Tokai J Exp Clin Med., Vol. 27, No. 3, pp.57-64, 2002

Myxoid Leiomyoma of the Vulva: A Case Report

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(Received May 16, 2002; Accepted July 11, 2002)

A case of myxoid leiomyoma of the vulva in a 29-year-old pregnant woman was encountered. The leiomyoma was a well-circumscribed solitary mass measuring 4 × 4 × 4.5 cm and, microscopically, composed of spindle-shaped cells and an abundant matrix characterized by a myxoid change. These spindle-shaped cells were arranged in a plexiform pattern. The cytological findings on the aspiration biopsy and the histological features were well correlated. Review of the reported smooth muscle tumors of vulval origin indicates that the myxoid change occurs invariably in younger women and, in some cases, association with pregnancy is suggested.

Key words : Vulva, Leiomyoma, Myxoid change, Pregnancy

INTRODUCTION

Smooth muscle tumors (SMMTs) of the vulva are uncommon. To the best of our knowledge, only 114 SMMTs have been reported [1-18]. As in skin elsewhere, most SMMTs in the vulva are thought to be derived either from the smooth muscle of the blood vessel walls, or from the arrector pili muscle [19]. Based on the literature review, the detailed clinical and pathological features of 36 SMMTs [7, 8, 17, 19], including our own two cases, provide a sufficient basis for discussion. Of those, 75 % (27/36) were typical leiomyomas. The remaining were 4 cases of atypical leiomyomas and 5 cases of leiomyosarcomas. The myxoid change in SMMTs of the vulva was shown to occur at the frequency of 36.1 % (13/36), and exclusively in younger women of 17 to 35 years of age. Nine (69.2 %) of the 13 cases with a characteristic myxoid change were pregnant. Thus, SMMTs of the vulva are clinicopathologically different from those arising in the uterus and skin elsewhere.

CLINICAL SUMMARY

A 29-year-old female was found to have a painless mass in the right labia majora of the vulva when she consulted the obstetric outpatient clinic at Isehara Kyoudo Hospital for a periodic health check for pregnancy at the gestational age of 4 weeks. Before becoming pregnant, she had noticed the mass. Ultrasonography indicated a hypoechoic feature with a well circumscribed margin (Fig. 1a, b). The aspiration cytology on the mass showed that spindle-shaped cells were accompanied by a myxoid change (Fig. 2). Under the diagnosis of probable leiomyoma, the mass was excised. After the excision the patient gave parturition to a baby by normal transvaginal delivery and has had an uneventful clinical course, without a recurrence.

PATHOLOGICAL FINDINGS

The tissue removed for light microscopy

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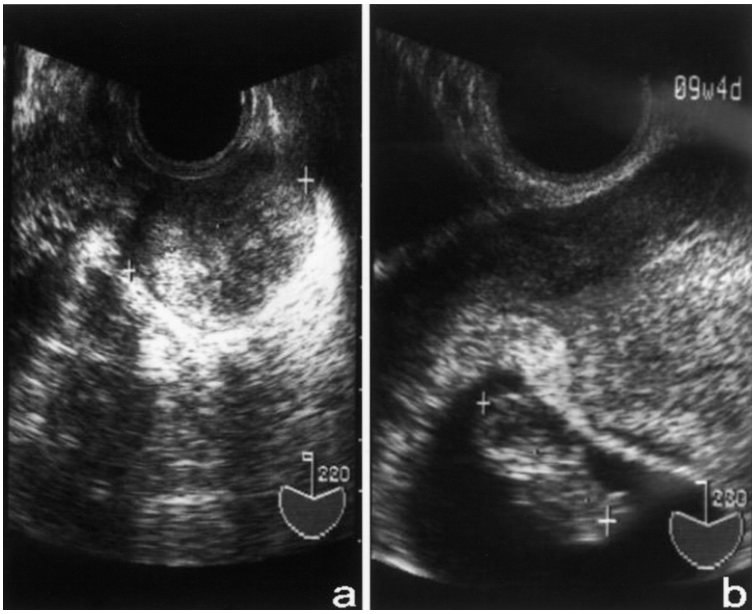

Fig. 1 Ultrasonography
(a) A hypoechoic solid mass with a well-circumscribed margin in the vulva and (b) a fetus in the first trimester.

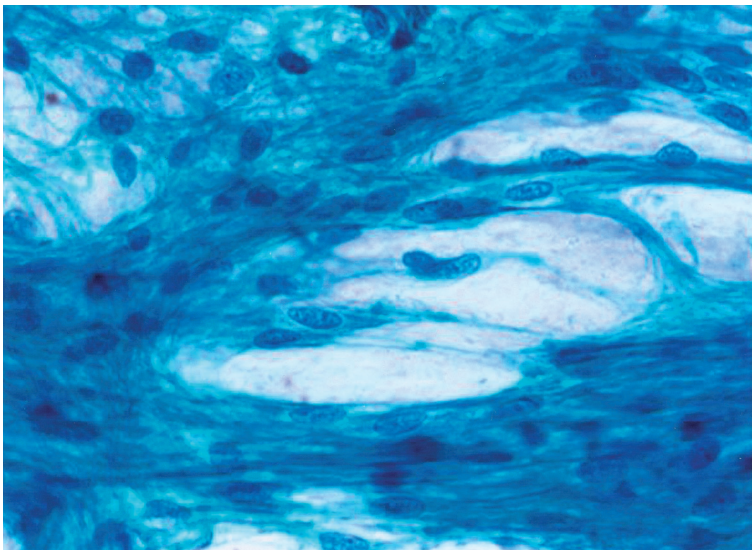

Fig. 2 Cytology
A cluster of tumor cells with ovoid to spindle-shaped nuclei by Papanicolaou's staining of an aspiration biopsy.

was subjected to routine histological procedures: fixation in 10 % neutral-buffered formalin, paraffin-embedding and hematoxylin and eosin staining. Immunohistochemical examinations were carried out using the streptavidin-biotin-peroxidase method. The antibodies used are shown in Table 1.

The excised mass measured 4.0 × 4.0 × 4.5 cm. The cut surface had a thin capsule, was uniformly pale-yellow in color, and appeared lobulated (Fig. 3). There were no necrotic or hemorrhagic changes in the mass. Microscopically, the mass consisted of cellular clusters and an abundant myxoid matrix (Fig. 4a). The proliferating tumor cells possessed ovoid to spindle-shaped nuclei,

Table 1 Antibodies used

Antibody to	Clone	Source	Dilution	Second antibody	Pre-treatment
Cytokeratin	Z622	Dako	× 200	Rabbit	proteinase
Vimentin	M0725	Dako	× 100	Envision	boiling
Desmin	M761	Dako	× 200	Envision	–
SMA	1A4	Sigma Chemical	× 800	Mouse	–
S-100	Z0311	Dako	× 200	Rabbit	–
ER	M7047	Dako	× 40	Mouse	boiling
PgR	328N	Bio Genex	× 20	Mouse	boiling
Ki-67	MIB-1	Dako	× 50	Envision	boiling

SMA: smooth muscle actine
ER: estrogen receptor
PgR: progesterone receptor

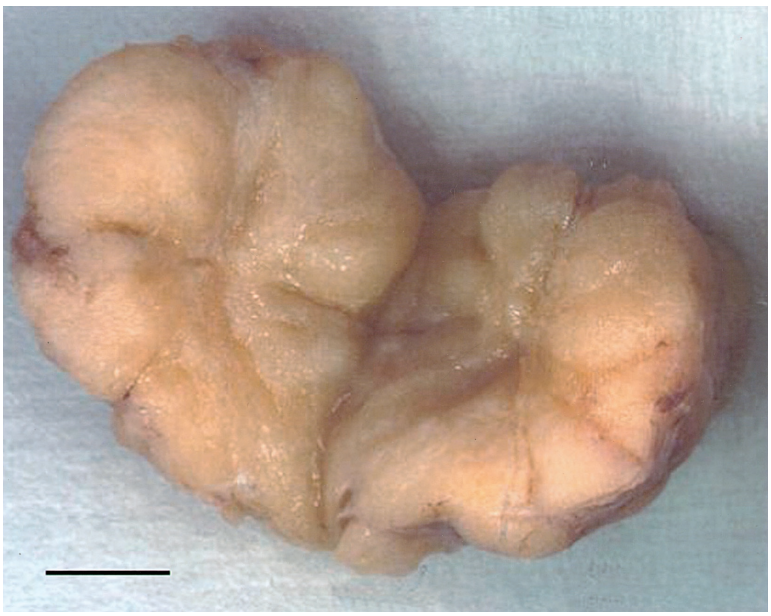

Fig. 3 Gross findings
The uniformly pale-yellow cut surface appearing lobulated with a thin capsule.

unclear cell membrane, and were arranged in a plexiform pattern (Fig. 4b). Nuclear pleomorphism was mild. Mitotic figures were rarely seen.

Immunohistochemically, the tumor cells were stained positive for desmin (Fig. 5a), smooth muscle actin (Fig. 5b) and vimentin, but negative for cytokeratin, CA125 and S-100 protein. Both ER and PgR were also negative for the nuclei. The MIB-1 (Ki-67 antigen) labeling index was less than 1 %. On the special stainings, the myxoid matrix was positive for alcian blue at pH2.5, (Fig. 6a) and high iron diamine (HID), but negative for PAS (Fig. 6b). The staining profiles demonstrated that the myxoid matrix contained a large amount of acid mucopolysaccharides.

DISCUSSION

SMMTs of the vulva are uncommon. According to the review by Stout with 95 solitary cutaneous leiomyomas, 4.2 % (4/95) were located at the vulva [19]. Reidel described only one leiomyoma (0.07 %) in the review of 144 vulval tumors [20]. Table 2 summarizes the 18 publications that we reviewed concern-

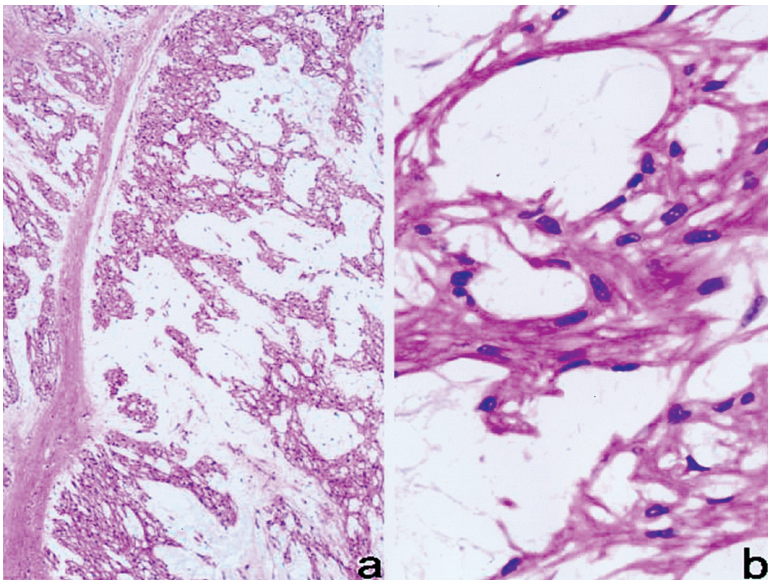

Fig. 4 Microscopic findings
(a) Clustered tumor cells accompanied by an abundant myxoid matrix and (b) a plexiform pattern of tumor cells possessing mildly atypical nuclei.

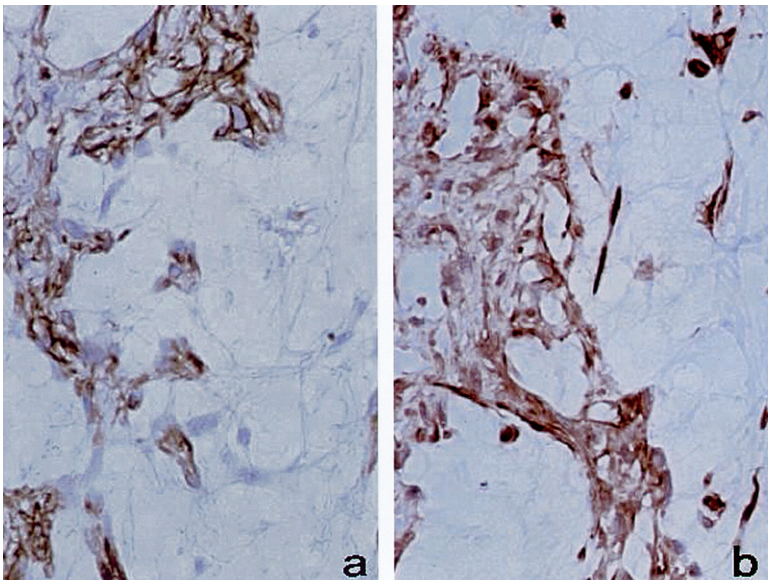

Fig. 5 Immunohistochemistry
Tumor cells clearly labeled for (a) desmin and (b) smooth muscle actin.

ing SMMTs of the vulva. Of a total of 114 reported SMMTs [1–18], 36 cases were chosen [7, 8, 17, 18], including our own two cases, and the clinical and pathological information was described in detail (Table 3: 17 to 71 years of age, mean 37 years). Regarding these 36 cases, 36.1 % (13/36) were shown to have the myxoid matrix. Interestingly, Newman *et al.* noted that myxoid or hyalinizing changes were more common in SMMTs of the vulva than in those that occurred elsewhere in the external genitalia [16]. In general, the secondary degeneration of tumors is closely related with the size. However,

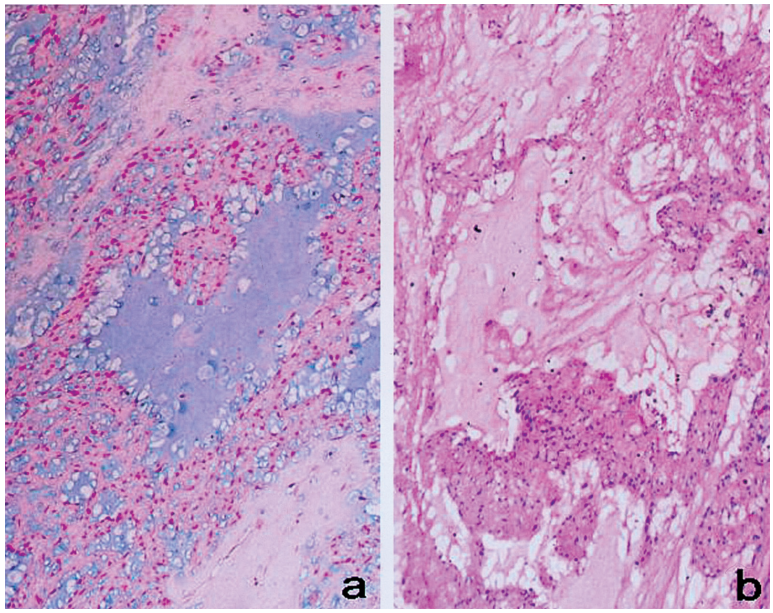

Fig. 6 Mucous stainings
The myxoid matrix positive for (a) alcian blue at pH2.5, and negative for (b) PAS, indicating a deposit of acid mucopolysaccharides.

the myxoid change in vulval SMMTs is not considered to be related to tumor size but to the age of the patient (17 to 35 years of age, mean 26 years). As evident in the profiles of the 13 cases with myxoid change shown in Table 4, nine patients (69.2 %) were pregnant. It should be emphasized that although the myxoid change was closely associated with the age of occurrence, the relationship between the myxoid change and pregnancy remains to be clarified. It is unclear whether any specific hormonal alterations that occur during pregnancy play an important role in the development of the myxoid change in SMMTs of the vulva.

Immunohistochemically, ER and PgR were expressed in 73.7 % (14/19) and 85.0 % (17/20) of SMMTs of the vulva, respectively (Table 3). No significant difference was apparent between them. Because of the evidence that mitotic activity increases in leiomyomas in the secretory phase of the menstrual cycle [22], Kawaguchi *et al*. speculated that leiomyomas of the uterus have a high growth activity under the hormonal milieu of high progesterone levels. In addition, in the uterine leiomyomas, ER expression was observed throughout the menstrual cycle, but was suppressed during pregnancy, whereas PgR was expressed throughout the menstrual cycle and pregnancy [22]. Regarding our present case, the leiomyoma of the vulva with myxoid change was negative for ER and PgR. The other two pregnant cases were positive and negative for ER and PgR, respectively (Table 3: no. 5, 21). The profiles of these 3 cases suggest that unlike in leiomyomas of the uterus, not only ER expression but also PgR expression are suppressed in SMMTs of the vulva.

Like SMMTs of the uterus, the major diagnostic problem with SMMTs of the vulva is the distinction between benign and malignant forms. It should be noted that 25 % (9/36) of SMMTs of the vulva were atypical leiomyomas (4 cases) and leiomyosarcomas (5 cases). In comparison with patients younger than 40 years and those of 40 years or older, there is no significant difference in the frequency of leiomyosarcomas; 10.5 % (2/19) for the former and 17.6 % (3/17) for the latter. It remains to be defined whether the criteria of the pathological grading used for SMMTs of the uterus are applicable to those arising elsewhere in the female genital tract. Gunnlauger *et al*. proposed that the most common findings in SMMTs of the vulva that recurred, metastasized or both, include a diameter of 5 cm

Table 2 Case reports of vulval SMMTs

Year	Author	No. of cases	Age	Size (cm)	Characteristic pathological findings (No. of cases)	Ref.
1940	Folsome	9	–	0.5–huge	sarcomatous change (1)	1
1941	Lovelady	2	–	6 × 3.5 × 3.5; 4		2
1964	Palermino	1	43	5	focal hemorrhage	3
1965	Kaufman	2	13; 35	8–9, 2.5	cellular leiomyoma (2)	4
1965	Wahlen	2	21; 59	pigeon egg size hazelnut size	hyalinization (1)	5
1973	Schapiro	2	23; 24			6
1979	Tavassoli	32	18–66 (median 35)	1.4–7	myxoid change (10) pregnancy (7)	7
1980	Katenkamp	1	71	1.5	fibroma-like	8
1982	Aneiros	1	26	4.5 × 3 × 3	epithelioid leiomyoma	9
1984	Smit	1	74	2 × 2 × 3		10
1986	Goto	1	44	3 × 3	cellular leiomyoma	11
1987	Yokoyama	13			hyalinization (10)	12
1988	Zaltkov	1	48	15		13
1989	Ienaga	1	29	goose egg size		14
1991	Faber	1	20	12 × 6		15
1991	Newman	18	23–66 (mean 41)	0.8–5 (mean 3.2)	myxoid change (3) hyalinization (8)	16
1995	John	1	44	6 × 4 × 3.5		17
1996	Gunnlauger	25	17–63	1.5–16	myxoid change (5) pregnancy (2)	18

SMMT: smooth muscle tumor

or greater, an infiltrative margin, a mitotic count of 5 or more per 10 HPFs, and grade 2 to 3 nuclear atypia [18]. We are aware that benign SMMTs have the potential to recur after a long interval, as shown in 2 cases in Table 4.

In summary, the vulval leiomyoma characterized by a distinct myxoid change, which arose in the pregnant woman, was discussed with the literature review.

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Table 3 Summary of vulval SMMTs

case no.	Age	Size (cm)	Cell types	Myxoid change	Keratin	Vimentin	Desmin	SMA	S-100	ER	PgR	Pregnancy	Diagnosis	Ref.
1	17	5	e	○	ND	ND	−	++	ND	ND	ND		L	18
2	17	3	s		ND	ND	ND	ND	ND	ND	ND		L	18
3	19	4	e	○	−	++	+	+++	−	−	+		L	18
4	19	6.5	s		−	+++	+++	+++	−	+	+		AL	18
5	20	2.8	s	○	−	+++	+++	+++	−	+	+	○	AL	18
6	20	3	e	○	ND	ND	−	+++	ND	ND	ND		L	18
7	24	−	e		ND	ND	ND	ND	ND	ND	ND		L	18
8	24	1.5	s	○	ND	ND	ND	ND	ND	ND	ND	○	L	7
9	25	3	s	○	ND	ND	ND	ND	ND	ND	ND	○	L	7
10	26	3	e		−	++	+	+++	−	−	+		L	18
11	26	1.5	s	○	ND	ND	ND	ND	ND	ND	ND	○	L	7
12	28	4.5	s	○	ND	ND	ND	ND	ND	ND	ND	○	L	7
☆ 13	29	3	s	○	−	+++	+++	+++	−	−	−	○	L	
14	30	11.5	s	○	ND	ND	ND	ND	ND	ND	ND	○	L	7
15	31	4	s	○	ND	ND	ND	ND	ND	ND	ND	○	L	7
16	33	5.5	s	○	−	+++	+++	+++	−	+	+		LS	18
17	34	3	s		ND	ND	ND	ND	ND	ND	ND		L	18
18	35	6	s	○	ND	ND	ND	ND	ND	ND	ND	○	L	7
19	37	5	s		−	+++	+++	+	−	+	+		LS	18
* 20	40	2	s		−	+++	+++	+++	−	+	+		L	
21	40	8	s		−	+++	+	+++	−	−	−	○	AL	18
22	40	−	m		ND	ND	++	ND	ND	ND	ND		L	18
23	41	4	m		−	+++	++	+++	−	UC	+		L	18
24	42	3	m		ND	ND	+++	ND	−	ND	ND		L	18
25	43	1.8	s		−	+++	+++	+	−	+	+		L	18
26	44	6	s		ND	ND	ND	ND	ND	ND	ND		L	17
27	45	11.7	s		−	+++	+++	+++	−	+	+		L	18
28	45	4	e		−	++	++	+++	−	+	+		L	18
29	46	10	s		−	+++	+	+++	−	+	+		LS	18
30	47	1.5	s		−	+++	+++	+++	−	+	+		L	18
31	47	1.6	e		−	+++	++	+++	−	+	+		L	18
32	52	4.5	s		−	−	−	+++	−	+	+		L	18
33	56	5.5	m		−	+++	−	+	−	−	−		LS	18
34	63	6	s		−	+++	+++	+++	−	+	+		AL	18
35	67	16	s		−	+++	−	+	−	+	+		LS	18
36	71	−	s		ND	ND	ND	ND	ND	ND	ND		L	8

☆ The present case, * Our previous case
Cell types: s, spindle; m, mixed; e, epithelioid
Evaluation of immunohistochemistry: −, negative; +, < 25% ; ++, 25-50% ; +++, > 50%
ND, not done; UC, unclear
Diagnosis according to criteria by Nielsen [18]: L, typical leiomyoma; AL, atypical leiomyoma; LS, leiomyosarcoma

Table 4 Vulval SMMTs with myxoid change

*	Age	Size (cm)	Cell types	Mitotic figures (/10HPF)	Atypia	Pregnancy	Diagnosis	Outcome
1	17	5	e	0	1 +		L	unknown
3	19	4	e	0	2 +		L	no recurrence
5	20	2.8	s	2	3 +	○	AL	no recurrence
6	20	3	e	0	1 +		L	recurrence after 10 years
8	24	1.5	s	0	1 +	○	L	no recurrence
9	25	3	s	0	1 +	○	L	unknown
11	26	1.5	s	2	1 +	○	L	no recurrence
12	28	4.5	s	2	1 +	○	L	no recurrence
13	29	3	s	0	1 +	○	L	no recurrence
14	30	11.5	s	0	1 +	○	L	recurrence after 6 years
15	31	4	s	1	1 +	○	L	unknowna
16	33	5.5	s	1	3 +		LS	recurrence after 4 months
18	35	6	s	1	1 +	○	L	unknown

* Case No. in Table 3
Cell types: s, spindle; e, epithelioid
Atypia: 1 +, mild; 2 +, moderate; 3 +, severe
Diagnosis, according to criteria by Nielsen [18]: L, typical leiomyoma; AL, atypical leiomyoma; LS, leiomyosarcoma

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