

An Audit of the Clinicopathological Spectrum of Benign Vascular Tumors of Female Genital Tract; with a Mini Narrative Review

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ABSTRACT

Background: Vascular tumors of the female genital tract (FGT) are very rare. The aim of this study was to analyze the spectrum of vascular tumors in FGT and to correlate their clinicopathological features. **Materials and Methods:** A retrospective study of 15 years, including clinical features, imaging studies, gross and microscopic features of 24 cases of benign vascular tumors of FGT were reviewed. The age range was 20–95 years. Presenting complaints were abdominal pain/mass, postcoital bleeding, and vaginal and vulval mass. The duration of symptoms varied from 3 months to 10 years. A diagnosis of vascular tumor was not considered in any of these on clinical grounds. **Results:** The most common benign vascular tumor was hemangioma (7 cases), followed by chorangioma (5 cases). The most common sites of occurrence of these benign tumors were ovary and vulva (8 cases each), the rarest site was cervix (1 case). The clinical symptom of ovarian vascular tumors was abdominal pain and lump. Among the vascular tumors of ovary, the most common was lymphangioma (4 cases) followed by hemangioma (3 cases). The least common tumor was angiomyolipoma. The most common vulval tumors were hemangioma and lymphangioma circumscriptum. An unusual case of multiplicity and complexity was observed with 3 neoplasms, one malignant and two benign with additional caseating tuberculous lymphadenitis. **Conclusion:** Benign vascular tumors in the FGT can present with symptoms similar to gynecological tumors and epithelial malignancies leading to unwarranted radical surgery. The pathological examination is necessary in all such cases to exclude the possibility of malignancy. Angiomyofibroblastoma and aggressive angiomyxoma of the vulva are very rare and both share similar clinical and histopathologic features causing diagnostic problems.

KEY WORDS: Angiomyolipoma, angiomyofibroblastoma, female genital tract, hemangioma, lymphangioma circumscriptum, vascular tumors

INTRODUCTION

The ovary itself is a highly vascularized organ but vascular tumors of female genital tract (FGT), especially those arising in the ovary, are very rare.^[1] The majority of vascular tumors are incidental findings due to their small size and asymptomatic nature. However, some cases present clinically with features simulating other more common gynecological tumors, even on radiological investigations like ultrasonography.^[2] Most of the reports in the literature are short series of these neoplasms confined to one organ of FGT.^[2]

This study describes the clinical profile, histopathological features, immunohistochemical findings, and differential

diagnosis of 24 cases of benign vascular tumors of the FGT observed over a period of 15 years.

MATERIALS AND METHODS

All the cases diagnosed as vascular tumor of the FGT in the Department of Obstetrics and Gynaecology and Pathology during a period of 15 years from 2000 to 2015, were retrieved from the files.

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The clinical features, imaging studies, laboratory investigations, and gross findings were analyzed. Histopathology slides were reviewed for morphological features, and special stains were done.

Immunohistochemistry was done in a case diagnosed as deep aggressive angiomyxoma (AAM).

RESULTS

Maximum cases were hemangiomas (29.16%) [Table 1].

The age ranged from 20 to 95 years with mean age of 43.4 years. Ovary and vulva were most frequently involved (33.33%) [Table 2].

Of 8 cases in the ovary, 4 were lymphangiomas, 3 were hemangiomas, and a case of angiomyolipoma (AML) noted.

These cases presented with nonspecific symptoms which ranged from abdominal masses and/pain, postcoital bleeding, and vulval or vaginal masses. A diagnosis of the vascular tumor was not considered in any of these cases on the clinical grounds.

The lymphangioma of ovary showed multiple cystic spaces on cut surface. Microscopy revealed several cystic spaces lined by bland endothelial cells and lumen showed lymph fluid [Figure 1].

The hemangiomas showed enlarged ovaries with a honeycomb appearance. Histologically dilated vascular spaces containing blood were noted [Figure 2].

A single case of AML was diagnosed. Cut section showed yellowish gray gelatinous appearance and histologically admixture of smooth muscle, fat, and vascular spaces seen [Figure 3 and Table 3].

Of 8 vulval tumors, most frequent were lymphangioma circumscriptum (LC), hemangiomas, and superficial angiomyxoma (SAM) (2 cases each) followed by single cases of deep AAM and angiomyofibroblastoma (AMFB).

Both cases of LC presented as edematous, multiple, grouped vesicles on mons pubis and labia majus. Microscopy revealed hyperkeratotic, hyperplastic squamous epithelium with multiple fluid filled spaces lined by flat endothelial cells in superficial and deep dermis [Figure 4].

Both cases of SAM were pedunculated skin covered masses of 5 and 4 cm diameter, respectively, with the clinical diagnosis of condyloma. Microscopy revealed hypocellular myxomatous tumor composed of spindle fibroblastic cells and numerous large caliber vessels having thickened endothelial lining [Figure 5a and b].

Table 1: Histological spectrum of benign vascular tumors

	Number	Percentage
Hemangioma	7	29.16
Lymphangioma	4	16.66
Angiomyolipoma	1	4.16
Superficial angiomyxoma	2	8.33
Deep aggressive angiomyxoma	2	8.33
Angiomyofibroblastoma	1	4.16
Lymphangioma circumscriptum	2	8.33
Chorangioma of placenta	5	20.83
Total	24	100.00

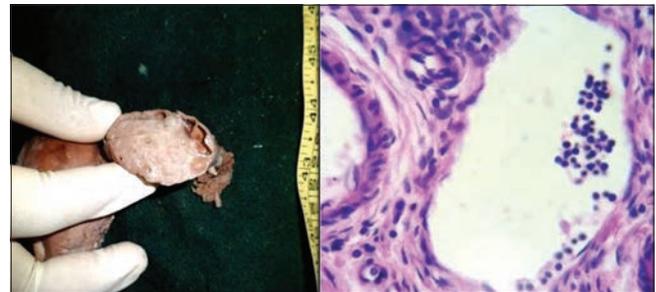


Figure 1: Gross specimen of ovary showing multiple cystic spaces, microscopy-several cystic spaces lined by bland endothelial cells containing lymph (H and E, ×200)

Table 2: Anatomic and age distribution and surgical procedure of benign vascular tumors

Anatomic site	Histopathological diagnosis	Surgical procedure	Number of cases and age (years)	Percentage	
Ovary n=8 (33.33%)	Left	Total abdominal hysterectomy with bilateral salpinxg-oophorectomy	Hemangioma	2 (35, 38)	8.33
			Lymphangioma	2 (45, 56)	8.33
	Right		Angiomyolipoma	1 (22)	4.16
			Lymphangioma	1 (35)	4.16
	Bilateral		Hemangioma	1 (55)	4.16
			Lymphangioma	1 (46)	4.16
Cervix (n=1)	Hemangioma	Polypectomy	1 (40)	4.16	
Vagina (n=2, 8.33%)	Hemangioma	Excision of mass	Hemangioma	1 (95)	4.16
			Deep aggressive angiomyxoma	1 (35)	4.16
			Angiomyofibroblastoma	1 (35)	4.16
Vulva (n=8, 33.33%)	Hemangioma		Hemangioma	2 (46, 71)	8.33
			Lymphangioma circumscriptum	2 (50, 56)	8.33
	Superficial angiomyxoma		2 (40, 70)	8.33	
	Deep aggressive angiomyxoma		1 (50)	4.16	
	Angiomyofibroblastoma		1 (35)	4.16	
	Chorangioma		5 (20-28)	20.83	
Placenta (n=5, 20.83%)	Chorangioma	Placenta with the mass removed	5 (20-28)	20.83	
Total number of cases			24	100.00	

The deep AAM of vulva was clinically diagnosed as Bartholin's cyst and excised. Grossly, soft gelatinous reddish-brown areas and microscopically, the lesions were moderately cellular with predominant stellate cells and few spindle cells in an abundant myxomatous stroma. The stromal cells were bland, oval, and showed no atypia. Plenty of pigmented macrophages were present. IHC with CD 34 was positive, confirming the diagnosis [Figure 5c and d].

One patient had mass in labia for last 10 years and was clinically diagnosed as Bartholin's cyst. Grossly, well-circumscribed and soft to rubbery in consistency with cut section showing grayish-white homogenous appearance. Microscopy revealed tumor consisting of hypo- and hyper- cellular areas with numerous delicate capillary sized blood vessels lined by endothelial cells. The stromal cells were plump to spindle with moderate cytoplasm and round to oval to spindly nucleus with fine chromatin and inconspicuous nucleoli. The cells were numerous in hypercellular areas and around the blood vessels. A diagnosis of AMFB of vulva was made [Figure 6].

A lesion received as cervical polyp was hemorrhagic and microscopic examination revealed cervical hemangioma [Figure 7].

In five cases, placenta was submitted after the delivery of baby. Placentas contained tumors ranging in size from 0.5 to 23 cm and placenta weighing from 400 to 800 g. Cut section showed large nodular lesions and dark brown appearance. Microscopically the lesion composed of numerous thin-walled fetal vessels of capillary or sinusoidal

Table 3: Clinical presentation of vulval tumors

Complaint	Local examination	Histopathological diagnosis
Labia majora growth since 10 years	Clinical impression-Bartholin's cyst	Angiomyofibroblastoma
Vulval swelling	Vulval mass-Bartholin's cyst	Deep aggressive angiomyxoma
Vulval growth	Many small warty lesions	Lymphangioma circumscriptum
Vulval growth	Warty lesion of 1.5 cm×1 cm	Lymphangioma circumscriptum
Vulval growth	Dark brown pedunculated mass of 4.5 cm×3 cm, clinical impression-melanoma	Cavernous hemangioma
Vulval growth	Reddish brown fleshy mass of 2.5 cm×2.2 cm	Hemangioma
Vulval growth	Soft pedunculated mass of 4 cm diameter	Superficial angiomyxoma
Vulval growth	Pedunculated skin covered mass of 5 cm×4 cm over clitoris	Superficial angiomyxoma

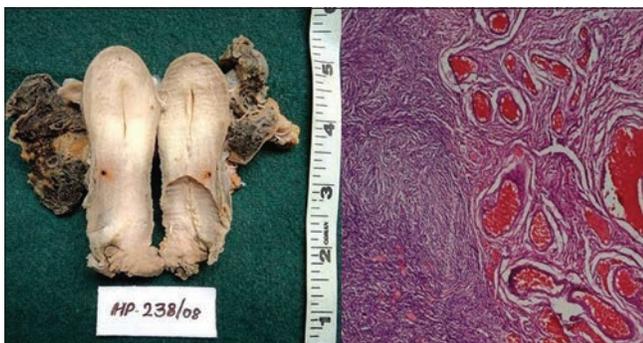


Figure 2: Gross-incidentally b/l cavernous hemangiomas in ovary, microscopy-numerous cavernous vascular channels and normal ovary seen on left side (H and E, ×200)

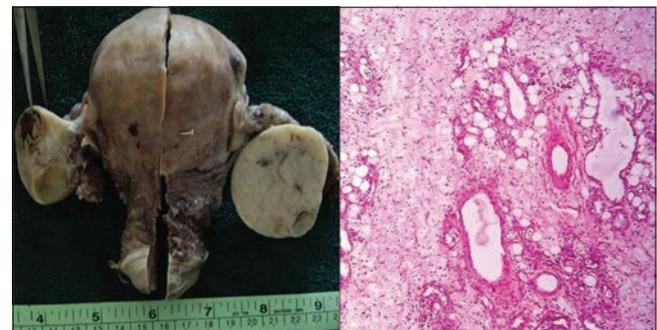


Figure 3: c/s yellow gelatinous with hemorrhagic areas. Microscopy revealed an admixture of smooth muscle bundles, large thick-walled blood vessels, and mature adipose tissue (H and E, ×200)



Figure 4: Edema and multiple, grouped, vesicles on the mons pubis and labium majus, Microphotograph showing hyperkeratotic hyperplastic squamous epithelium with multiple fluid filled spaces lined by flat endothelial cells in superficial and deep dermis (H and E, ×200)

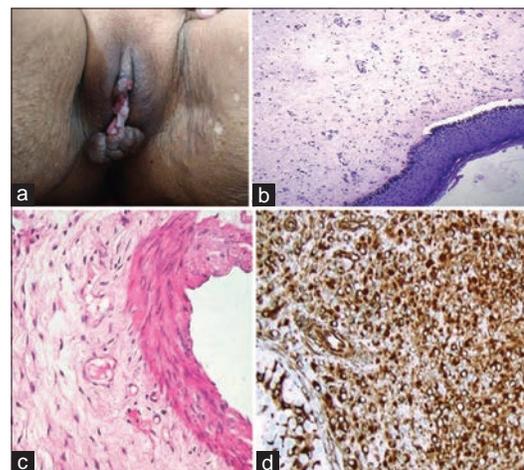


Figure 5: (a and b) Gross - pedunculated skin covered mass, microscopy revealed hypocellular myxomatous tumor composed of spindle fibroblastic cells and numerous large calibre vessels having thickened endothelial lining (H and E, ×200). (c and d) Abundant myxoid stroma with bland oval stromal cells with no atypia, large blood vessel with thickening and hyalinization of the walls (H and E, ×400), IHC- CD34 positive

caliber with scant intervening stroma with fibrous and myxoid areas. The diagnosis of chorangioma of placenta was made [Figure 8].

Bilateral cavernous hemangioma was detected as an incidental finding during the procedure of pan-hysterectomy in a diagnosed case of carcinoma of the cervix. Interestingly,

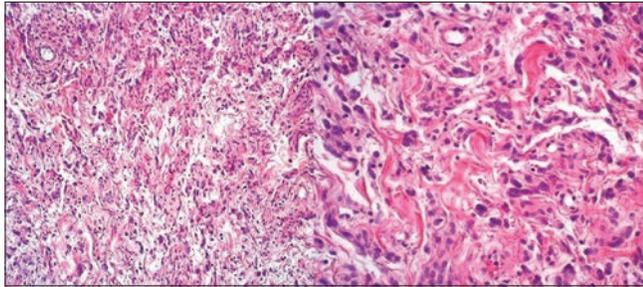


Figure 6: Photomicrograph showing hypo and hypercellular areas with numerous delicate capillary sized blood vessels lined by endothelial cells, stromal cells were plump to spindle with moderate cytoplasm and round to oval to spindle nucleus (H and E, x200)



Figure 7: Gross-mass was vascular, necrotic and friable, with a sessile base, microscopy-revealed a hyperplastic squamous epithelium with large dilated cavernous vascular channels which were lined by flattened endothelium (H and E, x200)

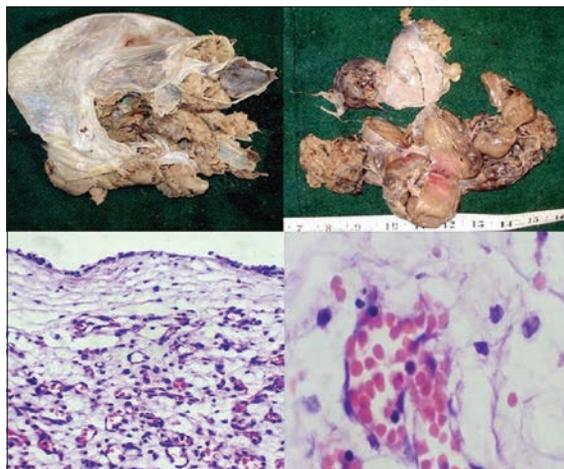


Figure 8: Gross showing a nodular mass attached to placenta, microscopy-increased capillary proliferation in enlarged villi covered by trophoblastic epithelium (H and E x100). Higher magnification showing capillaries resembling fetal vessels lined by flattened endothelial cells and scant intervening stroma (H and E, x200)

in this patient, small leiomyoma was present in the myometrium. The pelvic lymph nodes showed metastatic deposits. In addition, the lymph nodes showed necrotizing granulomatous inflammation compatible with tuberculous lymphadenitis.

In all the 24 cases, there was no atypia, no mitoses, and no necrosis.

DISCUSSION

Vascular tumors of FGT, especially of ovary constitute a very small proportion of all tumors of FGT. There are only a few case reports and short series of these neoplasms in literature. These have been reported in a wide age group, ranging from 4 months to 81 years.^[2] In the present series, age of patients ranged from 20 to 95 years. The majority of these patients were in age group of 30–40 years (12 cases). There was no specific clinical presentation which was suggestive of vascular tumor, as was noted in the present case series. However, these tumors can mimic other common neoplasm of FGT.

In a retrospective study, vascular tumors of FGT over 4 years were reviewed by Gupta *et al.* The age range of these cases was 12–52 years and the presenting complaint was abdominal pain/mass, postcoital bleeding, and vaginal and vulval mass. The vascular tumors occurred most commonly in the ovary (6 cases), followed by vulva (2 cases), and one each in cervix and vagina.

Clinical diagnoses ranged from cystadenoma in ovarian tumors to endocervical polyp in cervical tumor. Histologically, all were benign vascular neoplasms, hemangioma (five), lymphangioma (one), lymphangioma circumscriptum (one), angiomatosis (two), and arteriovenous malformation (one).^[2]

Hemangioma of ovary

Hemangioma of the ovary was first described by Payne in 1869.^[3] These are usually asymptomatic and present as incidental finding during operation or autopsy. Large lesions tend to present clinically as adnexal mass, frequently associated with lower abdominal pain, nausea, and vomiting, due to torsion or abdominal distension because of the mass itself.^[1] All cases in the present series were asymptomatic. Histologically, hemangiomas are benign lesions arising from vascular malformation, particularly in the canalizing process, forming abnormal vascular channels. There are two types, cavernous and capillary, with the cavernous type being the most common. Although they have been found in different parts of the ovaries, the medulla and Hilar region are the most common locations. This is consistent with the presence of larger vascular channels in these regions.^[3] In

the present series, all the five cases were of the cavernous type. Both the cortex and the medulla of the ovaries were involved. Although the etiology remains unknown, these lesions have been considered either hamartomatous malformations or true neoplasms in which pregnancy, other hormonal effects, or infection have been implicated as factors, enhancing the growth.^[1]

The preoperative diagnosis may be facilitated by radiological methods, to avoid radical surgery.^[2] In the present series, four cases were diagnosed as ovarian cysts on ultrasound examination and they underwent total abdominal hysterectomy with bilateral salpingo-oophorectomy. Simple oophorectomy is curative for ovarian hemangioma.^[2] So, a clinicopathologic correlation is essential.

Cervical hemangioma

Fewer than 40 cases of hemangioma of cervix are present in the literature.^[2] The uterine cervix cavernous hemangioma is a vascular benign tumor growth primarily made up of superficial and/or deep dilated large blood-vessels.^[4] Changes during pregnancy under hormonal influence can present a risk of obstetrical complications.^[4] In the present study, one case of cavernous hemangioma of the cervix presented clinically with postcoital bleeding. It was diagnosed as endocervical polyp and polypectomy was done.

Cervical hemangioma may be treated with hysterectomy, local excision, conization, or by laser ablation to preserve fertility in young patients. However, pathologic opinion is always to be considered necessary to rule out an underlying malignancy, including malignant vascular lesions.^[2]

Cavernous hemangioma of vagina

Cavernous hemangioma of the vagina is extremely rare and no cases have been reported in nonpregnant females in the literature over the past 35 years. A case of vaginal cavernous hemangioma was described by Bartsh in 1959 and a case of cavernous hemangioma during pregnancy was reported by Rizwan in 1997.^[5] The present case was a 95-year-old female who presented with a mass in the paraurethral region of the vagina, which bled on touch. It was clinically diagnosed as vaginal carcinoma and was excised. The mass was vascular, necrotic, and friable, with a sessile base. Microscopically, it was diagnosed as cavernous hemangioma.

Lymphangioma of the ovary

Lymphangioma of the ovary is an extremely rare lesion. There are only 19 cases reported in the literature. Lymphangioma is usually unilateral and asymptomatic, presenting as an incidental finding during routine gynecologic procedures. It is composed of aggregates of lymphatic spaces in ovarian stroma and the endothelial cells lining these spaces stain positively with CD-31 and CD-34 on immunostaining.^[6] In

the present series, four cases of ovarian lymphangiomas were encountered. Clinically, they simulated other cystic tumors of the ovary, which were similar to hemangioma and salpingo-oophorectomy was done. Therefore, a pathological examination is necessary to reach the correct diagnosis. Cystic lymphangioma should be included in the differential diagnosis of an ovarian cystic mass, and laparoscopic excision may be the method of treatment.^[7]

Angimyolipoma ovary

AML is a benign mesenchymal neoplasm that mainly occurs in the kidney either sporadically or in patients with tuberous sclerosis complex. Extrarenal AML is uncommon. Primary AML of ovary is extremely rare and only one case has been reported in literature as of our knowledge.^[8,9] In present study, a 22-year-old female presented with persistent cystic ovarian mass measuring 8 cm × 8 cm × 4 cm, c/s yellow gelatinous with hemorrhagic areas. Total abdominal hysterectomy with bilateral salpingo-oophorectomy was done. Microscopy revealed an admixture of smooth muscle bundles, large thick-walled blood vessels, and mature adipose tissue. Mitoses were rare. The main differential diagnosis is other oxyphilic tumors of the ovary. Typical smooth muscle cells are strongly immunoreactive for HMB-45 in AML.^[8]

Lymphangioma circumscriptum

LC is characterized by the appearance of persistent clusters of thin-walled vessels, usually filled with clear, colorless fluid over a thickened area of subcutaneous tissue on the skin.^[10] However, epithelial hyperplasia and hyperkeratosis give rise to firm lesions which are clinically suspected as genital warts or molluscum contagiosum.^[2] LC involving the vulva is very rare; only 33 cases are reported. In 12 of these LC was congenital and in 21 acquired. The most common predisposing condition for acquired LC of the vulva was radical surgery and/or radiotherapy.^[10] The two cases in the present series presented with small, nodular, warty/vesicular lesions in the labia without any previous history of malignancy. Excision biopsies of both the cases revealed the features of LC.

Superficial angiomyxoma vulva

Two cases of SAM were excised as vulval mass and histopathologically diagnosed, in a 40-year-old female and in a 70-year-old female with microinvasive vaginal squamous cell carcinoma. Giant SAMs of the vulva can mimic AAMs and AMFBs, as well as soft tissue sarcomas. Giant SAMs should be included in the differential diagnosis of vulvar soft tissue tumors.^[11]

Angiomyofibroblastoma vulva

AMFB is a recently described, rare benign soft tissue tumor that occurs mainly in the genital tract of premenopausal

women. AMFB of the vulva is a rare tumor with only 61 cases reported in the literature till date.^[12] The first case was diagnosed by Fletcher *et al.* in 1992. Patients usually present with painless mobile masses. The preoperative clinical diagnosis is that of a labial or Bartholin gland cyst in most cases. Some cases are misdiagnosed as vulval benign tumor, myxoid vulvar leiomyoma and lipoma.^[12,13] The tumors are subepithelial in location, well circumscribed, range from 0.5 to 25 cm in maximum diameter. The lesions present as a polypoidal or nodular mass with soft or elastic texture, light grey to tan in color, muco gelatinous on cut surface.^[12] In the present study, one case of AMFB was excised and reported as nonmalignant tumor on frozen section study, was histologically diagnosed. It presented clinically as Bartholin's cyst and was present for the past 10 years.

Aggressive angiomyxoma of vulva

AAM was first described by Steeper and Rosai in 1983. This is a rare, locally infiltrative tumor that arises in the pelvic and perineal soft tissues of young women.^[14] Approximately 150 cases have been reported.^[15] AAM has a high rate of local recurrence ranging from 50% to 60%, because of its infiltrative growth and anatomical location. The treatment of choice is wide local excision.^[14,15] Grossly, it is a nonencapsulated, gelatinous tumor with an infiltrative edge. There is no specific immunohistochemical marker for AAMs as yet.^[16] The tumor cells uniformly express vimentin and they heterogeneously express muscle specific actin and desmin. We encountered a case of AAM in a 50-year-old female, with the clinical presentation as Bartholin's cyst. The mass was excised. Based on the characteristic histological features, a diagnosis of deep AAM was made. There was no recurrence up to 9 months of follow-up.

The cases of AMFB and AAM in the present series illustrated that the differential diagnosis could be difficult. The tumors were rather similar in clinical presentation as well as at surgery and histopathologic examination. The cases presented as a soft non tender swelling in the vulva and were preoperatively diagnosed as Bartholin's cyst. The atypical and diagnostically misleading clinical features were the large size of the AMFB and the near absence of local infiltration of the AAM. Similar features were observed by Schotz *et al.* These tumors are so rare that many gynecological surgeons will never see one.^[13-15]

Chorangioma of placenta

Chorioangioma, originally described by Clarke in 1798, is the most common tumor of the placenta, with prevalence of 0.5–1.0%.^[17] It consists of a benign angioma arising from chorionic tissue. Three histological patterns have been described: Angiomatous, cellular and degenerate. The angiomatous is the most common, with numerous small

areas of endothelial tissue, capillaries and blood vessels surrounded by placental stroma. The cellular pattern has abundant endothelial cells within a loose stroma. The degenerate pattern has calcification, necrosis or hyalinization. These lesions are sometimes classified as placental hamartomas rather than true neoplasia.

Most chorioangiomas are of no clinical importance. Those measuring more than 5 cm in diameter may be associated with complications that can affect the mother, the fetus or the neonate.^[18] Chorioangioma is often confused with placental teratoma, degenerated myoma, and blood clot. Chorioangioma is differentiated from the rest by demonstration of vascular channels similar to fetal vessels on Echo pattern.^[19] In the present case series, placenta were received and histopathological analysis was done. Two out of five cases were more than 5 cm at preterm delivery and one case presented with preeclampsia, abruptio placenta and intrauterine fetal death.

Multiplicity and complexity of lesions in a surgically resected specimen

A 50-year-old female with previous cervical biopsy reported as squamous cell carcinoma was taken for surgery and Wertheim's hysterectomy was done. Specimen consisted uterus and cervix with bilateral adnexa and 2 pelvic lymph nodes. Cervix was showing a 1 cm × 1 cm grayish brown irregular mass at external Os which on microscopy showed moderately differentiated squamous cell carcinoma, large cell nonkeratinising type with metastatic deposits in bilateral pelvic lymph nodes. One of the lymph nodes showed caseating granuloma and the uterus showing a small leiomyoma. Both ovaries were dark brown with spongy consistency and honeycomb appearance on cut section. Microscopy showed multiple thin walled vascular spaces filled with red blood cells favoring a diagnosis of cavernous hemangioma. The occurrence of rare and multiple lesions in a surgically resected specimen of an organ or system is extremely rare, and there are no such reports in English literature until now.

CONCLUSION

The benign vascular tumor of the FGT present clinically simulating the common gynecological tumors, some asymptomatic and found incidentally. A detailed clinico radiological examination is essential. A pathological examination is necessary to exclude the probability of malignancy. Surgical excision is curative in most of the cases.

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Conflicts of interest

There are no conflicts of interest.

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