Stromomyomas of the uterus - importance of total circumferential evaluation of the margin

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Summary

Four stromomyomas were extensively dissected to represent the entire circumference of the uterus on sequential histologic sections. In all cases the smooth muscle component was extensive, and irregular interdigitation of stromal neoplasia with a smooth muscle component made evaluation of the margin difficult. It was impossible to determine where the smooth muscle component of the neoplasm ended and where peritumoral normal myometrium began. This makes the detection of vascular invasion more important. At the end of a thorough evaluation of sections, large vessel invasion was found on the circumference of three stromomyomas in a particular foci of the margin. Extensive circumferential evaluation of the margin has been evaluated as a promising procedure to allow effective distinction of stromomyomas with focal angioinvasion.

Key words: Uterus; Endometrial stromal tumors; Stromomyoma.

Introduction

Endometrial stromal tumor (EST) is rarely encountered and can be benign or malignant. Benign endometrial stromal tumors are called stromal nodules (SN). They are circumscribed, expansile and do not invade the myometrium [1] and they represent less than a quarter of EST [2, 3]. Low-grade endometrial stromal sarcoma (ESS) is the most common endometrial stromal neoplasm [4]. Distinction between SN and ESS depends on the nature of the margin and presence or absence of tumor in the uterine vascular spaces [4]. The generally accepted criterion is that SN has a margin that is either completely circumscribed or exhibits only minimal infiltration, arbitrarily defined in large case series of SNs as one to three protrusions with no more than 3 mm of myometrial penetration [5]. Dionigi *et al.* [6] reported that occasional tumors lack the typical permeable infiltration of an ESS and yet have > 3 mm of myometrial penetration. Rarely the infiltration is the permeable type but is so tiny as to make one wonder whether the neoplasm is likely to be other than benign. They proposed the term "endometrial stromal tumor with limited infiltration" (ESTLI) for these problematic cases.

It is common to see unequivocal smooth muscle elements (smooth muscle metaplasia) within EST [7]. Norris *et al.* defined "stromomyomas" as tumors containing stromal and smooth muscle cells where the lesser of the two elements made up at least 30% of the neoplasm [5]. Although the existence of such tumors is acknowledged in the World Health Organization classification of uterine tumors [8], the literature concerning this tumor is restricted to sporadic case reports or small series [6, 7, 9-16]. In some cases irregular interdigitation of stromal neoplasias with metaplastic smooth muscle at the margin of the tumor may erroneously suggest myometrial infiltration [6].

Therefore it is extremely important to sample the tumor margin extensively and search carefully for vascular invasion. Demonstration of vascular invasion is more important particularly in stromomyomas and ESTLI. Nevertheless, the extent and method of histopatologic examination of the margin necessary for reliable distinction is unenlighted. Therefore development of a thorough and complete examination method seems worthwhile. The present study was devised to introduce a new technique for extensive dissection of the entire margin area to more frequently aid the detection of vascular invasion.

Material & Method

Surgical specimens of uterine tumors obtained at Zeynep Kamil Maternity Hospital that had a diagnosis of stromomyoma (over the past three years) were evaluated. Preliminary diagnosis of EST was obtained either by evaluation of the curettage specimen or intraoperative frozen specimen. Three patients underwent total abdominal hysterectomy with bilateral salpingo-oophorectomy (TAH&BSO), and the remainder had local excision. The uterus was opened along the lateral margins from the external os to the origin of the fallopian tubes. A vertical cut through the tumor bulk and uterine wall was performed. Dissection was carried out after overnight formalin fixation. All cases were dissected circumferentially to examine the margins of the neoplasm *in toto* using the technique which is also used for dissection of follicular neoplasms of the thyroid [17]. In the process of dissection, peritumoral tissue beyond its invasive edges was trimmed off from the specimen, preserving a signifigant amount of paraneoplastic myometrial tissue. Then, the lesion was bisected in the midcenter and its diameter was measured. The remaining two pieces of dome-shaped tumors were

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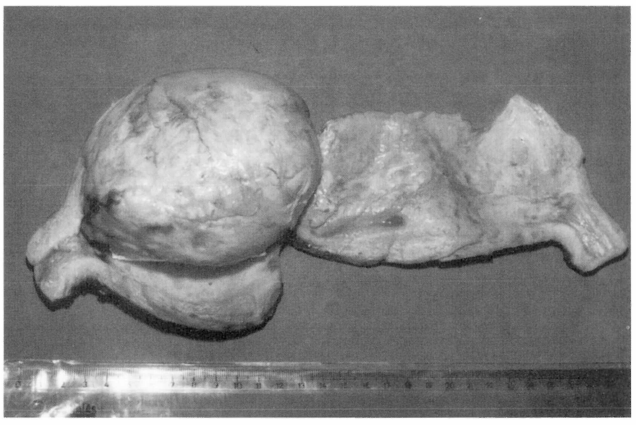
Fig. 1



Fig

Fig. 3

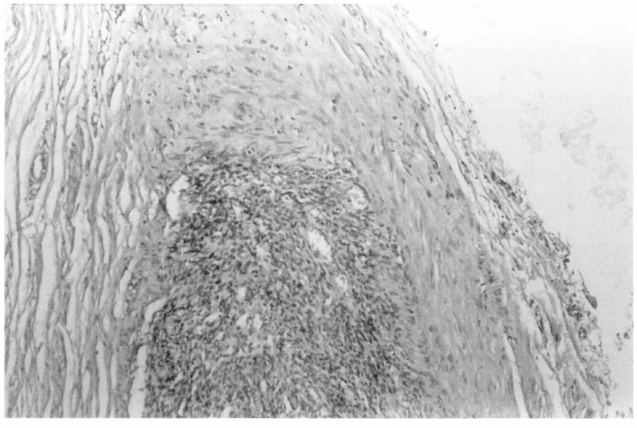


Figure 1. — All cases were dissected circumferentially to examine the margins of the neoplasm *in toto.*
Figure 2. — Two lesions were "typical leiomyomas" composed of white, firm, whorled tissue.
Figure 3. — Thick-walled vascular invasion in a particular portion of the margin.

placed with the cut surface on the cutting board with the maximum diameter of the specimen.

Incisions were made from the paraneoplastic tissue plane toward but not completely up to the line. After the entire dome had been incised in intervals of approximately 3 mm in the margin plane (Figure 1), the incisions were advanced completely to produce serial slices of the tumor. Only for margins of the tumor was careful attension paid to the subsequent process of paraffin embedding and sectioning. Therefore the tumor part was trimmed to minimize the number of paraffin blocks. All the sequential blocks of the entire margin were prepared to cut the largest section of each to represent the circumference of the tumor in the histologic section. We examined 32 to 64 (average 47) hematoxylin and eosin (H&E) stained slides showing the margins per case.

During the examination in all H&E-stained sections extent and number of sites where myometrial or vascular invasion was evident were recorded.

Results

Patient age ranged from 21 to 43 years (mean 36 years). Dysfunctional uterine bleeding was the presenting complaint and an enlarged uterus was detected in all women. Three patients underwent TAH & BSO and one had a local excision.

The tumors ranged from 4 to 13 cm in maximum dimension. All were submucosal or intramural and well circumscribed. The cut surfaces of two tumors were multinodular with a few tannish-yellow soft nodules, alternating with firm, white, whorled nodules embedded in a more pale, firmer tissue. The other two were "typical leiomyomas" composed of white, firm, whorled tissue (Figure 2). No cystic degeneration or necrosis was noted. The excised tumor was 6 cm in the greatest dimension with a signifigant amount of surrounding normal myometrial tissue.

The smooth muscle component predominated in all cases. The endometrial stromal component was characterized by a diffuse growth of closely packed small cells with inconspicous cytoplasm that enveloped numerous uniform arterioles. There was minimal cytologic atypia, and the mitotic rate varied from 0 to 2 mitotic figures per 10 high-power fields. In all tumors there was an abrupt transition from the endometrial stromal to the smooth muscle component. In areas of smooth muscle differentiation the cells were elongated and usually had abundent, eosinophylic cytoplasm, elongated nuclei with small nucleoli and minimal cytologic atypia. The mitotic rate varied from 0 to 3 mitotic figures per 10 high power fields. In all cases smooth muscle components of the tumor were also extensive at the periphery of the tumor. Determination of where the smooth muscle component ended and where the surrounding normal myometrium began was difficult. Appreciation of where the "true margin" was and whether focal and limited extensions of the endometrial stromal component was greater or less

than 3 mm was not possible. Only in one case was extensive myometrial invasion noted up to 1 cm beyond the estimated margin of the tumor. Among these four circumferentially dissected cases, three showed 3 to 5 foci of thick-walled vascular invasion per case, which were noted in a particular portion of the margin (Figure 3). These three cases were diagnosed as ESS. The fourth one showed minor irregularity of the margin but no vascular invasion, so the diagnosis was SN. Selected features of cases are summarized in Table 1.

Table 1. — *Selected features of cases.*

Case	Age	Treatment	Groos circumscription	Maximum diameter (cm)	Slides showing margins	Slides with irregular margins	Slides with vascular invasion
1	21	Excision	WC	6	43	8	2
2	34	TAH & BSO	WC	9	52	14	5
3	42	TAH & BSO	WC	13	64	4	4
4	47	TAH & BSO	WC	4	32	3	0

WC: Well circumscribed.

Discussion

In stromomyomas interdigitation of stromal neoplasms with a smooth muscle component may erroneously suggest myometrial infiltration [6]. Also in cases which are proposed as ESTLI by Dionigi *et al.* [6], evaluation of the tumor margin is problematic. Obviously in these cases and in stromomyomas detection of vascular invasion is more important and thorough sampling of margins is mandatory, however the question of what constitutes adequate sampling of stromomyomas and problematic stromal neoplasms has remained unanswered.

In Oliva *et al.*'s [7] publication reporting 15 cases of stromomyomas, 12 were from consultation files and the number of reviewed slides was limited. Two to 33 (average 11) H&E-stained slides were examined in each case. Microscopic evaluation disclosed that nine tumors were well circumscribed and six had infiltrating borders. No vascular invasion was detected. One tumor with infiltrating borders metastasized. Follow-up duration was from five to 156 months (mean, 47 months).

Yilmaz *et al.* [16] reported 24 ESSs in 12 patients. Ten were primary uterine ESSs with unusual histologic features including three with smooth muscle differentiation and one had metastasized to the lung. They examined an average of 17 slides per tumor. Seven tumors infiltrated the myometrium; one tumor had an indistinct interface with myometrium and only one showed both myometrial and vascular invasion.

In Dionigi *et al.'s* [6] series from four to 51 (average nine) H&E-stained slides showing margins belonging to seven ESTLI's were reviewed. No vascular invasion was detected. When four slides were examined per case, in two to three slides, margins were irregular with 1-2 mm of maximum infiltration. Of the 51 reviewed slides, six slides with irregular margins were seen with 5 mm maximum infiltration.

Chang *et al.* [17] studied 117 ESTs of which 109 were ESSs. They reviewed an average of six HE sections per case. The interface of the neoplasm with surrounding myometrium was assessed for the presence of myoinvasion or angioinvasion; 54% of ESS cases demonstrated intravascular growth.

Among our four cases dissected circumferentially, three stromomyomas showed thick-walled vascular invasion with two to five foci of invasion per case at a particular area of the margin. We examined 32 to 64 (average 47) H&E-stained slides showing margins per case.

It is obvious that vascular invasion appeared to be of greater importance for diagnosis than myometrial invasion in stromomyomas and ESTLI. Although we examined only four cases, we propose that an increase in the number of sections showing margins is associated with an increased chance of identifying foci of vascular invasion within the margins of the ESTs.

This conclusion supports the view that the more sections examined, the higher the chance of finding ESS. However, no correlation about the specific number of blocks can be drawn based on the results of this study even with nearly complete total dissection of the margin. More important in stromomyomas was the detection of vascular invasion at a particular area of the margin.

In conclusion, in view of our findings obtained through a complete evaluation of the margins, ESTLI and ESS with extensive smooth muscle components – causing difficulty in evaluation of the margin and questionable vascular invasion necessitating immunohistochemical identification of vascular endothelial components – are indicators that an extensive, even complete, examination of tumor margin is necessary until conclusive invasion is detected.

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