

## 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 HNF1 $\beta$ , 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

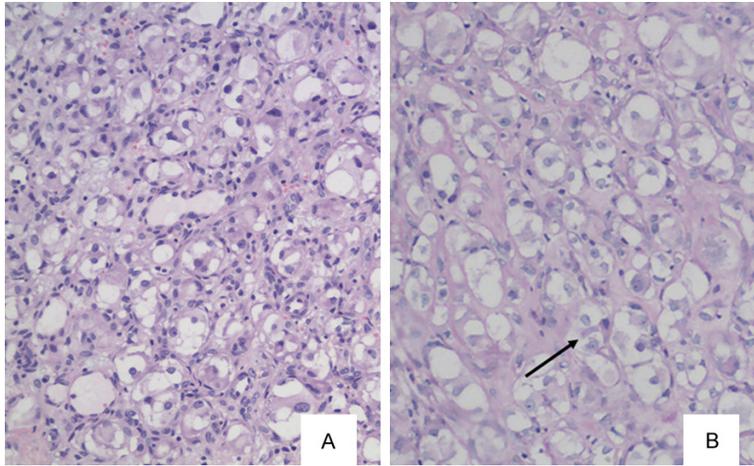
Alveolar soft part sarcoma (ASPS) is a rare soft tissue malignancy and is reported to have an incidence of 0.5%-1% among soft tissue sarcomas [1]. Even rare, ASPS can occur in female reproductive system, among which the uterine cervix is the most common sites [2]. ASPS mostly occurred in the second or 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

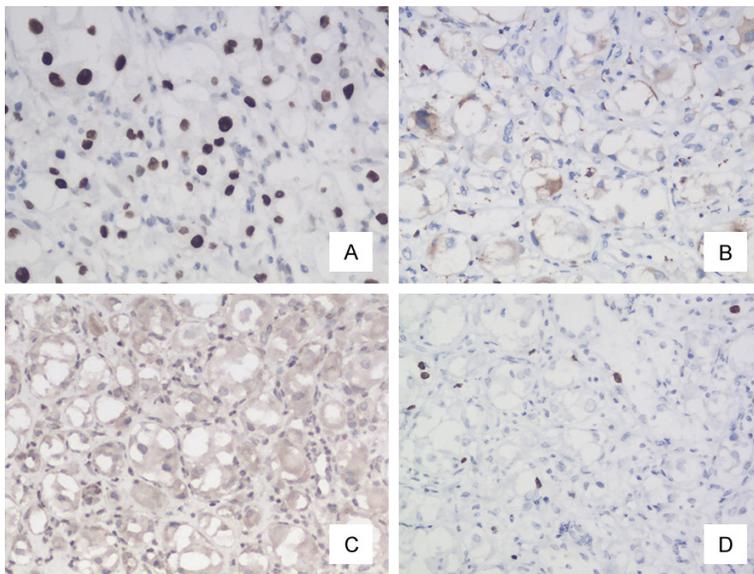
### *Clinical summary*

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.

## ASPS of uterine cervix



**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).

### *Pathological findings*

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-1 $\beta$ , 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. Periodic 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

## ASPS of uterine cervix

**Table 1.** Contradistinction in clinical pathology features of ASPS in uterine cervix versus soft tissue

Clinical pathology features	ASPS of uterine cervix	ASPS of soft tissue
Age of onset	Mean age 29.9 years (8-68 years)	Common in 15-35 years
Clinical features	Vaginal bleeding and/or menstrual cycle shortening	Various
Macroscopy	Well-defined borderline	Ill-defined borderline
Histopathology	Alveolar pattern (minority) + solid pattern (majority)	Alveolar pattern + solid pattern
Biological behaviour	The overall prognosis is better than that of the soft tissue. Neither distant metastasis nor deaths was found in most cases.	Metastasis in the early age occurred commonly.
Genetic profile	Both showed t(X;17)(p11;q25), resulting in ASPL/TFE3 gene fusion.	

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 diagnose 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 HNF1 $\beta$  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 hemangioma, 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 clear [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,

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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#### References

- [1] Chen J, Chen X, Wang Y, Chen H, Wang Z. Imaging findings and histologic appearances of alveolar soft part sarcoma in the prostate: a case report and review of the literature. *Clin Genitourin Cancer* 2015; 13: e315-9.
- [2] Fadare O. Uncommon sarcomas of the uterine cervix: a review of selected entities. *Diagn Pathol* 2006; 1: 30.
- [3] Singh A, Gupta S, Ghosh S, Yuwanati MB. Alveolar soft part sarcoma. *BMJ Case Rep* 2014; 2014.
- [4] Feng M, Jiang W, He Y, Li L. Primary alveolar soft part sarcoma of the uterine cervix: a case report and literature review. *Int J Clin Exp Pathol* 2014; 7: 8223-6.
- [5] Kang WD, Heo SH, Choi YD, Choi HS, Kim SM. Alveolar soft part sarcoma of the uterine cervix in a woman presenting with postmenopausal bleeding: a case report and literature review. *Eur J Gynaecol Oncol* 2011; 32: 359-61.
- [6] Lee HJ. Alveolar soft part sarcoma of the uterine cervix: a case report and review of the literature. *Korean J Pathol* 2014; 48: 361-365.
- [7] Mannan R, Bhasin TS, Kaur P, Manjari M, Gill KS. Prominent intracytoplasmic crystals in alveolar soft part sarcoma (ASPS): an aid in cytological diagnosis. *J Clin Diagn Res* 2014; 8: 145-146.
- [8] Cho YJ, Kim JY. Alveolar soft part sarcoma: clinical presentation, treatment and outcome in a series of 19 patients. *Clin Orthop Surg* 2014; 6: 80-6.
- [9] Mullins BT, Hackman T. Adult alveolar soft part sarcoma of the head and neck: a report of two cases and literature review. *Case Rep Oncol Med* 2014; 2014: 597291.
- [10] Kingler M, Chakrabarti P, Varma A, Doshi B. Alveolar soft part sarcoma of tongue in 14-year-old boy. *Ann Maxillofac Surg* 2014; 4: 240-2.
- [11] Kim JM, Im SA, Oh SN, Chung NG. Alveolar soft part sarcoma arising from the kidney: imaging and clinical features. *Korean J Radiol* 2014; 15: 381-385.
- [12] Zhang LL, Tang Q, Wang Z, Zhang XS. Alveolar soft part sarcoma of the uterine corpus with pelvic lymph node metastasis: case report and literature review. *Int J Clin Exp Pathol* 2012; 5: 715-719.
- [13] Khosla D, Patel FD, Kumar R. Sarcomas of the uterine cervix: a united and multidisciplinary approach is required. *Womens Health (Lond Engl)* 2013; 9: 501-4.
- [14] Roma AA, Yang B, Senior ME, Goldblum JR. TFE3 immunoreactivity in alveolar soft part sarcoma of uterine cervix: case report. *Int J Gynecol Pathol* 2005; 24: 131-135.
- [15] Gómez JA, Amin MB, Ro JY, Linden MD, Lee MW, Zarbo RJ. Immunohistochemical profile of MyoD1 does not support skeletal muscle lineage in alveolar soft part sarcoma: a study of 19 tumors. *Arch Pathol Med Lab* 1999; 123: 503-507.
- [16] Chamberlain BK, McClain CM, Gonzalez RS, Coffin CM, Cates JM. Alveolar soft part sarcoma and granular cell tumor: an immunohistochemical comparison study. *Hum Pathol* 2014; 45: 1039-1044.
- [17] Ritterhouse LL, Cykowski MD, Hassell LA, Slobodov G, Bane BL. Melanotic Xp11 translocation renal cancer: report of a case with a unique intratumoral sarcoid-like reaction. *Diagn Pathol* 2014; 9: 81.
- [18] Okamoto T, Mandai M, Matsumura N, Yamaguchi K, Kondoh H, Amano Y, Baba T, Hamanishi J, Abiko K, Kosaka K, Murphy SK, Mori S, Konishi I. Hepatocyte nuclear factor-1 $\beta$  (HNF-1 $\beta$ ) promotes glucose uptake and glycolytic activity in ovarian clear cell carcinoma. *Mol Carcinog* 2015; 54: 35-49.
- [19] Zhao C, Gao X, Yang J, Li Z, Cai X, Tan T, Hou T, Yan W, Yang X, Yang C, Liu T, Xiao J. Surgical management and outcome of spinal alveolar soft part sarcoma (ASPS): a case series of five patients and literature review. *World J Surg Oncol* 2017; 15: 39.