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PRIMARY EXTRAUTERINE ENDOMETRIAL STROMAL NODULE OF THE VULVA AND VAGINA – A RARE CASE REPORT AND REVIEW OF VULVO-VAGINAL ENDOMETRIAL STROMAL TUMORS

Pathology

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ABSTRACT

Endometrial stromal tumors are rare mesenchymal tumors with a reported incidence of 2 per million women. The broad spectrum of these neoplasms include endometrial stromal nodule, low-grade and high grade endometrial stromal sarcomas and undifferentiated uterine sarcomas. These tumors have been usually reported in the uterus and ovary. Tumor invasion with infiltrative borders, high mitotic activity and lymphovascular invasion define the malignant nature of these tumors. Endometrial stromal nodules (ESN) are rare non-invasive benign tumors described mainly in the uterus of premenopausal females. Endometrial stromal sarcoma (ESS) had been reported in vulva and vagina however, no case of endometrial stromal nodule involving vulva has been reported as per our knowledge. After extensive search of literature, we found only one such case reported in vagina so far. Here we report the first case of primary endometrial stromal nodule involving the right vulva and also the vaginal wall in a 32 year old nulliparous female. Also, we are presenting a brief review of endometrial stromal tumor reported in the vulvovaginal region.

KEYWORDS

Endometrial stromal tumour, vulva, vagina.

INTRODUCTION

Endometrial stromal tumors are rare mesenchymal tumors with a reported incidence of 2 per million women. These tumors have been usually reported in the uterus and ovary.[1,2] The World Health Organization classification of tumors of the female genital organs describes the uterine stromal neoplasms into four groups: benign endometrial stromal nodule (ESN), low-grade endometrial stromal sarcoma, high grade endometrial stromal sarcoma and undifferentiated uterine sarcomas.[2] Low-grade endometrial stromal sarcomas are found to be the second most common uterine malignant mesenchymal tumour.[2] After extensive search of literature, we found cases of endometrial stromal sarcoma (ESS) in cervix[3], vulva[4], vagina[5,6] and fallopian tube.[6] Some of these were associated with endometriosis.[7] Primary extrauterine ESS had also been described in intestine, pelvic peritoneum, rectovaginal septum[7] and sigmoid colon.[8] Endometrial stromal nodules are rare benign stromal neoplasms accounting for only one fourth of the endometrial stromal tumours.[9] ESN have been described in the uterus but very few cases of extrauterine ESN have been reported so far, only one such case in the vaginal wall [10] and one embedded in placenta [11]. Primary ESN involving the vulva is much more uncommon and no such case has been described till date.

Thus, here we report the first case of an exceptionally rare entity of primary extrauterine endometrial stromal nodule involving the right vulva and the vaginal wall in a 32 year old nulliparous female with no associated endometriosis. Also, a brief review of endometrial stromal tumors reported in the vulvovaginal region has been summarized.

Case Report

A 32-year-old nulliparous female presented with the complaint of swelling in the vagina and right vulva. On physical examination, multiple nodular swellings ranging from 1 cm to 9 cm were found in the right vulva, and also involving the vagina. Left vulva and the rest of the female genital tract were unremarkable. Abdominal and vaginal ultrasonography revealed multiple lobular growths in the right vulvo-vaginal region with unremarkable uterus and ovaries. Vaginal myomectomy was done and excision of the growth was done from the ischioanal space.

On gross examination, there were multiple irregular, grey-white firm globular tissues ranging in size from 1x1x0.5 cm to 9x6x2 cm. The external surface was bosselated. The cut surface was homogenous and grey-white. Microscopic examination of multiple sections taken from all the nodules showed well circumscribed nodule composed of tumour cells closely resembling normal proliferative-phase endometrial stromal cells. The tumour cells were arranged in diffuse sheets and there was whorling of tumor cells around small uniformly distributed arterioles. These cells had scant to moderate cytoplasm, uniform, small, darkly staining, round to oval nuclei with finely granular chromatin and inconspicuous nucleoli [Figure 1(a) and (b)]. Only one mitotic figure per 10 high power fields was seen. No cellular atypia or vascular invasion was seen.

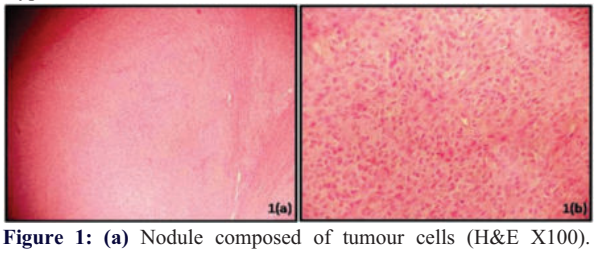

Figure 1: (a) Nodule composed of tumour cells (H&E X100). (b)Tumour cells resembling normal proliferative-phase endometrial stromal cells alongwith whorling of tumor cells around small uniformly distributed arterioles (H&E X400).

These tumour cells showed positive expression of estrogen receptor (ER) [Figure 2(a)] and progesterone receptor (PR) [Figure 2(b)]. CD10 was focally positive [Figure 2(c)]. Cytokeratin, EMA and smooth muscle actin (SMA) were negative.

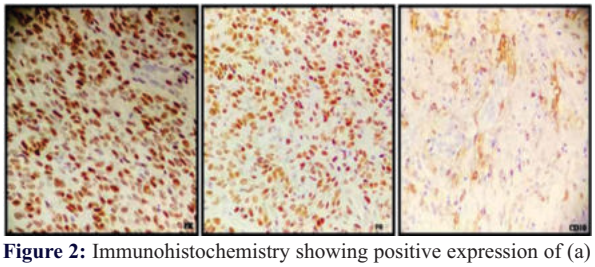

Figure 2: Immunohistochemistry showing positive expression of (a) ER (b) PR (c) CD10.

Based on the characteristic histopathological features and immunohistochemical profile, the final diagnosis of endometrial stromal nodule was rendered. Since no evidence of any primary in uterus or ovary was seen, the diagnosis of primary extrauterine endometrial stromal nodule in the vulvovaginal region was confirmed.

DISCUSSION

Endometrial stromal tumors are uncommon tumors accounting to less than 10% of all uterine malignancies.[1] Most of these cases were described in the uterus of women of age group 23 to 86 years. Almost three-fourth of the affected women were pre-menopausal, presenting with the chief complaint of abnormal uterine bleeding. Approximately in 10% of cases, this neoplasm is an incidental finding [1,2] as it was in the present case. The patient was operated for suspected fibroids.

We present a case of rare benign endometrial stromal neoplasm (endometrial stromal nodule) involving the vulvovaginal region in a premenopausal woman with no associated endometriosis. This case is unique since no case of endometrial stromal nodule in the vulva has been reported till date.

A brief review of endometrial stromal neoplasms reported in the vulva and vagina has been summarized in Table 1.

TABLE 1: Summary of reported cases of endometrial stromal tumors in the vulvo-vaginal region

No.	AUTHORS	YEAR	No. OF CASES	AGE	SITE	TYPE OF ENDOMETRIAL STROMAL NEOPLASM	IMMUNO HISTOCHEMISTRY
1	Ulbright TM et al [12]	1981	1	32y	Vagina	Endometrial stromal neoplasm	Not Done
2	Irvin et al [13]	1998	1	34y	Vulva	Sarcoma NOS	Not Done
3	Corpa et al [6]	2004	1	40y	Vagina	Low grade ESS	CD10(+),ER(+), PR(+)
4	Androulaki et al [14]	2007	1	46y	Vulva	Low grade ESS	Vimentin(+),ER(+), PR(+) Focal CD10(+)
5	Liu et al [15]	2013	1	32y	Vagina	Sarcoma NOS	CD10(+),ER(+), PR(+), Vimentin(+)
6	Masand et al [7]	2013	6	40 to 79 y	Vagina	Sarcoma NOS	ER(+),PR(+), CD10 (+)
7	Sanchez-Ferrer ML et al [16]	2014	1	47y	Vagina	Endometrial stromal nodule	CD10(+),ER(+), PR(+)
8	Zaza KJ el al [2]	2015	1	50y	Vulva	ESS	CD10(+), Vimentin(+), ER(+), PR(+)
9	Sanverdi et al [17]	2016	1	46y	Vagina	ESS	ER(+),PR(+), CD10(+), Vimentin(+)
10	Abu Jamea GA et al [17]	2017	1	58y	Vagina	Low grade ESS	CD10(+),ER(+), PR(+), Vimentin (+)
11	Tang Y et al [18]	2020	1	74y	Vagina	Low grade ESS	ER(+),PR(+), β-Caterin(+), Vimentin(+) CD10(-)
12	Agarwal K et al (Present case)	2021	1	32y	Vulva and vagina	Endometrial stromal nodule	ER(+),PR (+) Focal CD10(+)

Key: ESS: Endometrial stromal sarcoma, NA: Not avaliable

After extensive search of literature, we found 3 cases of endometrial stromal sarcomas in vulva [5,13,14] and 13 cases in vaginal wall [6,7,10,12,14-18]. Out of these, only 4 cases were associated with endometriosis. The age of the patients varied from 32 to 79 years. Most of these patients had been operated for suspected fibroids. Immunohistochemistry was done in most of these cases. ER, PR and CD10 were found to be the most used panel for diagnosing this rare entity. However, ESS with negative expression of CD10 had also been reported.[18]

Endometrial stromal nodule has been described as well-circumscribed endometrial stromal tumor, varying in size from <1 cm to >20 cm in diameter. Cut surface is fleshy yellow or tan. Two or more nodules are seen in approximately 5% of patients. [1] Multiple nodules resected from the right vulva and vagina were found in the present case. Microscopically, there is an expansile noninfiltrative margin, with no vascular invasion. The tumor is composed of cells that closely resemble normal proliferative-phase endometrial stromal cells. These cells have scant to moderate cytoplasm, uniform, darkly staining, round or oval nuclei with finely granular chromatin and inconspicuous nucleoli. Mitotic activity is usually low (<3 MF/10HPF). Whorling of tumor cells around small uniformly distributed arterioles are usually seen. Smooth muscle differentiation, hyaline plaques, areas of hyaline fibrosis and myxoid stroma can be seen. [1,2]

ESN is difficult to diagnose from highly cellular leiomyoma. [2]Cellular leiomyomas are composed of cells with spindle-shaped nuclei with a fascicular growth pattern and thick muscular-walled blood vessels. [19] No such features of cellular leiomyoma was seen in the present case. Immunohistochemistry also plays a very important role to rule out cellular leiomyoma. ESNs are typically positive for ER and PR. CD 10 is typically but not always positive. There is variable expression of smooth muscle actin and desmin. Areas showing smooth muscle differentiation show positive expression of these smooth muscle markers. There is negative expression of EMA. [1, 2, 19] Positive expression of ER and PR was seen in the present case and CD10 expression was seen focally.

The role of radiological investigations such as ultrasonography, contrast enhanced computed tomography and magnetic resonance imaging is limited. It has been discussed in few cases of endometrial stromal sarcomas. [20,21] In a study by Huang et al, the utility of magnetic resonance imaging in differentiating low grade and high grade endometrial stromal sarcoma based on features of extensive necrosis, haemorrhage and feather like enhacement has been described.[21] However, histopathological examination is very important for rendering a definitive diagnosis.

There are very limited reports on ESN and their clinical management. Local conservative surgery has been found to be curative in ESN. In the present case, vaginal myomectomy was done and the post-operative period was uneventful. The prognosis in ESN patients is good. [2] So, it is very important to exclude vascular and tumor invasion by extensive sampling of the specimen to rule out ESS.

To summarize, endometrial stromal nodule is a very rare type of endometrial stromal tumor with very few cases of extrauterine presentation. Proper histopathological examination alongwith immunohistochemitry play a very important role in differentiating these tumors from cellular leiomyoma. Keeping an open mind is thus, essential for such uncommon surprising histology as was seen in this case.

REFERENCES

1. Zaloudek CJ, Hendrickson MR, Soslow RA. "Mesenchymal tumors of the uterus," in Blaustein's Pathology of the Female Genital Tract, Kurman RJ, Ellenson LH, Ronnett BM (Eds).Springer, New York, USA 2001: 480-92.
2. Kurman RJ, Carcangiu ML, Herrington CS, Young RH (Editors.): WHO Classification of Tumours of Female Reproductive Organs. IARC: Lyon 2014: 141-4.
3. Dweep J, Manjusha J.Primary endometrial stromal sarcoma arising in cervix. IOSR Journal of Dental and Medical Sciences.2015; 14: 139-4.
4. Zaza KJ, Arafah MA, Al-Badawi IA. Vulvar extrauterine endometrial stromal sarcoma: A case report and literature review. Hematol Oncol Stem Cell Ther. 2015; 8:125-9.
5. Corpa MV, Serafini EP, Bacchi CE. Low-Grade Endometrial Stromal Sarcoma Presenting as Vaginal Nodule. Ann Diagn Pathol. 2004; 8:295–8.
6. Masand RP, Euscher ED, Deavers MT, Malpica A. Endometrioid stromal sarcoma: a clinicopathologic study of 63 cases. Am J Surg Pathol. 2013; 37:1635-47.
7. Alcázar JL, Guerriero S, Ajossa S, Parodo G, Piras B, Peiretti M, et al. Extragenital endometrial stromal sarcoma arising in endometriosis.GynecolObstetInvest. 2012;73:265-71.
8. Son HJ, Kim JH, Kang DW, Lee HK, Park MJ, Lee SY. Primary extrauterine endometrial stromal sarcoma in the sigmoid colon. Ann Coloproctol. 2015; 31:68-73.
9. Fdili Alaoui FZ, Chaara H, Bouguern H, Melhouf MA, Fatemi H, Belmlih A, Amarti A. Endometrial stromal nodule: report of a case. Case Rep Med. 2011; 2011:260647.
10. Sánchez-Ferrer ML, Ferri-Níguez B, Schuldt M, Nogales FF. Endometrial stromal nodule of the vaginal wall with a review of vulvovaginal endometrial stromal neoplasms. Gynecol Oncol Rep. 2014; 11:13-5.
11. Karpf EF, Poetsch B, Langner C, Nogales FF, Regauer S. Endometrial stromal nodule embedded into term placenta. Case report. APMIS. 2007; 115:1302–5.
12. Ulbright TM, Kraus FT. Endometrial stomal tumors of extra-uterine tissue. Am J Clin Pathol. 1981; 76:371-7.
13. Irvin W, Pelkey T, Rice L. Endometrial stromal sarcoma of the vulva arising in extraovarian endometriosis: a case report and literature review. Gynecol Oncol. 1998;71:313–6.
14. Androulaki A, Papathomas TG, Alexandrou P. Metastatic low-grade endometrial stromal sarcoma of clitoris: report of a case. Int. J. Gynecol. Cancer. 2007; 17:290–3.
15. Liu Z, Ding J, Li X, Yu K. Endometrial stromal sarcoma arising in vagina. Int J Clin Exp Pathol. 2013; 6:2997-02.
16. Sanverdi I, Temizkan O, Vural F, Koc N, Polat M. Primary vaginal endometrial stromal sarcoma associated with endometriosis: a case report with a review of the literature. Eur J Gynaecol Oncol. 2016; 37:717-21.
17. Abu Jamea GA, Al Rikabi AC, Akkour K. Primary low-grade endometrial stromal sarcoma arising in the vagina: report of an unusual case and literature review. J Surg Case Rep. 2017; 2017:rjx238.
18. Tang Y, Chen T, Tian L, Chen J, Yang P, Zhang D, et al. Vaginal Low-Grade Endometrial Stromal Sarcoma: An Extremely Rare Case Report and Review of the Literature. Int J Gynecol Pathol.2020; 39:447-51.
19. Zhu XQ, Shi YF, Cheng XD, Zhao CL, Wu YZ. Immunohistochemical markers in differential diagnosis of endometrial stromal sarcoma and cellular leiomyoma. Gynecol Oncol. 2004; 92:71-9.
20. Toprak U, Pasaoglu E, Karademir A, Gulbay M. Sonographic, CT and MRI findings of endometrial stromal sarcoma located in the myometrium and associated with peritoneal inclusion cyst. Am J Roentgen. 2004; 182: 1531-1533.
21. Huang YL, Ueng SH, Chen K, Huang YT, Lu HY, et al. Utility of diffusion-weighted and contrast-enhanced magnetic resonance imaging in diagnosing and differentiating between high- and low-grade uterine endometrial stromal sarcoma. Cancer Imaging. 2019; 19: 63.