

Review of the pathophysiology, diagnosis, and therapy of vulvar leiomyoma, a rare gynecological tumor

Chao Sun^{1,*}, Junkai Zou^{1,*}, Qing Wang¹,
 Qi Wang¹, Lu Han¹, Nasra Batchu¹,
 Qurat Ulain¹, Jiang Du¹, Shulan Lv¹,
 Qing Song^{1,2,3} and Qiling Li^{1,2}

Abstract

The objective of this article is to discuss the pathophysiology, diagnosis, differential diagnosis, and therapy of vulvar leiomyoma. We performed a review of all English-language reports of vulvar leiomyoma published in PubMed from 1978 to 2015 using the following search terms: “vulvar leiomyoma,” “vulvar leiomyoma,” “vulval smooth muscle tumor,” and “external genitalia smooth muscle tumor.” Vulvar leiomyomas, which are rare benign monoclonal tumors, most commonly occur in the fourth and fifth decades of life. The genetics of vulvar leiomyoma remain undefined. Three principal histological patterns have been identified: spindle, epithelioid, and myxoid. Imaging tests such as ultrasound, endoscopic ultrasound, and magnetic resonance imaging are used in diagnosis. Surgical excision is the only curative treatment for vulvar leiomyomas. Establishment of a full differential diagnosis list and correct final diagnosis before surgery are essential for optimal clinical management. Although recurrence of vulvar leiomyoma is extremely rare, long-term follow-up of all cases is advisable.

Keywords

Vulvar leiomyoma, gynecological tumor, histology, diagnosis, imaging, treatment, management

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¹Department of Obstetrics and Gynecology, the First Affiliated Hospital of Xi'an Jiaotong University, Xi'an, Shaanxi, China

²Center of Big Data and Bioinformatics, the First Affiliated Hospital of Xi'an Jiaotong University, Xi'an, Shaanxi, China

³Cardiovascular Research Institute, Morehouse School of Medicine, Atlanta, GA, USA

*These authors contributed equally to this work.

Corresponding author:

Qiling Li, Department of Obstetrics and Gynecology, the First Affiliated Hospital of Xi'an Jiaotong University, Xi'an, Shaanxi 710061, China.

Email: liqiling@mail.xjtu.edu.cn



Introduction

The vulva, or female external genitalia, refers to the exposed parts of the female reproductive organs. The component structures of the vulva include the pubic mound, labia majora, labia minora, clitoris, vaginal vestibule, Bartholin's glands, urethra, vagina, and hymen.¹

Among soft tissue tumors, smooth muscle tumors were originally classified as either superficial or deep-seated.² Superficial smooth muscle tumors include pilar leiomyoma and angioleiomyoma, which are considered to have similar criteria for malignancy. Smooth muscle tumors of the vulva were originally placed in this class. However, later studies³ showed that smooth muscle tumors of the vulva differ both clinically and histologically from pilar leiomyoma and angioleiomyoma. Thus, smooth muscle tumors of the soft tissue are now classified as superficial (e.g., nipple), genital (e.g., vulva, scrotum), or deep-seated.

Leiomyomas are well-circumscribed, benign soft tissue tumors of mesenchymal origin. Around 3.8% of all benign soft tissue tumors⁴ are leiomyomas. Smooth muscle tumors of the vulva are usually classified into three categories⁵: leiomyomas, atypical leiomyomas, and leiomyosarcomas. Vulvar leiomyomas originate from the smooth muscle within the round ligament, erectile tissue, and dartos muscle. Although leiomyomas can develop wherever smooth muscle is present, they most commonly develop in the uterus.⁶ Leiomyomas are relatively rare in the vulva, but they are the most common benign solid tumor of the vulva. Vulvar leiomyomas account for only 0.03% of all gynecologic neoplasms⁷ and 0.07% of all vulvar tumors.⁸

The objective of this review is to discuss the pathophysiology, diagnosis, differential diagnosis, and therapy of vulvar leiomyoma.

Methods

A search of the English-language literature published from 1 January 1978 to 1 September 2015 in the PubMed database was performed using the following search terms: "vulval leiomyoma," "vulvar leiomyoma," "vulval smooth muscle tumor," and "external genitalia smooth muscle tumor." All literature related to vulvar leiomyoma was collected. Articles regarding other types of fibroids in the vulva and lesions that were misdiagnosed as vulvar leiomyoma were excluded. From more than 140 relevant titles, we identified 46 publications related to our study topic. Of these, 31 focused on vulvar leiomyoma and 15 focused on diseases of the vulva that were misdiagnosed as leiomyoma; all of these publications were excluded. From 31 relevant case reports, we obtained 27 full papers and 4 abstracts. Of the 27 full papers, 21 were case reports. Additional publications were identified via a systematic review of the reference lists within the initially identified publications and retrieved from PubMed.

This review was approved by the Ethics Committee at First Affiliated Hospital of Xi'an Jiaotong University. Informed consent for use of the figures was obtained from Dr Gurkan Kiran at Kahramanmaraş Sutcu Imam University of Kahramanmaraş in Turkey and Dr Burak Karadag at Ankara Training and Research Hospital of Ankara in Turkey. They offered the original pictures for use in this report.

Results (Table 1)

In this review, the age of the patients ranged from 15 to 73 years (mean, 41 years) (Table 1).^{9,10} According to these case reports, the personal and family histories of patients with vulvar leiomyoma generally revealed no abnormal findings.^{2,4,5,7,8,11-14}

Table 1. Summary of patients with vulvar leiomyoma.

Patient No.	First author and year	Age/duration	Clinical symptoms	Size (cm)	Histological pattern	Treatment	Outcome
1	Roy KK, 1998 [12]	47 y/6 mo	Multiple protruding masses in the vulva; difficulty walking	6 × 6 to 2 × 2	Spindled leiomyoma	Local excision	No recurrence in 2 y
2	Keriakos R, 1998 [28]	41 y/1 y	Painless left vulval swelling	3 × 2.8 × 2.5	Myxoid epithelial leiomyoma	Local excision	No recurrence in 2 y
3	Hopkins-Luna AM, 1999 [35]	45 y/-	Left labial mass and vaginal bleeding	10.5 × 9.0 × 5.2	Epithelioid leiomyoma	Local excision	-
4	Kajiwara H, 2002 [18]	29 y/-	-	4 × 4 × 4.5	Myxoid epithelial leiomyoma	-	-
5	Youssef A, 2003 [7]	39 y/4 y	Solid mass on external genitalia	14 × 12.5 × 11.5	Leiomyoma; weakly positive for ER and PR	Local excision	-
6	Darbhamura A, 2004 [31]	48 y/-	Firm, mobile lump in the right labium majus	2	Spindled leiomyoma; strong positivity for ER	Local excision	Recurrence in 6 mo
		49 y/-	Similar swelling in the left labium majus	No abdominal masses	Spindled leiomyoma; strong positivity for ER	Local excision	Recurrence in 5 y
		54 y/-	5-cm swelling in the perineum	5	Spindled leiomyoma; strong positivity for ER	Wide local excision; selective ER modulator	No recurrence in 1.5 y
7	Al Azzam M, 2004 [9]	15 y/2 y	Vulval pain associated with a swelling	4.0	Myxoid hyaline leiomyoma	Local excision	-
8	Horton E, 2006 [16]	47 y/1 y	Vulvar mass	3.0 × 2.0 × 0.7	Leiomyoma; strong positivity for ER	Local excision	-
9	Zhou J, 2006 [5]	29 y/6 mo	Vulvar mass with history of pregnancy	8.5 × 7.5 × 6.5	Myxoid epithelioid leiomyoma	Local excision	No recurrence in 29 mo
10	Koc O, 2010 [32]	47 y/2 y	Painless swelling on right side of vulva	6.5 × 4 × 2.3	Leiomyoma	Local excision	No recurrence in 1 y

(continued)

Table 1. Continued.

Patient No.	First author and year	Age/duration	Clinical symptoms	Size (cm)	Histological pattern	Treatment	Outcome
11	Guardiola MT, 2010 [17]	47 y/1 y	Slowly enlarging vulvar mass	2.3 × 2.0 × 2.0	Spindled leiomyoma; strong positivity for ER	Local excision	–
12	Oliveira-Brito LG, 2011 [33]	36 y/1 y	Perineal tenderness and local pain	1.5 × 6.5 × 7.5	Spindled leiomyoma	Local excision	–
13	Ngo Q, 2011 [19]	27 y/8 y	Firm perineal mass	9.0 × 7.5 × 5.5	Spindled leiomyoma	Local excision	No recurrence in 2.5 y
14	Kurdoglu M, 2011 [13]	39 y/–	Giant subcutaneous pedunculated mass in right labium majus during pregnancy	9 × 6 × 5	Leiomyoma	Local excision	–
15	Celik H, 2012 [14]	73 y/15–20 y	Solid large pedunculated mass	10 × 6 × 5	Leiomyoma	Local excision	–
16	Francis SA, 2012 [34]	56 y/1 y	Lump in the vulva	5 × 3 × 3	Spindled leiomyoma	Local excision	–
17	Kim HR, 2013 [8]	25 y/–	Right perineal mass in fifth week of pregnancy	5.5 × 4.3	Epithelioid leiomyoma	Local excision	–
18	Tian W, 2013 [27]	64 y/20 y	Bilateral masses between labia majora and labia minora	11 × 9 × 7 and 14 × 12 × 9	Leiomyoma	Local excision	No recurrence in 3 mo
19	Pandey D, 2014 [24]	20 y/6 mo	Labial swelling on left side with signs of inflammation	6 × 4 × 3	Epithelioid leiomyoma	Local excision	–
20	Levy RA, 2014 [4]	50 y/5 y	Large left labial mass	6.5 × 5.5 × 2.5	Spindled leiomyoma	Local excision	–
21	Zhao T, 2015 [22]	30 y/7 y	Mass in left labium majus with history of pregnancy	7	Myxoid epithelial leiomyoma	Local excision	–

ER, estrogen receptor; PR, progesterone receptor

Genetic findings

Uterine leiomyomas are monoclonal in origin, and approximately 40% to 50% harbor a cytogenetic abnormality.⁶ The most common abnormal chromosomes are 6, 7, 12, and 14.¹⁵ With respect to vulvar leiomyomas, however, only two reports have discussed cytogenetic abnormalities,^{16,17} and no conclusion regarding possible genetic causes can be drawn from these reports. Horton et al.¹⁶ described a unique clonal translocation (7;8)(p13;q11.2) in a leiomyoma of the vulva. The transcription factor gene pleomorphic adenoma gene 1 (*PLAG1*), with one allele in the long arm of normal chromosome 8 and the second allele in the derivative chromosome 7, was not modified by the translocation in this tumor. The authors mentioned some other possible genes: the one-carbon metabolism gene (*OCM*) at 7p13–p11, which codes for the calcium-binding oncodevelopmental protein oncomodulin; the *c-mos* proto-oncogene; and the *RBI*-inducible coiled-coil 1 gene (*RBICCI*) at 8q11, which codes for a key regulator of the tumor suppressor gene *RBI*.

In addition, Guardiola et al.¹⁷ published a case of a vulvar leiomyoma with the karyotype 46,XX,inv(12)(p12q13–q14). The breakpoint site may either involve or flank the high-mobility group AT-hook 2 gene (*HMG A2*) at 12q14.3 because this gene has been shown to be activated by rearrangement. The *HMG A2* gene encodes a protein member of the non-histone chromosomal high-mobility group family. This gene is often overexpressed in uterine leiomyomas. However, these findings do not explain how aberrant smooth muscle cells of leiomyoma survive and develop; therefore, additional genetic research is warranted.

Histological findings

The tumors ranged from 2 to 15 cm (mean, 7.1 cm) along their greatest dimension. Grossly, the tumors were well-circumscribed

and had a gray, white, tan, or yellow cut surface.^{2,3,5,7–9,12,14,16–22} Vulvar leiomyomas, like other smooth muscle tumors of the vulva, exhibit three principal histological patterns: spindled, epithelioid, and myxoid.²³ These patterns can be mixed or pure. Among the reviewed cases, seven tumors were spindled leiomyomas, three were epithelioid leiomyomas, and five were myxoid leiomyomas; the histological patterns of six tumors were not clearly reported. In the spindled pattern, which is a relatively common type of vulvar leiomyoma,²² the neoplastic tissue exhibits a fascicular proliferation of spindle-shaped cells with ovoid to elongated nuclei and richly eosinophilic cytoplasm.^{4,24} Compared with the spindled pattern, the epithelioid pattern is much less common.^{2,3,25} In this pattern, microscopic examination often shows a combination of spindle and epithelioid cells with abundant eosinophilic or clear cytoplasm.^{5,8,23} In contrast to vulvar angioleiomyomas, in which the cells are usually arranged in anastomosing cords, the cells in vulvar leiomyomas usually are arranged in nests. Microscopically, the myxoid pattern consists of small round or oval cells arranged in nests and an interlacing network of spindle cells, which are filled with mucous material.^{5,22,26}

Diagnosis and assessment

Most patients presented with a long history of a painless mass.^{4,12,14,27,28} Because the mass usually remains small (often for 10–20 years)^{10,12,27} and grows slowly in the early period, many patients do not initially see a physician. As the mass increases in size, patients often have difficulty walking, sitting, or having intercourse.^{2,4,7,8,12,14,19,22} The mass gradually causes pain,^{14,29} which we can infer is due to stimulation of the peripheral nerves by larger leiomyomas. Pruritus and erythema,² although uncommon, may also be signs of vulvar

leiomyoma. Roy et al.¹² described a patient with vulvar leiomyoma who developed severe pruritus over the swelling of the mass. Reports of compression of the bladder or rectum by the mass are relatively infrequent.

Vulvar leiomyomas usually occur in the clitoris and labium minora.²⁴ On physical examination, palpation usually reveals a non-tender mass with firm consistency and partial mobility.^{12,14,19} Occasionally, palpation also reveals a peduncle in a superficial mass⁷ or simply a swelling in a deeper mass.²⁴ Tenderness may also be present in those patients who experience pain. Based on the patients' histories, symptoms, and physical examination findings, the masses are often misdiagnosed as Bartholin's gland cysts on first impression.^{5,8,22} A sufficient differential diagnosis list should be established in such cases.

Once a leiomyoma is suspected based on the patient's history or physical examination findings, imaging should be undertaken to confirm the presence, location, characterization, and size of the vulvar leiomyoma.¹² Ultrasonography is most often used to assess vulvar leiomyomas because of its low cost, high accessibility, and helpfulness in establishing the correct diagnosis.²⁴

With the exception of its higher cost, magnetic resonance imaging (MRI) is also an excellent imaging tool for the characterization and diagnosis of vulvar leiomyoma because of its multiplanar capability and superior soft tissue contrast resolution.³⁰ The key to diagnosis of vulvar leiomyoma is the low signal intensity mimicking that of smooth muscle on T2-weighted images.⁸ Most investigators agree that MRI is not ideal for differentiating benign and malignant forms in doubtful cases because some benign-appearing lesions behave aggressively with time.^{5,8,21} In the present review, auxiliary examination with imaging was performed in six cases: two patients underwent ultrasound,^{8,17,31} three patients

underwent MRI,^{8,32-34} and one patient underwent both ultrasound and MRI.⁸

Differential diagnosis

The differential diagnosis includes benign and malignant entities such as Bartholin's cysts, AAM, atypical leiomyoma, leiomyosarcoma, and dermatofibrosarcoma.

As mentioned above, vulvar leiomyoma often presents as a painless mass that enlarges over time, and it is usually initially misdiagnosed as a Bartholin's cyst or abscess.^{5,8,11,12,19,24,35} The most common clinical findings²⁰ of a Bartholin's cyst or abscess is a painful lump that is often associated with fever and inflammation. The presence of tenderness should be determined by physical examination. When an abscess forms, local fluctuation and the inguinal lymph nodes will also be palpable. Hence, any cases initially diagnosed as a Bartholin's cyst or abscess need to be reexamined once the inflammation subsides. Transperineal ultrasonography, pelvic computed tomography, and pelvic MRI are also helpful in confirming the diagnosis.³³

AAM is a rare soft tissue tumor that usually occurs in female patients of reproductive age.³⁶ This disease can be easily misdiagnosed because its clinical features are similar to those of vulvar leiomyoma. MRI is an efficient method with which to reach a diagnosis before surgery.^{8,37} AAM is isointense to muscle on T1-weighted images and exhibits high signal intensity on T2-weighted sequences because of its loose and sometimes myxoid stroma.³⁷ The most definitive diagnostic method is histologic analysis of an excisional biopsy specimen along with confirmatory immunohistochemical evaluation.^{36,37} AAM is usually composed of bland spindle and spindle cells with round or ovoid nuclei and pale eosinophilic cytoplasm with thin cytoplasmic processes.³⁸⁻⁴⁰ The most distinguishing feature of AAM is the presence of thick-walled

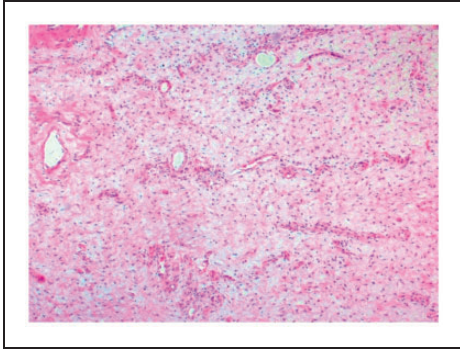


Figure 1. Low-magnification view of spindle-shaped cells evenly distributed in a myxoid stroma. Prominent vessels are apparent (original magnification, $\times 40$).

vessels, which are not seen in vulvar leiomyoma (Figure 1).⁴¹

Dermatofibrosarcoma protuberans (DFSP) is an uncommon soft tissue tumor characterized by a low propensity for metastasis and a high rate of local recurrence; it rarely presents in the vulva.^{13,42} The main clinical feature of this disease is painless, persistent, slow growth of a single nodule with a hump-like pattern or plaque, similar to vulvar leiomyoma.⁴²⁻⁴⁴ Color Doppler images can show a rich color flow signal inside the DFSP.¹⁴ On MRI, DFSP is isointense or slightly low to muscle on T1-weighted images and exhibits high signal intensity on T2-weighted sequences.^{45,46} The main diagnostic method relies on pathology: DFSP cells show a typical spindle shape similar to fibroblasts, are often arranged around a central axis or exhibit a "basket"-like arrangement, stretch along the subcutaneous fat and connective tissue, and infiltrate the lobular septal deep tissue. Tumor cell atypia is not obvious, and the mitotic spectrum varies.^{42,43}

The most difficult problem in diagnosing vulvar smooth muscle tumors is distinguishing benign from malignant forms; that is, leiomyoma from atypical leiomyoma and leiomyosarcoma. Tavassoli and Norris²⁵

proposed the following diagnostic criteria for leiomyosarcoma⁴⁷ (Figure 2): (1) ≥ 5 cm in the greatest dimension, (2) infiltrating margins, and (3) ≥ 5 mitotic figures per 10 high-power fields. Nielsen et al.² added a fourth criterion: (4) moderate to severe cytological atypia. It has been suggested⁴⁸ that if at least three of these criteria are met, the diagnosis is leiomyosarcoma. If only two criteria are met, a diagnosis of atypical leiomyoma is warranted, and if only one criterion is met, the diagnosis is leiomyoma. Nucci and Fletcher²³ reported that coagulative tumor necrosis is also a feature of malignancy and that its presence in combination with any of the four aforementioned criteria should seriously raise the possibility of leiomyosarcoma. The expression of estrogen, progesterone, and androgen receptors, along with a moderate number of Ki-67-positive cells and lack of p53 protein overexpression, are also considered markers of low-histologic-grade vulvar leiomyosarcoma.^{49,50}

Therapy and follow-up

Decisions regarding therapy for vulvar leiomyoma should be made based on the individual case presentation and pathological evaluation. Patients who accept local excision should be informed about the risk of injury to the levator muscles, rectum, vagina, or pubic ramus as well as the risk of recurrence.^{2,13,31} Due to the low incidence of the tumor, no evidence-based diagnostic algorithms or published recommendations for treatment have been established. Excision of vulvar leiomyomas is the only viable surgical option to ensure complete cure.^{2,3,14,19} Usually, the most important consideration for women who undergo surgery is simply the inconvenience.^{2,4,7,12,22,35}

Follow-up information was available for eight patients, and the follow-up duration ranged from 3 months to 5 years (mean,

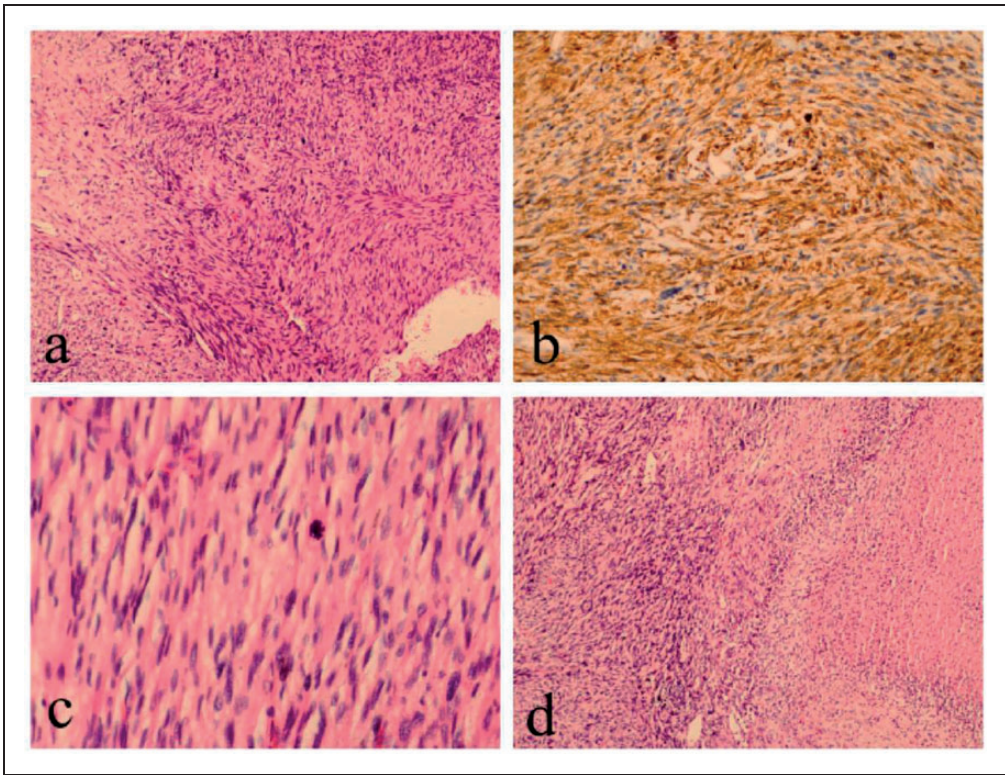


Figure 2. Representative leiomyosarcoma. (a) Fusiform-shaped pleomorphic cells with hyperchromatic nuclei and rare bizarre-shaped atypical cells. (b) Necrotic tumor fields. (c) Atypical mitosis. (d) Tumor cells exhibiting diffuse positive staining for calponin.

25 months). The vulvar leiomyoma in one patient (Patient 7 in Table 1) recurred twice: first after 6 months and again after 5 years. For the first two therapies, only local excision was adopted. The third time, the patient was given a selective estrogen receptor (ER) modulator after local excision, and no further recurrence developed after 1.5 years.

Discussion

Vulvar leiomyomas are rare and account for only 0.03% of all gynecologic neoplasms⁷ and 0.07% of all vulvar tumors.⁸ Affected patients range in age from 15 to 73 years (mean, 41 years), and the diameter of the tumors ranges from 2 to 15 cm (mean, 7.1 cm). Only two reports of cytogenetic

abnormalities of vulvar leiomyomas have been published [a unique clonal translocation (7;8)(p13;q11.2) and karyotype 46,XX,inv(12)(p12q13-q14)].^{16,17} No conclusion regarding possible genetic causes can be drawn from these reports.

ERs and progesterone receptors (PRs) are highly expressed in uterine leiomyoma, and both estrogen and progesterone can promote the development of uterine fibroids.⁵¹⁻⁵³ These findings may suggest that uterine leiomyomas originate from ER- and PR-expressing myometrial smooth muscle cells.²² Conventional wisdom suggests that vulvar leiomyoma is also an estrogen-dependent neoplasm,^{29,31} like uterine leiomyoma. However, Hodgins et al.⁵⁴ reported that ER staining of

epidermis and fibroblasts with monoclonal antibodies significantly declined when moving from the vagina toward the labia minora, labia majora, and suprapubic skin. The round ligament, erectile tissue, and dartos muscle, which may lack intrinsic ER/PR expression, are considered to be the sites at which vulvar leiomyomas originate.^{12,22} Additionally, in a review of more than 30 years of literature, no reports of enlargement of vulvar leiomyomas during pregnancy were found.^{5,8,13,22} In contrast, some postmenopausal women have exhibited enlargement of their vulvar leiomyomas in the absence of estrogen therapy.^{14,34} Hence, the relationship between hormones and the growth of vulvar leiomyomas warrants further study.

Most of the tumors in our series were composed of spindle cells. Nielsen et al.² found that 14 of 25 vulvar leiomyomas consisted mainly of spindle cells arranged in fascicles. Compared with the spindled pattern, the epithelioid pattern is much less common, occurring in only about 12% of vulvar leiomyomas.^{2,3,25} The myxoid pattern is speculated to be a degenerative phenomenon related to hormonal changes during pregnancy.^{5,18,26} However, Zhao et al.²² review reports of 11 women with vulvar leiomyomas complicated by pregnancy. Two of these women exhibited negative staining for ER and PR or weak ER and PR positivity in local areas. Consequently, the relationship between pregnancy and myxoid morphology warrants further study. In addition, vulvar leiomyomas are immunopositive for muscle markers, including smooth muscle actin, desmin, and muscle-specific actin^{18,29,31} and focally positive for S-100 and cytokeratin.^{5,19,22}

Most investigators initially assumed that vulvar leiomyomas develop at reproductive ages and usually regress after menopause, similarly to uterine leiomyomas.^{8,29,31} However, no evidence suggests that leiomyomas shrink or disappear during

the menopausal or postmenopausal periods. Some vulvar leiomyomas in postmenopausal patients even continue to grow, as mentioned above. Therefore, in both older women and women of reproductive age, suspected leiomyomas should be followed up and surgery performed if needed.

Endoscopic ultrasound and MRI are common imaging tools for the diagnosis and differential diagnosis of vulvar leiomyoma. The differential diagnoses include Bartholin's cysts, AAM, atypical leiomyoma, and leiomyosarcoma. Because of their similar clinical features, Bartholin's cysts must be ruled out first. The above-described diagnostic criteria have been established to distinguish leiomyoma from atypical leiomyoma and leiomyosarcoma.

One report suggested that vulvar leiomyomas are subject to relapse if the tumor shows strong ER immunopositivity.²⁰ Although the relationship between hormones and the growth of vulvar leiomyoma is still ambiguous,¹⁸ a selective ER modulator may be given to prevent recurrence following surgery.²⁰ Recurrence of tumors with negativity or weak positivity for ERs and PRs is extremely rare.^{8,14,13,33}

Conclusions

The most common presentation of vulvar leiomyoma is a painless mass^{4,12,14,27,28} in the clitoris or labium minora.²⁴ On physical examination, palpation usually reveals a non-tender mass with firm consistency and partial mobility.^{12,14,19} Before establishing a preoperative diagnosis, endoscopic ultrasound or MRI are suggested to aid in the differential diagnosis from Bartholin's cysts and AAM. Postoperative pathological examination can distinguish vulvar leiomyoma from atypical leiomyoma and leiomyosarcoma. Excision of vulvar leiomyomas is the most useful surgical option to completely cure leiomyomas.^{22,3,14,19}

Although recurrence is uncommon, short-term follow-up is still suggested.

Because only two reports of cytogenetic abnormalities were found in the literature, further studies of how vulvar leiomyomas develop and survive are warranted. Additionally, the relationships between pregnancy and myxoid morphology and between hormones and the growth of vulvar leiomyomas warrant further study.

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Declaration of conflicting interest

The authors declare that there is no conflict of interest.

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References

- Hoffman BL and Williams JW. *Williams gynecology*. 2nd ed. New York: McGraw-Hill Medical, 2012, p.940.
- Nielsen GP, Rosenberg AE, Koerner FC, et al. Smooth-muscle tumors of the vulva - A clinicopathological study of 25 cases and review of the literature. *Am J Surg Pathol* 1996; 20: 779-793.
- Newman PL and Fletcher CD. Smooth muscle tumours of the external genitalia: clinicopathological analysis of a series. *Histopathology* 1991; 18: 523-529.
- Levy RA, Winham WM, Bryant CS, et al. Smooth muscle neoplasms of the vulva masquerading as Bartholin gland duct cysts. *Proc (Bayl Univ Med Cent)* 2014; 27: 25-27.
- Zhou J, Ha BK, Schubeck D, et al. Myxoid epithelioid leiomyoma of the vulva: a case report. *Gynecol Oncol* 2006; 103: 342-345.
- Owen C and Armstrong AY. Clinical management of leiomyoma. *Obstet Gynecol Clin North Am* 2015; 42: 67-85.
- Youssef A, Neji K, M'Barki M, et al. Leiomyoma of the vulva. *Tunis Med* 2013; 91: 78-80.
- Kim HR, Yi BH, Lee HK, et al. Vulval epithelioid leiomyoma in a pregnant woman. *J Obstet Gynaecol* 2013; 33: 210-211.
- Al Azzam M, Orrell JM and Vasey DP. Vulval leiomyoma with a myxoid hyaline stroma. *J Obstet Gynaecol* 2004; 24: 936.
- Celik H, Bildircin FD, Kefeli M, et al. Labial leiomyoma growing gradually in the vulva of an elderly woman. *J Obstet Gynaecol* 2012; 32: 816.
- Aneiros J, Beltran E, Garcia del Moral R, et al. Epithelioid leiomyoma of the vulva. *Diagn Gynecol Obstet* 1982; 4: 351-356.
- Roy KK, Mittal S and Kriplani A. A rare case of vulval and perineal leiomyoma. *Acta Obstetrica Et Gynecologica Scandinavica* 1998; 77: 356-357.
- Messalli EM, D'Aponte ML, Luise R, et al. An apparently benign vulvar mass: possibly a rare malignancy. *Eur J Gynaecol Oncol* 2012; 33: 441-444.
- Kransdorf MJ and Meis-Kindblom JM. Dermatofibrosarcoma protuberans: radiologic appearance. *AJR Am J Roentgenol* 1994; 163: 391-394.
- Ligon AH and Morton CC. Leiomyomata: heritability and cytogenetic studies. *Hum Reprod Update* 2001; 7: 8-14.
- Horton E, Dobin SM, Debiec-Rychter M, et al. A clonal translocation (7;8)(p13;q11.2) in a leiomyoma of the vulva. *Cancer Genet Cytogenet* 2006; 170: 58-60.
- Guardiola MT, Dobin SM, Dal Cin P, et al. Pericentric inversion (12)(p12q13-14) as the

- sole chromosomal abnormality in a leiomyoma of the vulva. *Cancer Genet Cytogenet* 2010; 199: 21–23.
18. Kajiwara H, Yasuda M, Yahata G, et al. Myxoid leiomyoma of the vulva: a case report. *Tokai J Exp Clin Med* 2002; 27: 57–64.
 19. Ngo Q and Haertsch P. Vulvar leiomyoma in association with gastrointestinal leiomyoma. *Aust N Z J Obstet Gynaecol* 2011; 51: 468–469.
 20. Saeed NK and Al-Jufairi ZA. Bartholin's gland abscesses caused by streptococcus pneumoniae in a Primigravida. *J Lab Physicians* 2013; 5: 130–132.
 21. von-Waagner W, Liu H and Picon AI. Giant perineal leiomyoma: a case report and review of the literature. *Case Rep Surg* 2014; 2014: 629672.
 22. Zhao T, Liu X and Lu Y. Myxoid Epithelial Leiomyoma of the Vulva: A Case Report and Literature Review. *Case Rep Obstet Gynecol* 2015; 2015: 894830.
 23. Nucci MR and Fletcher CD. Vulvovaginal soft tissue tumours: update and review. *Histopathology* 2000; 36: 97–108.
 24. Pandey D, Shetty J, Saxena A, et al. Leiomyoma in vulva: a diagnostic dilemma. *Case Rep Obstet Gynecol* 2014; 2014: 386432.
 25. Tavassoli FA and Norris HJ. Smooth muscle tumors of the vulva. *Obstet Gynecol* 1979; 53(2): 213–217.
 26. Nemoto T, Shinoda M, Komatsuzaki K, et al. Myxoid leiomyoma of the vulva mimicking aggressive angiomyxoma. *Pathol Int* 1994; 44: 454–459.
 27. Tian W, Wang Y, Zhang H, et al. Androgen insensitivity syndrome with gynandroblastoma and vulvar leiomyoma: case report and literature review. *J Low Genit Tract Dis* 2013; 17: 335–339.
 28. Keriakos R, Rahman KM and Dixon GR. Atypical vulvar leiomyoma-a diagnostic challenge. *J Obstet Gynaecol* 1998; 18: 299–300.
 29. Siegle JC and Cartmell L. Vulvar leiomyoma associated with estrogen/progestin therapy. A case report. *J Reprod Med* 1995; 40: 147–148.
 30. Misumi S, Irie T, Fukuda K, et al. A case of deep soft tissue leiomyoma: CT and MRI findings. *Radiat Med* 2000; 18: 253–256.
 31. Darbhamulla A, Watson AJ and Benatar B. Recurrent vulval fibroids—an unusual indication for selective oestrogen receptor modulators (SERMs). *J Obstet Gynaecol* 2004; 24: 95–96.
 32. Koc O, Sengul N and Gurel S. Perineal leiomyoma mimicking complex Bartholin mass. *Int Urogynecol J* 2010; 21: 495–497.
 33. McKenzie M, Pintilie H, Wilkinson N, et al. A rare case of vulval leiomyosarcoma: management and an updated review of the literature. *J Obstet Gynaecol* 2011; 31: 675–676.
 34. Francis SA, Wilcox FL and Sissons M. Bartholin's gland leiomyoma: a diagnostic and management dilemma. *J Obstet Gynaecol Res* 2012; 38: 941–943.
 35. Hopkins-Luna AM, Chambers DC and Goodman MD. Epithelioid leiomyoma of the vulva. *J Natl Med Assoc* 1999; 91: 171–173.
 36. Zizi-Sermpetzoglou A, Myoteri D, Koulia K, et al. Aggressive angiomyxoma of the vulva: a bizarre perineal lesion. *Case Rep Oncol Med* 2015; 2015: 292304.
 37. Karwacki GM, Stockli M, Kettelhack C, et al. Radiographic diagnosis and differentiation of an aggressive angiomyxoma in a male patient. *J Radiol Case Rep* 2013; 7: 1–6.
 38. Choi H, Park C and Ji YI. Alternative surgical approaches for aggressive angiomyxoma at different sites in the pelvic cavity. *Obstet Gynecol Sci* 2015; 58: 525–529.
 39. Miguez Gonzalez J, Dominguez Oronoz R, Lozano Arranz P, et al. Aggressive angiomyxoma: Imaging findings in 3 cases with clinicopathological correlation and review of the literature. *J Comput Assist Tomogr* 2015; 39: 914–921.
 40. Kiran G, Yancar S, Sayar H, et al. Late recurrence of aggressive angiomyxoma of the vulva. *J Low Genit Tract Dis* 2013; 17: 85–87.
 41. Wu H, Liu W, Xu H, et al. Aggressive angiomyxoma of the pelvis: a series of four cases and literature review. *Eur J Gynaecol Oncol* 2015; 36: 610–614.
 42. Wiszniewska J, Roy A and Masand RP. Myxoid Dermatofibrosarcoma Protuberans of the Vulva: Case Report of a Rare Variant in an Unusual Location, With Unusual Morphologic and Immunohistochemical

- Features. *Am J Dermatopathol* 2016; 38: 226–230.
43. Edelweiss M and Malpica A. Dermatofibrosarcoma protuberans of the vulva: a clinicopathologic and immunohistochemical study of 13 cases. *Am J Surg Pathol* 2010; 34: 393–400.
 44. Bernardez C, Machan S, Molina-Ruiz AM, et al. Dermatofibrosarcoma Protuberans of the Vulva With Myoid Differentiation. *Am J Dermatopathol* 2015; 37: e107–e111.
 45. Djilas-Ivanovic D, Prvulovic N, Bogdanovic-Stojanovic D, et al. Dermatofibrosarcoma protuberans of the breast: mammographic, ultrasound, MRI and MRS features. *Arch Gynecol Obstet* 2009; 280: 827–830.
 46. Hakozaki M, Yamada H, Hasegawa O, et al. Radiologic-Pathologic Correlations of Fibrosarcomatous Dermatofibrosarcoma Protuberans With Various Histological Features on Enhanced MRI and PET/MRI. *Clin Nucl Med* 2016; 41: 241–243.
 47. Korkmaz V, Kurdoglu Z, Karadag B, et al. A rare case of leiomyosarcoma localized in the Bartholin's gland area and review of the literature. *J Obstet Gynaecol Res* 2016; 42: 589–592.
 48. Heller DS. Benign Tumors and Tumor-like Lesions of the Vulva. *Clin Obstet Gynecol* 2015; 58: 526–535.
 49. Chokoeva AA, Tchernev G, Cardoso JC, et al. Vulvar sarcomas: Short guideline for histopathological recognition and clinical management. Part 1. *Int J Immunopathol Pharmacol* 2015; 28: 168–177.
 50. McKenzie M, Pintilie H, Wilkinson N, et al. A rare case of vulval leiomyosarcoma: management and an updated review of the literature. *J Obstet Gynaecol* 2011; 31: 675–676.
 51. Fields KR and Neinstein LS. Uterine myomas in adolescents: case reports and a review of the literature. *J Pediatr Adolesc Gynecol* 1996; 9: 195–198.
 52. Buttram VC Jr. and Reiter RC. Uterine leiomyomata: etiology, symptomatology, and management. *Fertil Steril* 1981; 36: 433–445.
 53. Tropeano G, Amoroso S and Scambia G. Non-surgical management of uterine fibroids. *Hum Reprod Update* 2008; 14: 259–274.
 54. Hodgins MB, Spike RC, Mackie RM, et al. An immunohistochemical study of androgen, oestrogen and progesterone receptors in the vulva and vagina. *Br J Obstet Gynaecol* 1998; 105: 216–222.