Case Report

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Angiomyofibroblastoma of the uterine cervix in a patient with triple negative breast cancer: a case report

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ABSTRACT

Angiomyofibroblastoma is an uncommon, benign mesenchymal tumor which generally occurs in the vulvovaginal region. Uterine cervix localisation is uncommon. A 40-year-old female patient, who had been operated becasue of breast carcinoma, presented vaginal bleeding. Examination revealed a polypoid mass located in both vagina and cervix. She underwent total abdominal hysterectomy and bilateral salpingectomy. With the help of typical histopathology and immunohistochemical findings, a diagnosis of "angiomyofibroblastoma" was made. Angiomyofibroblastoma is a benign mesenchymal tumor of unknown pathogenesis. A recognition of this entity is important to avoid misdagnosis of other angiomyxoid neoplasms such as aggressive angiomyxoma.

Keywords: Angiomyofibroblastoma, cervix uteri, breast carcinoma

INTRODUCTION

Angiomyofibroblastoma (AMFB) is characterized myofibroblastic differentiation and neoplastic stromal cell proliferation (1). AMFB is usually seen perineal and vulva–vaginal region in females and scrotum in males (2). AMFB needs to be distinguished from other stromal tumors especially angiomyxoma which is aggresive behaviour (3). Uterine cervix localization is unexpected in this tumor. To the best of our knowledge, 5 cases have been reported and this is the second reported AMFB of the uterine cervix in a patient with breast cancer in English literature (1,2,4–6). Tamoxifen treatment is thought to be effective in the development of AMFB (7). In this report, we discussed the histogenesis, immunohistochemical features, differential diagnosis, and relationship with tamoxifen of this uncommon entity and reviewed the English literature.

CASE REPORT

A 40-year-old female patient admitted to the hospital with vaginal bleeding. In medical history, she had a triple negative invasive ductal breast carcinoma which was treated with conservative breast surgery with axillary dissection and adjuvant chemo and radiotherapy in 2007. The gynecologic examination revealed a polypoid mass located in both vagina and cervix. The patient was diagnosed with cervical leiomyoma and underwent total abdominal hysterectomy and bilateral salpingectomy (TAH+BS) and sent intraoperative consultation. Macroscopically, TAH +BS was 10x6x4 cm size and a well-defined mass which was 6x5 cm in size was detected in the posterior cervix. The mass cut surface was solid and light yellow in appereance **Figure 1**. As a result of intraoperative consultation, the mass was reported as a benign mesenchymal tumor except leiomyoma. Histologically, the tumor was characterized by hypocellular edematous areas mixed with thin walled small blood vessels. The tumor cells were uniform eosinophilic, spindle-shaped or epitheloid without mitotic figures or atypia (**Figure 2-3**). The immunohistochemistry tumor had shown a strong positivity with desmin, vimentin, estrogen receptor (ER), progesterone receptor (PR), focal positivity with CD117 and caldesmon but CD34 and smooth muscle actin (SMA) were negative. According to these findings, the tumor was diagnosed as a "angiomyofibroblastoma". No tumor recurrence was reported.

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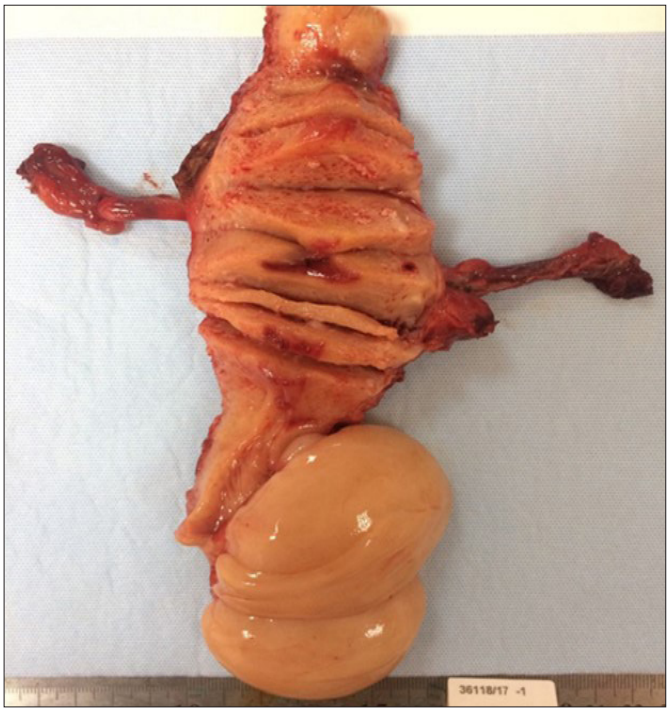

Figure 1. A well-defined mass which was 6x5 cm in size was detected in the posterior cervix

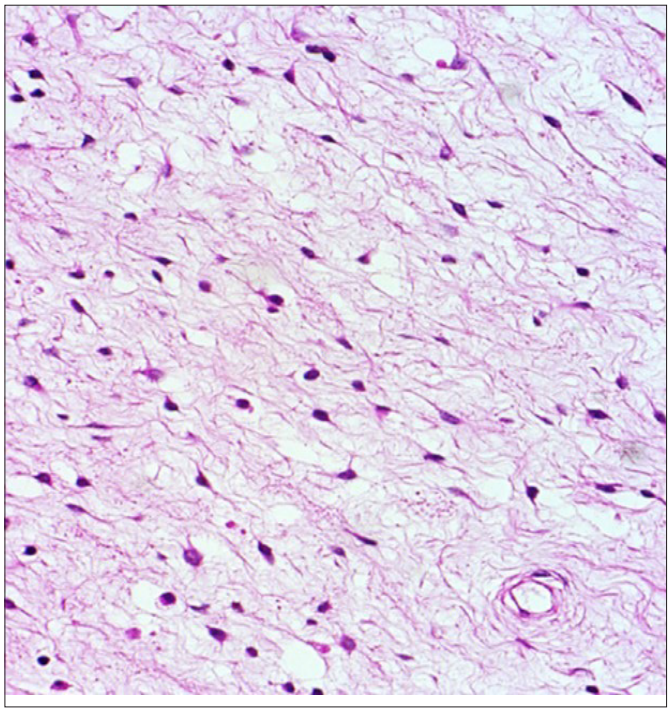

Figure 3. The neoplastic cells are bland-looking, spindle or oval shaped with scanty cytoplasm. H&E x400

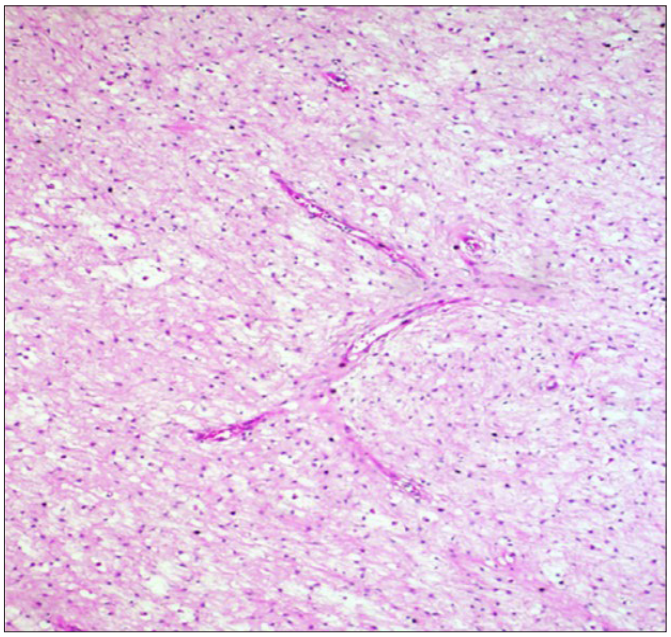

Figure 2. Tumor composed of hypocellularity in oedematous stroma and thin-walled blood vessels H&E x100

DISCUSSION

Angiomyofibroblastoma is frequently seen in vulva and vagina and between the ages of 20-50 (4,5). However, there are unusual cases reported in males (4,8). AMFB of the cervix is rarely seen with only 5 reports so far, ages range from 32- 53 and our case is 40 yearsold (1,2,4–6). The clinical and pathological features of AMFBs seen in cervix localization are shown in **Table 1**.

The tumor size varies between 10-40 mm (1,6). In our case, the tumor was the biggest diameter of 60 mm. Histologically, AMFB is characterized by variable hypocellular and hypercellular regions with spindle and round shaped cells (3,7). Stromal cells tend to collect around vessels. The immunohistochemistry shows strong positivity with desmin, vimentin, ER, PR, focal positivity with SMA and S100 protein, and negativity with cytokeratin and myoglobin (4,5). The imunohistochemical features of the cervical AMFB cases seen are listed in **Table 2.**

Table 1. The clinical and pathological features of AMFBs seen in cervix localization

Case Number	Age (Years)	Clinical Presentation	Treatment	Tumor size (cm)	Referance
1	53	Vaginal mass	Local excision	4x3	Lee CL et al. (1)
2*	43	Asymtomatic cervical mass	Local excision	3x3x2.5	Min Ji Kim et al. (2)
3	44	Polypoid mass	N/A	2	Babala et al. (4)
4	32	Vaginal spotting	N/A	1.2	Y.P.Wong et al. (5)
5	48	Intermens spotting	Cone biopsy	1	Roncati et al (6)
6*	40	Vaginal bleeding	TAH+BS	6x5	Present case

*breast carcinoma history cases, N/A: Not available, TAH+BS: Total abdominal hysterectomy and bilateral salpingectomy

Table 2. The imunohistochemical features of the cervical AMFB cases in the literature.

Case Number	Positive IHC	Negative IHC	Referance
1	Desmin CD 34 SMA	N/A	Lee CL et al. (1)
2	Desmin Vimentin	CD34 SMA	Min Ji Kim et al. (2)
3	Desmin Vimentin CD44	Ki67 Sarkomeric actin	Babala et al. (4)
4	ER PR	CD34 Desmin S100	Y.P.Wong et al. (5)
5	SMA Desmin ER PR	CD34 C Kit	Roncati et al. (6)
6	Desmin Vimentin ER PR	CD34 SMA	Present case

SMA: Smooth Muscle Actin, ER: Oestrogen receptor, PR: Progesterone receptor

The most important differential diagnosis is aggressive angiomyxoma (AAM). Other entities that should be considered in the differential diagnosis include cellular angiofibroma (CA), superficial myofibroblastoma (SM) fibroepithelial stromal polyp (FSP) (9). The clinical, histopathological, and immunohistochemical features of AMFB and differantial diagnosis are listed in the **Table 3.**

Aggressive angiomyxoma (AAM), described in 1983 by the first Steeper (4) and Rosai (9). AAM, with a high risk of recurrence, usually shows infiltrative growth with entrapped muscles, nerves, and mucous glands (5,10). AMFB has well circumscipred and benign clinical course. AAM is consisted of bland-looking stellate tumor cells with myxoid stroma, which has numerous variable-thickness blood vessels in contrast AMFB higher cellularity more numerous blood vessels more frequent plump, spindle shape cells (5). Dispersed inflammatory cells, especially neutrophils are always present (4). Immunohistochemistrically, AMFB and AAM express similar markers (5). Unlike AMFB, the CA occurs as a small and well-defined mass, grossly. The tumor consists of bland spindle cells arranged in intersecting fascicles mixed with wispy collagen bundles and hyalinised thickwalled blood vessels (4,5). CA is negative for desmin, and expresses variable estrogen receptor (ER), progesterone receptor (PR), CD34 and SMA (5). Superficial myofibroblastoma (SM) is composed of bland stellate or ovoid cells, within edematous and myxoid stroma (5,11). The neoplastic cells are separated by a non-neoplastic stromal band (Grenz zone) (5). SM shows variable immunoreactivity for ER, PR, CD34, desmin, and SMA (5,11). Fibroepithelial stromal polyp (FSP) is specific to the vulvovaginal region which is often incidentally encountered as a pedunculated polyp (5). It is overlied by squamous epithelium and typically contains central fibrovascular core (5).

Table 3. The clinical, histopathological, and immunohistochemical features of AMFB and differantial diagnosis.

	AMFB	AAM	CA	SM	FSP
Age (Years)	20-50	20-50	Middle-aged	40-70	Reproductive age
Clinical presention	Painless mass	Slow growing mass	Painless mass	Painless Mass	Asymptomatic
Tumor size (cm)	<5 cm	>10 cm	2-3 cm	<5 cm	1-3 cm
Margin	Well circumscipred	Infiltrative	Well circumscipred	Well circumscipred	Polypoid
Histological features	Alternating zone of cellularity Spindle-ovoid cells Stromal cells around vessels	Bland-looking stellate-spindle cells Myxomatous stroma Variable thickness blood vessels Inflammatory cells	Bland spindle cells Collagen bundles Hyalinised thick walled blood vessels	Bland stellate-ovoid cells Edematous or myxoid stroma (Grenz zone)	Overlied squamous epithelium Central fibrovascular core
Positive IHC	Desmin Vimentin ER, PR Focal positivity; SMA and S100	Desmin ER, PR Variable; CD34 and SMA	Variable; ER, PR CD34 SMA	ER, PR CD34 Desmin SMA	Desmin ER, PR Variable; CD34 and SMA
Negative IHC	Cytokeratin Myoglobin CD34	Cytokeratin S100 Myogenin	Desmin S100	Cytokeratin S100	Myogenin Myo D1
Treatment	Local excision	Surgical excision & Adjuvant chemotherapy	Local excision	Local excision	Simple excision

AMFB: Angiomyofibroblastoma, AAM: Aggressive angiomyxoma, CA: Cellular angiofibroma, SM:Superficial myofibroblastoma, FSP: Fibroepithelial stromal polyp

Histogenesis and pathogenesis of angiomyofibroblastoma have not been eluciated yet. However, some authors suggested that the neoplasm is probably derived from primitive mesenchymal cells of subepithelial myxoid stroma which may undergo differentiation to myofibroblasts under hormonal stimuli (12). The relationship between AMFB and tamoxifen which is used in treatment of breast cancer was firstly determined by Varras et al (7). In this study, it has been suggested that tamoxifen treatment may cause proliferation in mesenchymal cells of the vagina by estrogenic stimulation. Due to this effect, it has been reported to increase the incidence of endometriosis, adenomyosis, endometrial hyperplasia, leiomyoma, ovarian cysts, cervical and endometrial polyps especially in postmenopausal patients (7). Other previous studies have shown that in breast cancer patients, tamoxifen and similar drugs cause the development of vaginal AMFB (7,12–15). Although AMFB of the cervix is rare, cervical AMFB is much rarer due to tamoxifen and only 1 case has been reported in the literature so far.

CONCLUSION

Angiomyofibroblastoma located in uterine cervix is an unusual case, which creates a challenging diagnosis. The ethio-pathogenesis of AMFB is not clear yet. There are cases supporting the claim that says hormonal stimulation and usage of tamoxifen might have an effect on AMFB development. Since in our case the breast carcinoma is triple negative, there is no history of tamoxifen usage. As a result, more studies are needed to be made in order to show the relation between tamoxifen and AMFB development.

ETHICAL DECLARATIONS

Informed Consent: Written informed consent was obtained from all participants who participated in this study.

Referee Evaluation Process: Externally peer-reviewed.

Conflict of Interest Statement: The authors have no conflicts of interest to declare.

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