Gynecologic Oncology Reports 11 (2015) 13–15

Contents lists available at ScienceDirect

Gynecologic Oncology Reports

journal homepage: www.elsevier.com/locate/gore

Endometrial stromal nodule of the vaginal wall with a review of vulvovaginal endometrial stromal neoplasms

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ARTICLE INFO

Article history:
Received 14 September 2014
Accepted 11 November 2014
Available online 20 November 2014

Keywords:
Endometrial stromal tumors
Endometrial stromal nodule
Vagina
Vulva

Introduction

Endometrial stromal tumors (ESTs) are usually found in both uterus and ovary. Histologically, they can exhibit a wide range of differentiations (Chew and Oliva, 2010), and their malignant potential is often defined by their mitotic activity and presence of invasive borders and eventual lymphovascular invasion. Low grade sarcomas represent the more frequent types, while benign endometrial stromal nodules (ESNs), which are non-invasive, are less common (Chew and Oliva, 2010).

We have done a systematic review on PubMed with the key words "extrauterine endometrial stromal tumor"; 77 results were found and 15 were selected (4 of them are included in our references), we also read 11 articles regarding other extrauterine locations. Indeed extrauterine locations are also rare but not exceptional (Chang et al., 1993) with most cases originating in endometriotic foci. Thus, primary cases have been reported in the colon (Chen et al., 2007), the rectovaginal septum (Bosincu et al., 2001), and even implanted in the placenta of a newborn (Karpf et al., 2007). Vulvovaginal involvement is much more exceptional and there is not any article that summarizes them. This is the reason why we made the revision of the cases reported on this localization. We made searches with "vulvovaginal endometrial stromal tumor/sarcoma/nodule", "vaginal endometrial stromal tumor/sarcoma/nodule" and "vulvar endometrial stromal tumor/sarcoma/nodule" and we only found ten reported cases of sarcomas in the vagina and two in the vulva (Androulaki et al., 2007; Berkowitz et al., 1978; Corpa et al., 2004; Irvin et al., 1998; Kondi-Paphitis et al., 1998; Liu et al., 2013; Masand et al., 2013), half of them being metastases from other sites. Bibliographical analysis demonstrated various types of endometrial stromal sarcoma, often associated to endometriosis, but no cases of stromal nodules like the one we are submitting.

This paper reports, for the first time, the occurrence of an asymptomatic, non-recurring, polypoid primary endometrial stromal nodule (ESN) in the vagina of a 47 year-old female that was not associated with endometriosis and that was successfully treated by local resection. We also review the available cases of vulvovaginal ESTs.

Case report

A 47-year-old nulliparous patient, with an otherwise unexceptional gynecological history, consulted for a sensation of foreign body in the vagina. On clinical examination the vulva was unremarkable and a polypoid, pediculated mass of approximately 2 cm on the posterior aspect of the vagina, practically at the introitus was found. The rest of the female genital tract was unexceptional. The nodule was completely resected. No other lesions were detected in either vagina or vulva. Hysteroscopy and abdomino–pelvic MRI performed after resection were normal. Ca125 serum levels were within normal range. The patient has been followed regularly for a period of six years without recurrence.

Pathology

On gross examination, the 2 cm round, white yellow mass was homogeneous and elastic. Microscopically the vaginal epithelium lined surrounded the external circumference of the nodule which enclosed a homogeneous proliferation of endometrial stromal-type cells that had clear-cut lineal borders. No invasion of the pedicle or any surrounding vessels (Fig. 1A) was seen. Cells without atypia and lacking mitoses grew in diffuse sheets and had abundant collagen tracts and extensive hyalinization of perivascular distribution (Fig. 1B). Minor foci of calcification and foamy macrophages were present. Immunohistochemistry confirmed the endometrial stromal nature of the tumor by its

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http://dx.doi.org/10.1016/j.gore.2014.11.003

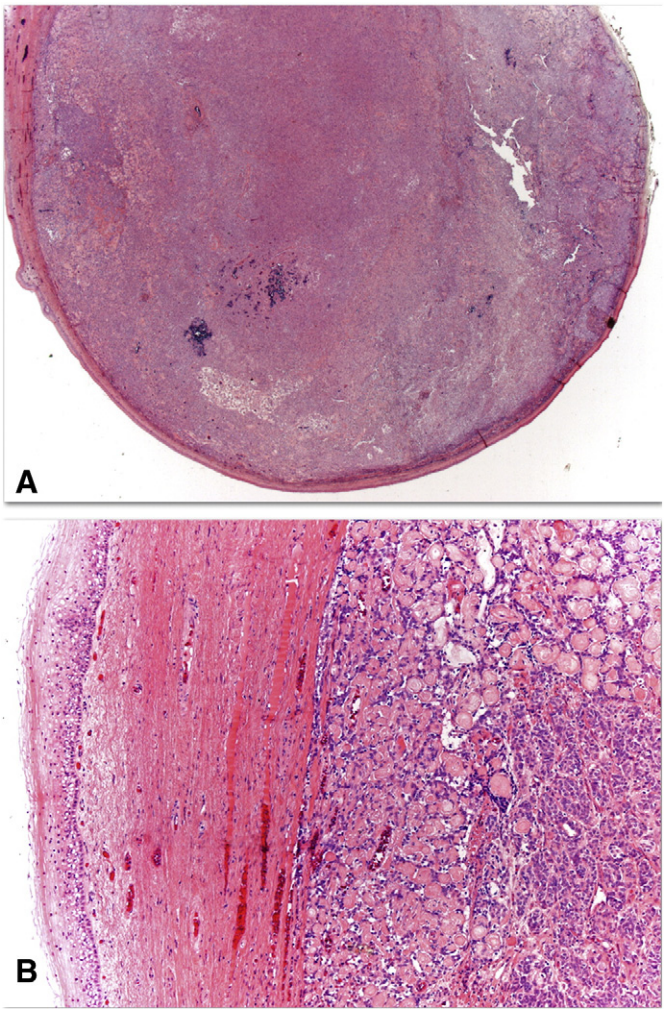

Fig. 1. Homogeneous stromal nodule surrounded by thin capsule and lined by vaginal squamous epithelium (A). Higher magnification (B) shows clear-cut lineal borders and a cellularity with fibrous tracts and perivascular sclerosis. H&E.

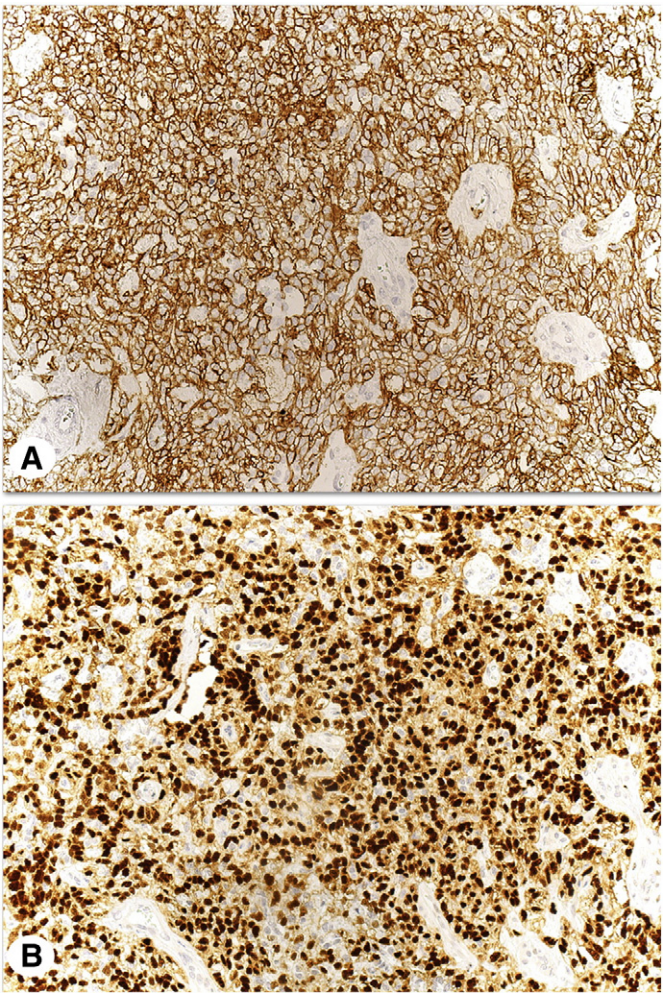

Fig. 2. Immunohistochemistry of stromal nodule showing marked co-expression of membranous CD10 (A) and nuclear progesterone receptors (B).

conspicuous coexpression of CD10 and estrogen and progesterone receptors (Fig. 2A–B). Smooth muscle markers such as h-caldesmon and desmin were negative.

Discussion

We report a case of an endometrial stromal nodule in the vagina in a premenopausal patient. Our case is unique, since no instances of this variant of EST, a benign endometrial stromal lesion, have been previously reported outside the uterus. Histologically, ESNs have lineal, smooth, pushing margins, minimal atypia or mitoses and often present a yellow color; possibly due to the presence of foamy macrophages. Characteristically they are non-invasive and do not permeate the capsule or adjacent vessels. The present case exemplifies such a lesion in a highly unusual location. Its benign nature is confirmed by the absence of local recurrence after a long follow-up. However, it must be borne in mind that some ESSs may experience very late recurrences (Chew and Oliva, 2010).

In contrast, all cases of ESNs reported in the vulvovaginal region (Table 1) have corresponded to endometrial stromal sarcomas of various grades of differentiation. In at least five cases (Androulaki et al., 2007; Berkowitz et al., 1978; Corpa et al., 2004; Kondi-Paphitis et al., 1998; Liu et al., 2013; Masand et al., 2013) the tumors appeared to be primary neoplasms, while the remaining ones were likely to be metastatic in nature (Irvin et al., 1998; Kondi-Paphitis et al., 1998; Liu et al., 2013; Masand et al., 2013), since tumor was also found in pelvic locations, colon and lung. Association with endometriosis, locally or elsewhere, was found in 6 cases.

In the present case, a metastasis from any other site was discarded since there was no evidence of either utero–ovarian primaries. Furthermore, an origin from endometriosis is unlikely since no such areas were detected in the vicinity of the neoplasm or elsewhere. This would support the possibility of a locally originated endometrial stromal neoplasm that could represent a type of Müllerian differentiation in the vagina, an organ whose partly Müllerian origin is well known (Sanchez-Ferrer et al., 2006).

Histopathological diagnosis was relevant to the management of this case, with characterization of its endometrial stromal cellularity based on both cell morphology and coexpression of characteristic markers such as CD10, estrogen and progesterone receptors. In the differential diagnosis, the immunohistochemical absence of smooth muscle markers excluded the more commonly found leiomyoma of the vagina (Imai et al., 2008), a tumor, especially their cellular variants, that may resemble ESN. An accurate diagnosis of ESN is important since local conservative surgery is curative. Core biopsy is not indicated since the diagnostic features of a pushing, non-invasive margin cannot be diagnosed with this procedure.

Consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the

Table 1
Clinicopathological features of reported cases of endometrial stromal sarcoma of the vulvovaginal region.

	Nr	Site	ESS type	Organ involvement	Associated endometriosis
Berkowitz et al. (1978)	1	Vagina	Sarcoma NOS	−	+
Kondi-Paphitis et al. (1998)	1	Vagina	Sarcoma NOS	−	+
Corpa et al. (2004)	1	Vagina	LGESS	−	−
Liu et al. (2013)	1	Vagina	Sarcoma NOS	−	−
Masand et al. (2013)	1	Vagina	Sarcoma NOS	Pelvic	+
Masand et al. (2013)	1	Vagina	Sarcoma NOS	−	−
Masand et al. (2013)	1	Vagina	Sarcoma NOS	Pelvic	−
Masand et al. (2013)	1	Vagina	Sarcoma NOS	Metastases	NA
Masand et al. (2013)	1	Vagina	Sarcoma NOS	Colon	+
Masand et al. (2013)	1	Vagina	Sarcoma NOS	Pelvic	+
Irvin et al. (1998)	1	Vulva	Sarcoma NOS	Lung	+
Androulaki et al. (2007)	1	Vulva	LGESS	Late metastases	NA

Key: LGESS: low grade endometrial stromal sarcoma. NA: not available.

written consent is available for review by the Editor-in-Chief of this journal on request.

Conflict of interest

The authors declare that they have no conflict of interest.

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