Case Report
Alveolar soft part sarcoma of uterine cervix in a postmenopausal woman: a case report and review of literature

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Abstract: We report a case of alveolar soft part sarcoma (ASPS) in a 68-year-old woman’s uterine cervix. Macroscopic observation revealed an unencapsulated lesion confined to the cervical stroma, measuring 10 mm in diameter. Microscopic examination showed large, round or polygonal tumor cells, arranging in a well-defined nests pattern with scanty vascular stroma. Immunohistochemistry was performed. Tumor cells showed positivity for Ki-67 (2%), TFE-3, CD68, and myoD1 (cytoplasm), while negative for HNF1β, CD10, RCC, PAX-8, CK7, CK18, CK8, CR, EMA, HMB-45, S-100, CgA, and Syn. Periodic acid-Schiff stain after diastase digestion (PAS-D) had revealed rod-like or rhomboid crystals of some cells. The diagnosis of ASPS was confirmed. ASPS was a rare soft tissue malignancy in female reproductive system. After a detailed study of the reported cases, we summarized some clinicopathological differences between cervical and soft tissue ASPS.

Keywords: Alveolar soft part sarcoma, postmenopausal bleeding, sarcoma, uterine cervix

Introduction

Alveolar soft part sarcoma (ASPS) is a rare soft tissue malignancy and is reported to have an incidence of 0.5%-1% among soft tissue sarcomas [1]. Even rare, ASPS can occur in female reproductive system, among which the uterine cervix is the most common sites [2]. ASPS mostly occurred in the second or third decade of life, between the age of 15 and 35, with a predilection for females over males [3]. The long-term prognosis of ASPS has a low tendency of local recurrence and metastasis. As far as we know, there are 41 cases of ASPS in uterine cervix have been reported (including our case), with an age ranging from 8 to 68 years old [2, 4-6]. We report a case of ASPS originating in the uterine cervix in a 68-year-old female. As a rare sarcoma in an uncommon site with an unusual age, we hope that our report could be helpful in the study of the rare tumor.

Materials and methods

Clinical summary

With full approval of local ethic committee, we reported a case of ASPS in a postmenopausal woman’s uterine cervix. A 68-year-old female presented to our hospital with an increasing abnormal uterine bleeding in 4 years duration. In the first, ultrasonic examination was done, which revealed an ill-defined mass of solid heterogeneously hyper echoic in the uterine cervix. Then Color Doppler Flow Imaging (CDFI) revealed a color flow streak, and arterial flow spectrum measuring Vmax 0.27 m/s, Vmin 0.16 m/s, RI00.42, and PI00.57. The data suggested that the cervical lesion might be malignant. She had a history of pulmonary tuberculosis in 1995 and an involvement of left thumb in 2010, which underwent an exsection then. The past history was otherwise unremarkable.
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She subsequently underwent radical hysterectomy. Macroscopic observation revealed an unencapsulated lesion which confined to the cervical stroma, measuring 10 mm in diameter. The cervical canal, corpus uteri, and adnexa uterus were all free of tumor. Microscopic examination of the biopsy specimen showed that tumor cells were large, round or polygonal, arranging in a well-defined nests pattern with scanty vascular stroma (Figure 1A). The cells had finely granular, eosinophilic cytoplasm and large, vesicular nuclei with prominent nucleoli, and diagnostic significance crystalline material [7] was noted within cell cytoplasm of a few tumor cells (Figure 1B). Based on the specific pattern, the initial diagnosis of ASPS was made. Differential diagnoses were considered for perivascular epithelioid cell tumor (PEComa), alveolar rhabdomyosarcoma, neuroendocrine tumor, granular cell tumor, mesothelioma, or possibly metastatic carcinoma.

In order to confirm the diagnosis, immunohistochemistry was performed. All the tumor cells were negative for HNF-1β, CD10, RCC, PAX-8, CK7, CK-18, CK8, CR, EMA, HMB-45, S-100, CgA, and Syn. However, they showed positivity for Ki-67 (2%), TFE-3, CD68, and myoD1 (cytoplasm) (Figure 2A-D). Fibrovascular septa were clearly seen by the positivity of vascular endothelial cells for CD31 and CD34. Periiodic acid-Schiff stain (PAS) was also done, which had revealed intracellular diastase-resistant granules. After diastase digestion (PAS-D), PAS-positive rod-like or rhomboid crystals of some cells were identified. The diagnosis of ASPS was confirmed.

Discussion

ASPS is an unusual soft tissue malignancy with a wide anatomical distribution. Common locations are reported in the literatures including prostate [1], muscle and soft tissues of the extremities [3, 8], trunk [8], head and neck [3], larynx [9], tongue [10], and retroperitoneum [11] et cetera. In even rare occasions, ASPS are also found in female reproductive system, with a predilection for uterine cervix. About 41 cases have been reported so far. After a detailed study of the reported cases, we summarized some clinicopathological differences between

Pathological findings

Figure 1. Photomicrograph showing large, round or polygonal tumor cells arranging in a well-defined nests pattern with scanty vascular stroma (A) (H&E×100). Arrow shows rod-like crystals within cell cytoplasm (B) (PAS-D×200).

Figure 2. Immunohistochemistry showing positivity for TFE-3 (A), CD68 (B) (H&E×200), myoD1 (C) and Ki-67 (D) (H&E×100).
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Table 1. Contradistinction in clinical pathology features of ASPS in uterine cervix versus soft tissue

<table>
<thead>
<tr>
<th>Clinical pathology features</th>
<th>ASPS of uterine cervix</th>
<th>ASPS of soft tissue</th>
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<tbody>
<tr>
<td>Age of onset</td>
<td>Mean age 29.9 years (8-68 years)</td>
<td>Common in 15-35 years</td>
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<td>Clinical features</td>
<td>Vaginal bleeding and/or menstrual cycle shortening</td>
<td>Various</td>
</tr>
<tr>
<td>Macroscopy</td>
<td>Well-defined borderline</td>
<td>III-defined borderline</td>
</tr>
<tr>
<td>Histopathology</td>
<td>Alveolar pattern (minority) + solid pattern (majority)</td>
<td>Alveolar pattern + solid pattern</td>
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<tr>
<td>Biological behaviour</td>
<td>The overall prognosis is better than that of the soft tissue. Neither distant metastasis nor deaths was found in most cases.</td>
<td>Metastasis in the early age occurred commonly.</td>
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<td>Genetic profile</td>
<td>Both showed t(X;17)(p11;q25), resulting in ASPL/TFE3 gene fusion.</td>
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cervical and soft tissue ASPS [Table 1]. In most cases, ASPS occurs in the second or third decade of life, between 15-35 years of age. However, age of onset spans larger in the primary cases of female reproductive system, ranging from 8 to 68 years old (including our case) [2, 5, 6, 12-14]. As for the ASPS in the uterine cervix, this is the oldest patient ever has been reported. We report could be helpful in furthering investigation of the rare tumor.

A female of 19-year-menopausal presented with gradually increasing abnormal uterine bleeding for about 4 years. Ultrasonic examination as well as CDFI revealed a mass with malignant possibility in the uterine cervix. Then radical hysterectomy was done on her. Subsequent surgical pathology detection revealed that the tumor has the typical structure of ASPS. IHC, PAS and PAS-D stain were all done to confirm the diagnosis. A number of previous studies have done with the IHC profiles of ASPS, which suggested that TFE-3 [14], CD68, and myoD1 [15] can help in diagnosis of this entity. The neoplastic nuclei were strongly positive for TFE-3, while CD68 and myoD1 were found positive in cytoplasm.

Histologically, ASPS shows certain overlap with some other tumors. First of all, not only tumor cells but also nests pattern of ASPS are similar to those of granular cell tumor. However, IHC staining of S-100 together with PAS-D staining were helpful in the differential diagnosis between the two tumors with highly sensitivity and specificity [16]. Next, vascular structures and shape of epithelioid cells made PEComa another differential diagnosis, which was rejected for the negative expression of HMB-45 and S-100. One more, mesothelioma was ruled out because of particular nests pattern and negative expression of CR as well. In addition, the nests pattern and vascular separation structures can also be found in neuroendocrine tumors, which show positivity with CgA and/or Syn, while ASPS are negative with both. Alveolar structure accompanied with a positive expression of myoD1 and negative of EMA make alveolar rhabdomyosarcoma another differential diagnosis. Typical polygonal cells with abundant eosinophilic cytoplasm accompanied with PAS-D staining are valuable in obviating diagnosis of alveolar rhabdomyosarcoma. Also, the suspicion of metastatic renal cell carcinoma (RCC) or ovarian clear cell carcinoma (OCCC) is made, but is soon ruled out, because the cells are negative for CD10, RCC, PAX-8, CK7 and HNF1β on immunohistochemical staining [17, 18]. Negative expression of CK18 and CK8 are helpful in excluding some other epithelial tumors. Because of a close clinical and imaging resemblance, ASPS may also be misdiagnosed as benign vascular tumors such as hemangiomma, resulting in delayed treatment and metastasis. If the vascular tumors are concerned, a biopsy or fine needle aspiration for pathological diagnosis could be necessary.

Although substantial progress has been achieved in the histological appearance and IHC markers, ASPS is still not characterized well in the origin and differentiation. Precise guidelines for their treatment protocols are insufficient because of their rarity too. Complete surgical resection with adequate margins is the treatment of choice for ASPS of the cervix for now [19]. The role of lymph node dissection on the clinical outcome of cervical ASPS, however, is not yet clears [13]. And also, the effect of chemotherapy or radiotherapy has neither been defined for ASPS in the cervix nor in soft tissues. In a review of the literature by Fadare,
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it is found that the prognosis is good for the patients with cervical ASPS after surgical intervention [2].

We reported a case with the age of 68, the oldest patient ever been reported. Surgical pathology detection revealed a typical histological, histochemical, and IHC appearance of ASPS. Subsequently, we will follow-up the patient to detect local recurrence and distant metastasis.

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Disclosure of conflict of interest

None.

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