bowel; ovarian hila PEComatosis MP - N/S</td>
<td>No one</td>
<td>Yes</td>
<td>Hysterectomy + BSO</td>
<td>NERM at 35 mo</td>
</tr>
<tr>
<td>2. Folpe 2005 [3]</td>
<td>28</td>
<td>Cervix -3 cm MP - N/S</td>
<td>No one</td>
<td>No</td>
<td>Hysterectomy + pelvic LN-dissection</td>
<td>NERM at 36 mo</td>
</tr>
<tr>
<td>6. Wagner 2010 [12]</td>
<td>61</td>
<td>Cervix – 9 cm Lung mts at pres. MP-Malignant</td>
<td>Size &gt; 5 cm</td>
<td>No</td>
<td>mTORi</td>
<td>DOD at 8 mo</td>
</tr>
<tr>
<td>7. Yamamoto 2010 [13]</td>
<td>24</td>
<td>Cervical membraneous tissue MP - LG malignancy</td>
<td>Infiltrative margin</td>
<td>No</td>
<td>Local excision</td>
<td>Cervical recurrence at 4 mo and 7 mo later NERM at 12 mo</td>
</tr>
<tr>
<td>8. Lim 2011 [14]</td>
<td>59</td>
<td>Uterus - AML, cervix -PEComa diffuse LAM in both MP - N/S</td>
<td>Not available</td>
<td>Yes</td>
<td>Hysterectomy + BSO</td>
<td>Not available</td>
</tr>
<tr>
<td>10. Celik 2014 [16]</td>
<td>41</td>
<td>Cervix – 4 cm Abdominal PEComatosis at pres. MP - N/S</td>
<td>Multinucleated cells, Infiltrative margin, 1MF/50HPF necrosis</td>
<td>Yes</td>
<td>Hysterectomy + BSO</td>
<td>NERM at 36 mo</td>
</tr>
<tr>
<td>11. Natella 2014 [17]</td>
<td>52</td>
<td>Cervix – 12 cm MP - Malignant</td>
<td>Size &gt; 5 cm</td>
<td>No</td>
<td>Radical pelvectomy /uterus, vagina, bladder, anal canal + Adj CT</td>
<td>NERM at 12 mo</td>
</tr>
<tr>
<td>12. Liu 2014 [18]</td>
<td>34</td>
<td>Cervix-9 cm MP - Malignant</td>
<td>Size &gt; 5 cm, Infiltrative margin, necrosis</td>
<td>No</td>
<td>Mass resection</td>
<td>Local recurrence at 2 mo, pelvic LN mts at 5 mo</td>
</tr>
<tr>
<td>14. Herein presented case 2019</td>
<td>57</td>
<td>Cervix-11 cm MP - Malignant</td>
<td>Size &gt;5cm, Infiltrative margin, high nuclear grade, necrosis, &gt;4MF/10HPF</td>
<td>No</td>
<td>Hysterectomy + BSO + pelvic LN dissection</td>
<td>NERM at 6 mo</td>
</tr>
</tbody>
</table>

Legend: MP-malignant potential; at pres-at presentation; N/S- not specified; BSO- bilateral salpingo-oophorectomy; NERM-no evidence of recurrence or metastasis; mo-months; LN-lymph node; Adj-adjuvant; RT-radiotherapy; mTORi-mammalian target of rapamycin inhibitor; DOD-death of disease; IT-immunotherapy; y-years; LG-low grade; CT-chemotherapy; Mts – metastasis.
**Table 3.** Uterine PEComas with malignant and uncertain malignant potential.

<table>
<thead>
<tr>
<th>Reference</th>
<th>age</th>
<th>Folpe category</th>
<th>Spread at pres.</th>
<th>Folpe criteria of aggressive behavior</th>
<th>TSC</th>
<th>Treatment</th>
<th>Follow-up</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Ruco 1998 [21]</td>
<td>56</td>
<td>Malignant</td>
<td>Ov and ileum involv.</td>
<td>5 cm, high nuclear grade, high cellularity, 11MF/50MF/HPF necrosis, vi</td>
<td>no</td>
<td>Hysterectomy+BSO +bowel resection</td>
<td>Local recurrence at 7 y</td>
</tr>
<tr>
<td>2. Bonnetti 2001 [22]</td>
<td>41</td>
<td>Malignant</td>
<td>Ov involv.</td>
<td>6 cm, high nucl grade, necrosis, vi</td>
<td>yes</td>
<td>Hysterectomy+BSO</td>
<td>NERM at 6 mo</td>
</tr>
<tr>
<td>3. Bonnetti 2001[22]</td>
<td>19</td>
<td>MalignantVaginal, pelvic/ inguinal LN involv.</td>
<td>5,5 cm, high nuclear grade, necrosis, vi</td>
<td>Hysterectomy+ BSO+pelvic and inguinal LN dissection+Adj CT and RT</td>
<td>Local recurrence at 1 mo, Lung and bone mts at 11 mo, AWD at 18 mo</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4. Vang 2002 [23]</td>
<td>40</td>
<td>UMP</td>
<td>12 cm, infiltrative margin</td>
<td>no excision</td>
<td>Not given</td>
<td></td>
<td></td>
</tr>
<tr>
<td>5. Vang 2002 [23]</td>
<td>75</td>
<td>UMP</td>
<td>5 cm, infiltrative margin</td>
<td>no Hysterectomy+BSO + Adj RT</td>
<td>NERM at 31 mo</td>
<td></td>
<td></td>
</tr>
<tr>
<td>7. Greene 2003 [25]</td>
<td>79</td>
<td>Malignant</td>
<td>13 cm, infiltrative margin, high nuclear grade, high cellularity, 8MF/10HPF, necrosis, vi</td>
<td>Hysterectomy+BSO +CT</td>
<td>Pelvic, abdominal recurrence, DOD at 24 mo</td>
<td></td>
<td></td>
</tr>
<tr>
<td>8. Park 2003 [26]</td>
<td>32</td>
<td>Malignant Right broad ligament involv.</td>
<td>8 cm, infiltrative margin, necrosis</td>
<td>no Hysterectomy+RSO</td>
<td>NERM at 18 mo</td>
<td></td>
<td></td>
</tr>
<tr>
<td>9. Nikolova 2004 [27]</td>
<td>43</td>
<td>Malignant</td>
<td>7 cm, infiltrative margin, high nuclear grade</td>
<td>no Hysterectomy+BSO+ Adj CT</td>
<td>Bone mts at 3 y and DOD</td>
<td></td>
<td></td>
</tr>
<tr>
<td>10. Folpe 2005 [3]</td>
<td>56</td>
<td>Malignant</td>
<td>9 cm, high nuclear grade, high cellularity, &gt;50MF/HPF</td>
<td>Surgery+Adj CT and RT</td>
<td>Lung and bone mts at 11 mo</td>
<td></td>
<td></td>
</tr>
<tr>
<td>12. Folpe 2005[3]</td>
<td>36</td>
<td>Malignant</td>
<td>Large, high nuclear grade, high cellularity, &gt;50MF/HPF, necrosis</td>
<td>no Hysterectomy+ Adj CT</td>
<td>Lung mts at 12 mo, liver mts at 36 mo DOD at 39 mo</td>
<td></td>
<td></td>
</tr>
<tr>
<td>13. Folpe 2005[3]</td>
<td>59</td>
<td>Malignant</td>
<td>14,5 cm, high nuclear grade, high cellularity, 10MF/50MF/HPF, necrosis, vi</td>
<td>no Surgery+Adj CT</td>
<td>Lung and liver mts at 30 mo</td>
<td></td>
<td></td>
</tr>
<tr>
<td>14. Fukunaga 2005 [20]</td>
<td>40</td>
<td>MalignantRight ov and omental involv.</td>
<td>30 cm, necrosis, 11MF/10HPF</td>
<td>no Hysterectomy+BSO+ omentectomy+ Adj CT and RT</td>
<td>Intestinal and lung mts at 16 mo, DOD at 17 mo</td>
<td></td>
<td></td>
</tr>
<tr>
<td>15. Jeon 2005 [28]</td>
<td>9</td>
<td>Malignant LN mts.</td>
<td>6,5 cm</td>
<td>no NA CT +hysterectomy +Adj CT and RT</td>
<td>NERM at 18 mo</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>First Name</td>
<td>Last Name</td>
<td>Age</td>
<td>Tumor Type</td>
<td>Tumor Size</td>
<td>Location</td>
<td>Stage</td>
</tr>
<tr>
<td>---</td>
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<td>------------</td>
<td>------------</td>
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<td>-------</td>
</tr>
<tr>
<td>16.</td>
<td>Bosincu</td>
<td>2005 [29]</td>
<td>59</td>
<td>Malignant</td>
<td>13 cm, high cellularity, 1MF/10HPF, necrosis</td>
<td>no</td>
<td>Hysterectomy+BSO+omentectomy</td>
</tr>
<tr>
<td>17.</td>
<td>Bosincu</td>
<td>2005 [29]</td>
<td>48</td>
<td>Malignant</td>
<td>11 cm, infiltrative margin, 5MF/10HPF, necrosis,</td>
<td>no</td>
<td>GnRH analogus, hysterectomy+Adj HT</td>
</tr>
<tr>
<td>18.</td>
<td>Iravanlo</td>
<td>2006 [30]</td>
<td>33</td>
<td>Malignant</td>
<td>20 cm, high nuclear grade, necrosis, high mitotic rate</td>
<td>N/S</td>
<td>Hysterectomy+Resection of mts</td>
</tr>
<tr>
<td>19.</td>
<td>Armah</td>
<td>2007 [31]</td>
<td>59</td>
<td>Malignant</td>
<td>6 cm, high nuclear grade, 45-60MF/50HPF, necrosis, vi</td>
<td>no</td>
<td>Hysterectomy+BSO+nephrectomy+lobectomy/lung/</td>
</tr>
<tr>
<td>20.</td>
<td>GAN Mei-fu</td>
<td>2007 [32]</td>
<td>33</td>
<td>UMP</td>
<td>8.5 cm, infiltrative margin</td>
<td>no</td>
<td>Hysterectomy</td>
</tr>
<tr>
<td>21.</td>
<td>GAN Mei-fu</td>
<td>2007 [32]</td>
<td>44</td>
<td>UMP</td>
<td>5.5 cm</td>
<td>no</td>
<td>Hysterectomy</td>
</tr>
<tr>
<td>22.</td>
<td>Cho</td>
<td>2008 [33]</td>
<td>9</td>
<td>Malignant</td>
<td>External iliac LN involv.</td>
<td>5 cm, infiltrative margin, necrosis</td>
<td>N/S</td>
</tr>
<tr>
<td>23.</td>
<td>Liang</td>
<td>2008 [34]</td>
<td>59</td>
<td>Malignant</td>
<td>PEComatosis of uterus,cervix, Ov hilum, pelvic LN –LAM</td>
<td>2.6 cm, infiltrative margin, high nuclear grade, 2MF/50HPF, necrosis, vi</td>
<td>yes</td>
</tr>
<tr>
<td>24.</td>
<td>Liu</td>
<td>2009 [35]</td>
<td>33</td>
<td>Malignant</td>
<td>Retroperitoneal LN involv.</td>
<td>8.1 cm, infiltrative margin, high nuclear grade, necrosis, 2MF/10HPF</td>
<td>no</td>
</tr>
<tr>
<td>26.</td>
<td>Italiano</td>
<td>2010 [36]</td>
<td>55</td>
<td>Malignant</td>
<td>Not given</td>
<td>N/S</td>
<td>Hysterectomy+BSO+ resection of mts + CT + mTORi</td>
</tr>
<tr>
<td>27.</td>
<td>Yamashita</td>
<td>2010 [37]</td>
<td>42</td>
<td>Malignant</td>
<td>Mts in humerus.</td>
<td>15 cm,</td>
<td>N/S</td>
</tr>
<tr>
<td>28.</td>
<td>Bleeker</td>
<td>2012 [38]</td>
<td>50</td>
<td>Malignant</td>
<td>Ov involv.</td>
<td>22 cm, infiltrative growth, high nuclear grade, 2MF/50HPM</td>
<td>no</td>
</tr>
<tr>
<td>29.</td>
<td>Chamsy</td>
<td>2012 [39]</td>
<td>46</td>
<td>Malignant</td>
<td>Vaginal mts.</td>
<td>9 cm, infiltrative margin, high nuclear grade, necrosis, 4MF/10HPF</td>
<td>N/S</td>
</tr>
<tr>
<td>30.</td>
<td>Cossu</td>
<td>2014 [40]</td>
<td>52</td>
<td>Malignant</td>
<td>Not available</td>
<td>N/S</td>
<td>Surgery</td>
</tr>
<tr>
<td>31.</td>
<td>Kang</td>
<td>2014 [41]</td>
<td>49</td>
<td>Malignant</td>
<td>8.5 cm, high nuclear grade, necrosis, 20MF/10HPF, vi</td>
<td>N/S</td>
<td>Hysterectomy+BSO + Adj CT</td>
</tr>
</tbody>
</table>
PEComas are diagnosed only by histological examination because neither their clinical presentation nor appearances are sufficiently specific to allow for preoperative diagnosis [41, 43, 45]. Therefore, morphological features are essential for making the diagnosis together with the cellular immunophenotype. PEComas are mesenchymal tumours, typically presenting with a mixture of epithelioid and spindle cells, and with a delicate vascular network [2]. While most reported PEComas were epithelioid, their cytological presentation ranged from purely spindled to purely epithelioid, and a combination of the two [8].

Vang and Kempson divided uterine PEComas into two histological groups: group A tumours composed of cells with abundant clear to pale eosinophilic cytoplasm with a tongue-like growth pattern. They express HMB45 diffusely, and muscle markers are expressed only focally. Group B tumours have fewer HMB45-positive clear cells, a large number of cells that express muscle markers and a diminished tongue-like growth pattern [23]. The most sensitive melanocytic marker of PEComas is HMB-45, followed by MelanA. The most sensitive muscle marker being is muscle actin, while desmin is less sensitive [2, 3, 46]. Expression varies with morphology: tumours with predominant spindle-cell morphology show strong expression of muscle markers and limited expression of melanocytic markers; predominantly epithelioid tumours may strongly express melanocytic markers with limited muscle marker expression [8].

We consider two main challenges in the morphological diagnosis of gynaecological tract PEComas. The first is an adequate diagnosis, which is of great clinical importance. Folpe criteria are accepted in The World Health Organization classification of tumours of female reproductive organs as “parameters that impact prognosis”, but PEComas with UMP in the uterus and soft tissues are not included in the International Classification of Diseases for Oncology (ICD-O) [1, 2]. It is unclear how to categorise PEComas with a single worrisome feature not typical for the UMP-category such as infiltrative growth pattern, elevated mitotic count, necrosis, or vascular invasion. Recently, a revised system was proposed by Schoolmeester et al., according to which the threshold of malignancy is suspected in the presence of four or more features. Tumours with less than four features were placed in a group of benign and UMP [46]. In 2015, Conlon et al. tested a modification of the Folpe criteria. Using histological and outcome data from 78 reported uterine PEComas, they applied Folpe, modified-Folpe and Schoolmeester criteria one after the other. The three systems are presented in Table 1. The authors concluded that Folpe and modified-Folpe criteria showed higher sensitivity and negative predictive values than the Schoolmeester criteria. However, malignant PEComas assessed by the Schoolmeester system often recurred early. They also suggested that a note is to be included in the pathology report to explain the reason for diagnostic uncertainty when using the term UMP [8]. Since PEComas are so rare, firm minimal criteria for their malignancy have not been established yet, and a prognostic classification system is currently under development [1, 2, 8, 47].

The second challenge in making the morphological diagnosis of gynaecological tract PEComas is the differential diagnosis with smooth muscle tumours, especially leiomyosarcomas (LMS). Conventional uterine LMS is an unequivocal diagnosis. LMS with epithelioid features presents diagnostic dilemmas because of their histomorphological overlapping with PEComas, especially in cases of aberrant expression of melanocytic markers. Vang and Kempson described four uterine tumours in all of which less than 20% of cells were positive for HMB-45 and defined them as a group B PEComas. They concluded that HMB-45 staining is the only way to distinguish PEComa from epithelioid smooth muscle tumours [23]. Silva et al. documented four uterine epithelioid leiomyosarcomas containing 5% to 80% HMB-45 positive, clear cells but they suggested they should be defined as uterine LMS and concluded that the HMB-45 expression is insufficient to identify these tumours as PEComas and separate them from epithelioid smooth muscle tumours [48]. Some authors have
suggested that tumours with diffuse melanocytic differentiation be regarded as related to the PEComa family. They claim that focal and weak melanocytic expression can be ignored because such an expression does not warrant the diagnosis of PEComa. They have proposed that only tumours with absolutely characteristic morphologic and immunophenotypic features can be diagnosed as PEComas, but they have not specified these “absolutely characteristic” features [7]. These are not the only contradictory findings, and controversy still exists regarding the minimum criteria for separating malignant PEComas from uterine epithelioid LMS. So the differential diagnosis is still a challenge. However, most authors have agreed with Vang and Kempson that all HMB-45+ positive epithelioid uterine tumours should be distinguished from other epithelioid tumours because some patients may have TSC [7, 23, 48].

The case herein presented showed typical morphological and immunohistochemical features: the mixture of epithelioid and spindle cells with the nested, perivascular and fascicular arrangement; diffuse HMB-45 expression in the epithelioid component and diffuse smooth muscle actin and desmin positivity in the spindle-cell component. It had unequivocal features of malignancy: 11 cm in diameter, infiltrative growth, high nuclear grade, mitotic rate > 4MF/50HPF, and necrosis. All these features allowed us to make a diagnosis of malignant cervical PEComa. Optimal treatment for PEComas has not been established yet. Surgery seems to be the only approach for aggressive cases, as chemo- and radiotherapy has not shown significant results [7]. Radical hysterectomy with bilateral salpingo-oophorectomy should be considered in patients with PEComas spreading or localised in the uterine cervix, and adjuvant therapy is not efficient [9]. Most sporadic and syndromic tumours demonstrate inactivation of the TSC1 and TSC2 genes with subsequent activation of the mTOR pathway. These tumours may respond to mTOR inhibitor therapy [2].

CONCLUSION

We consider that it is important to report and describe in details each one case of PEComa with aggressive behaviour or worrisome histological features. Such reports would help to establish firm minimal criteria for malignancy of these tumours. The extended follow-up of patients with preceding PEComas is also of great importance because it could provide information about the predictive value of morphological features. All gynaecological tract sarcomas with epithelioid cell component should be tested with melanocytic markers to distinguish them from PEComas.

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