Cervical Angiomyolipoma Coexisting with Endometrial Carcinoma in the Absence of Tuberous Sclerosis: A Rare Case Report

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Abstract

Angiomyolipoma (AML) is a rare benign mesenchymal neoplasm composed of variable admixture of blood vessels, smooth muscle, and adipose tissue; most commonly located in kidney, and is usually associated with tuberous sclerosis. Extrarenal AML has been reported in various sites, although infrequently in female genital tract (FGT). AML in cervix is extremely rare and only six cases have been reported so far. A 46-year-old postmenopausal female presented with lower abdominal pain, bleeding for 4 days and a polypoidal mass protruding through the cervical os. Endometrial curettings were suggestive of endometrial adenocarcinoma—endometrioid type (World Health Organization [WHO]). The subsequent hysterectomy specimen confirmed the diagnosis and the histologic grade was International Federation of Obstetrics and Gynecology (FIGO) grade I and stage was pT1aN0 (American Joint Committee on Cancer [AJCC], 8th edition). Cervical polyp showed AML. CD34 and smooth muscle actin (SMA) showed diffuse positivity in blood vessels and smooth muscle cells, respectively. HMB-45 was negative. This is the first ever reported case of AML coexisting with endometrial carcinoma in the absence of tuberous sclerosis. CD34 is a good marker for delineating the blood vessels and SMA for both the smooth muscle and vascular components. S100 is generally not needed to prove the adipose tissue component. HMB-45 is not consistently expressed in AML of female genital tract.

Keywords
- angiomyolipoma
- cervix
- endometrial carcinoma
- tuberous sclerosis
- HMB-45

Introduction

Angiomyolipoma (AML) is a rare tumor first reported in kidney by Morgan et al in 1951.[1] It is a benign mesenchymal neoplasm that is composed of variable admixture of blood vessels, smooth muscle, and adipose tissue.[2-6] Most common location of this tumor is kidney, in which case, it is associated with tuberous sclerosis.[2,4-10] Extrarenal AML has been reported in liver, retroperitoneum, mediastinum, lung, nasal cavity, oral cavity, ear lobe, salivary glands, pharynx, heart, large intestine, bone, soft tissue, skin, thoracic spine, spermatic cord, penis, thigh, foot and infrequently in female genital tract.[2-6,8,11] In female genital tract, body of uterus is the most common site of AML and other sites are

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cervix, fallopian tube, ovary, broad ligament, parametrium, vaginal wall, and vulva[2-5,7-13] AML in cervix is extremely rare and only six cases have been reported so far (►**Table 1**).[4,13]

AML belongs to the family of tumors called perivascular epithelioid cell tumors.[4] In general, AML is associated with tuberous sclerosis in 5 to 50% of cases.[3,8,] Most of the AML arising from female genital tract is not reported to be associated with tuberous sclerosis.[7,10]

Clinical presentation of AML is variable and may be asymptomatic or presents with menorrhagia/menometrorrhagia/abdominal pain/pelvic mass.[2,4,5,11] Ultrasonographic findings are also nonspecific.[4,10] Per speculum, it appears as firm globular mass.[3,4] Cut surface is yellowish white, soft in consistency.[4,5,11] Microscopically, it presents as unencapsulated, polypoidal tumor lined by stratified squamous epithelium.[3] It is composed of three components: the smooth muscle fascicles, thick walled hyalinized blood vessels, and mature adipose tissue.[2-6,11] Verhoeff Van Gieson demonstrates the lack of elastic fibers in blood vessels in this tumor.[3]

We report the first case of AML of cervix that presented along with adenocarcinoma of endometrium in the absence of tuberous sclerosis.

Case Report

P3L3, a 46-year-old female, presented with lower abdominal pain and postmenopausal bleeding for the last 4 days. Patient has attained menopause before 7 years. She had history of menorrhagia with passage of clots for the past 4 days. She did not have any other medical illness. No features of tuberous sclerosis were identified. Per speculum examination revealed a firm to hard, 4 × 4 cm polypoidal mass protruding through the cervical os. On ultrasonogram, there was a 4.2 × 3.6 cm posterior fibroid with cervical polyp and the endometrial thickness was 8.6 mm. Fractional curettage was done along with cervical polypectomy. The endometrial curetting yielded copious material. Microscopically, the curettings showed tumor composed of atypical cells arranged in villoglandular, complex glandular, papillary configuration and in solid sheets with six to seven mitotic figures/10 high power field (hpf). Clear cell change was noted in many foci. Some of the endocervical glands also showed cellular atypia. All features suggested malignancy. The polypectomy specimen from the cervix measured 3.5 × 2 × 1.5 cm and external surface was firm and gray white. Cut surface was homogenous and tan

Table 1 List of cases of angiomyolipoma reported in the female genital tract and their HMB-45 immunoreactivity

S. No.	Author(s)	Journal	Year	Parts involved	HMB-45 status
1	McKeithen et al	Obstet Gynecol	1964	Uterine corpus	Not done
2	Jacobs DS et al	Am J Clin. Pathol	1965	3 cases in uterine corpus	Not done
3	Demopoulos et al	Am J Clin Pathol	1973	4 cases in Uterine corpus	Not done
4	Katz DA	Am J Obstet Gynecol	1984	Fallopian tube	Negative
5	Lo Re et al	Appl Pathol	1987	Uterine corpus	Not done
6	Peth SC et al	Br J Obstet Gynaecol	1988	Vaginal wall	Not done
7	Sieinski et al	Int J Gynecol Pathol	1989	1 case in uterine corpus and 2 cases in cervix	Not done
8	Chen KT et al	Gynecol Oncol	1990	Vaginal wall	Not done
9	Laffargue et al	Gynecol Oncol	1993	Uterine corpus	Negative
10	Shintaku et al	Pathol Int	1996	Uterine corpus	Not done
11	Huang et al	Chinese Med J	2000	Cervix	Negative
12	Chetty et al	J Gynecol Surg	2000	Uterine corpus	Not done
13	Yaeghashi et al	Pathol Int	2001	Uterine corpus	Negative
14	Anderson et al	Int J of Gynec Pathol	2002	Ovary	Positive
15	Cli AP et al	Gynecol Oncol	2004	Uterine corpus	Positive (associated with Tuberous sclerosis)
16	Daraï E	J Reprod Med	2004	Uterine corpus	Negative
17	Sharma NH et al	The Inter J of Pathol	2006	Ovary	Positive
18	Jungsuk An et al	J of Women's Med	2010	Parametrium	Negative
19	Shakuntala PN et al.	Ind J Surg Onco	2012	Broad ligament	Negative
20	Yilmaz et al	Eur J Gen Med	2013	Uterine corpus	Negative
21	Totev TP et al	J Biomed Clin Res	2014	Uterine corpus	Negative
22	Garg M et al	J Can Res Ther	2015	Vulva	Not done
23	Sharma NH et al	Int J Medi Upd	2017	Cervix	Negative
24	Monteiro R et al	Int J Res Med Sci	2019	Cervix	Negative
25	Walke V et al	JMSCR	2019	Cervix	Not done
26	Dutta S et al	Autops Case Rep	2020	Broad ligament	Negative
27	Present case	–	2020	Cervix	Negative

white in color. On microscopic examination, the cervical polyp showed a benign tumor lined by cervical epithelium that had been partially eroded. The tumor had been composed of an admixture of smooth muscle fascicles, lobules of adipocytes, and numerous blood vessels with hyalinization in varied proportions (►**Figs. 1B** and **C**). No atypia or mitosis was seen. The polypoidal tumor of cervix showed CD34 (►**Fig. 2A**) and smooth muscle actin (SMA) (►**Fig. 2B**) diffuse positivity in blood vessels, and smooth muscle cells, respectively. HMB-45 was completely negative (►**Fig. 2C**). Based on these findings, the cervical tumor was diagnosed as AML.

Magnetic resonance imaging abdomen with contrast was done that showed enlarged bulky uterus, fairly defined, homogenous enhancing lesion with a broad base, measuring 3.8 × 3 × 2.6 cm projecting into the endometrial cavity abutting the posterior myometrium with suspicious endocervical invasion, suggesting the features of endometrial carcinoma. Hence, a staging laparotomy was done. Later total abdominal hysterectomy specimen was received with bilateral salpingo-oophorectomy, pelvic, paraaortic lymph nodes, and attached peritoneum. Externally, uterus appeared unremarkable. Cut surface showed dilated uterine cavity. Endometrium showed diffuse polypoidal, gray brown, friable growth measuring 2.3 × 1 × 0.5 cm (►**Fig. 3A**) and grossly myometrial invasion was identified.

Microscopically, sections from the posterior aspect of the body of uterus and fundus showed a tumor arising from the endometrium, which is composed of atypical columnar cells arranged in solid sheets, complex glandular and trabecular patterns with two to four mitotic figures/10 hpf (►**Fig. 3B–E**). Less than 50% of the myometrium was seen to be invaded. The anterior aspect of uterine corpus, bilateral parametria, fallopian tubes, and ovaries was free of tumor. There were 9 paraaortic nodes and 24 pelvic nodes that were free of tumor deposits. It was diagnosed as Endometrial adenocarcinoma—endometrioid type (World Health Organization [WHO]), histologic grade I (International Federation of Obstetrics and Gynecology [FIGO]) and pT1aN0 (American Joint Committee on Cancer [AJCC], 8th edition).

Left ovary showed a cortical inclusion cyst and left fallopian tube showed a paratubal cyst. The right adnexa were unremarkable.

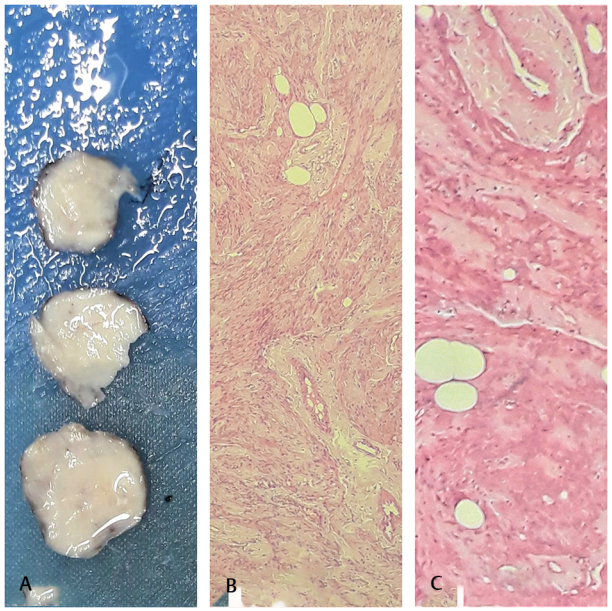

Fig. 1 (**A–C**) Gross picture and photomicrographs of angiomyolipoma of cervix.

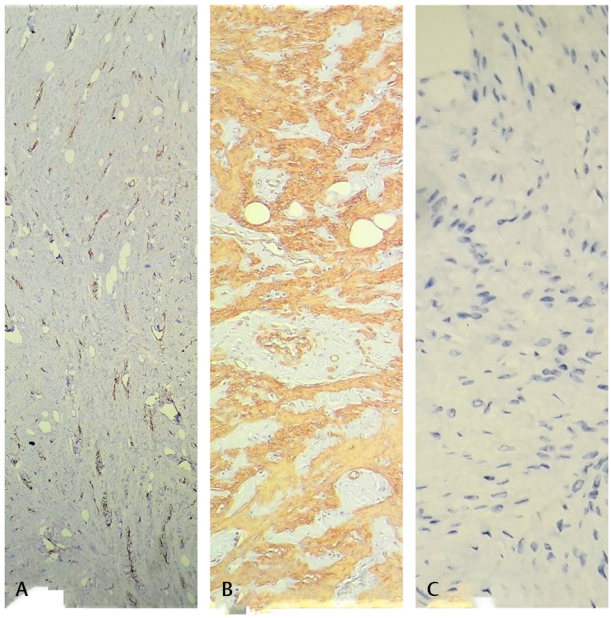

Fig. 2 (**A–C**) Immunohistochemical staining of angiomyolipoma: CD34 highlights the blood vessels (**A**); smooth muscle actin highlights the smooth muscle cells (**B**); HMB-45 is negative **(C).**

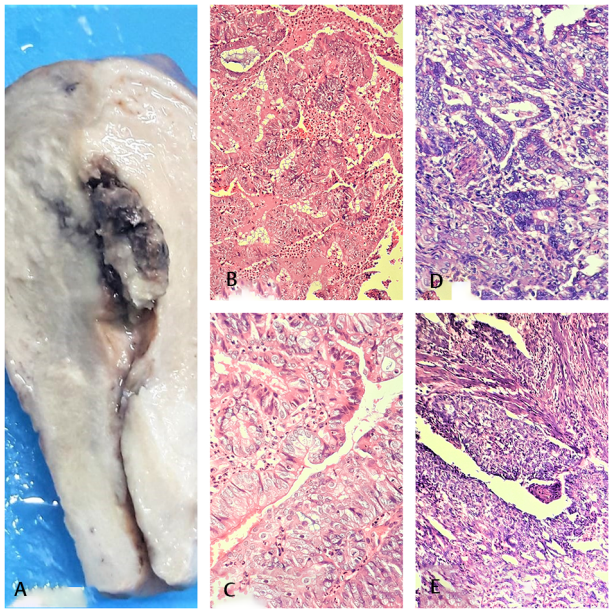

Fig. 3 (**A–E**) Gross picture (**A**) and photomicrographs (**B–E**) of endometrial adenocarcinoma.

Discussion

AML belongs to the family of PEComas.[4,6,14,15] PEComas include clear cell sugar tumors, myomelanocytic tumors, lymphangioleiomyomatosis, and AML.[4-6]

AML is extremely rare in the female genital tract.[3,5,6] AML in female genital tract usually arises in women over 40 years of age.[6] It is not included in the WHO classification of tumors of the female genital tract.[3,5,6,10,13]

AML is generally associated with tuberous sclerosis.[3,6,8,] Patients with tuberous sclerosis have increased risk of developing renal tumors and 5 to 80% risk of developing AML[3-6,10]

In tuberous sclerosis, hamartomas have been described in various organs such as adenoma sebaceum and angiofibromas in skin, AML in kidney, lymphangiomyomas in lung, sclerotic lesions in bone, tubers in brain, rhabdomyomas in heart, and phakomas in eyes.[6] Until their clonal neoplastic proliferation was proven, these tumors were considered as hamartomas.[2,4,8] No atypia/increased mitotic activity is seen in AML.[3,6,11,13] It may rarely show invasion of surrounding organs.[3,4]

The differential diagnoses of AML include lipoleiomyoma, degenerated myoma, vascular leiomyoma, benign lipomatous tumor, and angiolipoma.[2-4,6,7,14] Lipoleiomyoma is composed of adipose tissue and smooth muscle cells, but lacks the thick-walled blood vessels.[3,4,14] The thick-walled and hyalinized blood vessels in AML are appreciated better with trichrome stain.[4,11] Degenerated myoma is distinguished from AML by ultrasonographic findings, without shadowing and irregular margins.[3,6] Benign lipomatous tumor comprises only adipose tissue and lacks the other two components.[5] In AML, SMA is positive in the smooth muscle component and blood vessel wall; CD34 is positive in the endothelial cells; S100 in the mature adipose tissue component.[5,12] In our case, similar immunohistochemistry findings were found. But S100 staining was not performed.

All PEComas and hamartomas in tuberous sclerosis express HMB-45.[8] HMB-45 is positive in the nonvascular smooth muscle cells in AML. This feature has been reported in AML arising from kidney, lymph node, parametrium, colon, but not in most of the AML from the female genital tract.[2-5,10,12-14,16] Twenty percent of AML are negative for HMB-45.[3,6,14,16] Except in liver, most of the extrarenal AML are negative for HMB-45. Hence, it is proposed that HMB-45 reactivity is more related to abnormal TSC genotype, rather than AML.[8]

AML of cervix is rare and this is the first ever reported case of AML coexisting with endometrial carcinoma in the absence of tuberous sclerosis. CD34 is a good marker for delineating the blood vessels and SMA for both the smooth muscle and vascular components. S100 is generally not needed to prove the adipose tissue component. HMB-45 is not consistently expressed in AML of female genital tract. It is useful in the diagnosis of AML. But it is certainly not the definitive marker for AML[3,14,16]

Conclusion

AML is a tumor that can be diagnosed with the morphological findings alone without applying immunohistochemistry and even in the absence of tuberous sclerosis. The recurrence risk associated with AML is negligible as compared with malignant PEComas that has increased risk of recurrence and metastasis in the gynecological and genitourinary tract. This tumor is resected surgically, without any radical intervention, unless it is associated with endometrial carcinoma as reported in this case. The routine follow-up strategy for AML is mere observation with periodic pelvic and systemic examination.

Declaration of Patient Consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient has given her consent for images and other clinical information to be reported in the journal.

Conflict of Interest

None declared.

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