

Combined Stromal Smooth Muscle Tumour of Endometrium: Report of Two Cases

Sakshi Sirswal*, Charanjeet Ahluwalia, Sufian Zaheer, Amit Kumar Yadav and Ashish Kumar Mandal

Department of Pathology, Vardhman Mahavir Medical College & Safdarjung hospital, New Delhi, India

Keywords: *Cellular Leiomyoma, Endometrial Stromal Nodule, Endometrial Stromal Sarcoma, Immunohistochemistry, Myometrium*

ABSTRACT

Endometrial stromal tumours account for < 10% of all mesenchymal uterine tumours. If smooth muscle differentiation comprises $\geq 30\%$ of the tumour mass, the neoplasm is referred to as combined stromal smooth muscle tumour. We report here two cases of benign combined stromal smooth muscle tumour of endometrium, each discovered as an incidental finding in a hysterectomy specimen with a clinical diagnosis of fibroid uterus, where each of the two components- stromal and smooth muscle comprised more than 30% of the tumour. Although none of them showed features of malignancy. This report of two cases of benign combined stromal smooth muscle tumours of endometrium adds to the morphological spectrum of the endometrial mesenchymal tumours.

***Corresponding author:**

Dr Sakshi Sirswal, room number 409, fourth floor college building, Vardhman Mahavir Medical College & Safdarjung hospital, New Delhi-110029, INDIA
Phone: +91 9968529822
E-mail: sakshisirswal@gmail.com

Introduction

Endometrial stromal tumours (ESTs) are the second most common mesenchymal tumours of the uterus, even though they account for < 10% of all such tumours. [1] Uterine tumours exhibiting both endometrial stromal and smooth muscle differentiation are relatively rare. [2-8] Small areas of smooth muscle differentiation are commonly seen in otherwise typical endometrial stromal neoplasms, combined smooth muscle–stromal tumors were arbitrarily defined as neoplasms having at least 30% of each component. [2, 9, 10]

We are reporting here the morphological features of two cases of combined endometrial stromal- smooth muscle tumour.

Case Report(S)

Case 1: A 43-year-old lady, P₂L₂, presented with menorrhagia of 6 months duration following which she underwent total abdominal hysterectomy and right sided salphingo-oophorectomy with a clinical diagnosis of dysfunctional uterine bleeding. During surgery, a diagnosis of intramural fibroid was made.

Grossly, the uterus contained a well-circumscribed intramural tumour measuring 2.5 cm in diameter which on cut section showed homogenous grey white soft to firm areas.

For light microscopy, conventional haematoxylin and eosin (H&E) stained slides were examined. Sections revealed a well delineated tumour in the myometrium that contained areas of both endometrial stromal and smooth muscle differentiation. The endometrial stromal component, which made up approximately 30% of the tumour, was composed of uniform small ovoid to spindle shaped cells with scanty cytoplasm and round nuclei (fig1). Small thin-walled blood vessels were scattered uniformly throughout the stromal component. The remainder of the neoplasm was comprised of smooth muscle component with the smooth muscle cells arranged in interlacing fascicles, individual cells being spindle shaped with abundant eosinophilic cytoplasm and a spindle shaped nucleus with blunt ends (fig2). Large, thick-walled blood vessels featured the smooth muscle areas. The two components were well demarcated from each other. The stromal component showed absence of nuclear pleomorphism and mitotic activity.

On immunohistochemistry, the stromal component showed positivity for CD-10 and the smooth muscle component showed positivity for SMA and the final diagnosis of benign combined stromal smooth muscle tumour was made.

Case 2: A 49 year old lady P₂L₂, presented with history of heaviness in lower abdomen and menorrhagia for duration

of 9 months. On clinical examination, the uterus was found to be bulky and firm. Ultrasound revealed multiple leiomyomas (ranging from 7x7cm to 4.5cm in diameter). Based on these features, a clinical diagnosis of fibroid uterus was made. Total abdominal hysterectomy with left sided salpingo-oophorectomy was performed. The postoperative course was uneventful.

we received one container containing an already cut open uterus with cervix with two intramural tumours measuring 1.5x1x0.6cm and 1x1x0.5cm. Each of these tumours were well circumscribed which on cut showed grey white homogenous surface with whirling pattern. Second container had a globular soft tissue piece measuring 5x4x3cm, the cut surface showed grey white homogenous tumour with whirling pattern and few focal cystic areas. The left ovary and fallopian tube were received in the third container.

On light microscopic examination, the two intramural tumours were identified as leiomyomas. H&E sections from the globular soft tissue received in the second container revealed a well delineated tumour composed of stromal and smooth muscle components, each comprising more than 30% of the tumour (fig3). There was cystic change in the stromal component with a cyst lined by flattened epithelium and surrounded by stromal cells. The tumour was not invading the adjacent myometrium and the part of cervix attached to it, though the two components merged with each other. No atypia, necrosis or abnormal mitosis was seen.

On immunohistochemistry, the stromal cells were positive for CD-10 (fig4) and the smooth muscle cells were positive for SMA and desmin (fig5). The final diagnosis of benign combined stromal smooth muscle tumour was made.

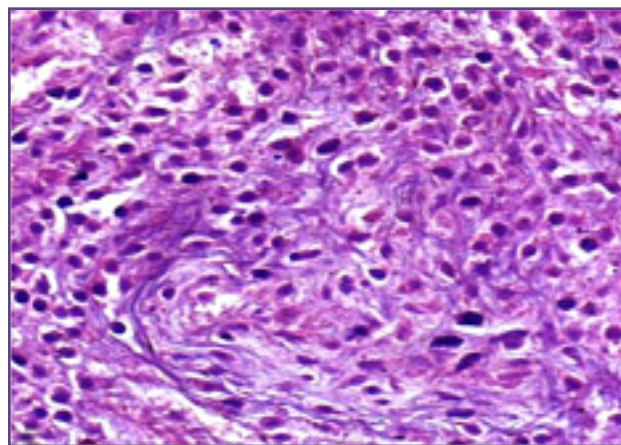


Fig. 1: (H&E, 40X) The tumour showing stromal component comprised of uniform small ovoid cells with scant amount of cytoplasm and a large round nucleus.

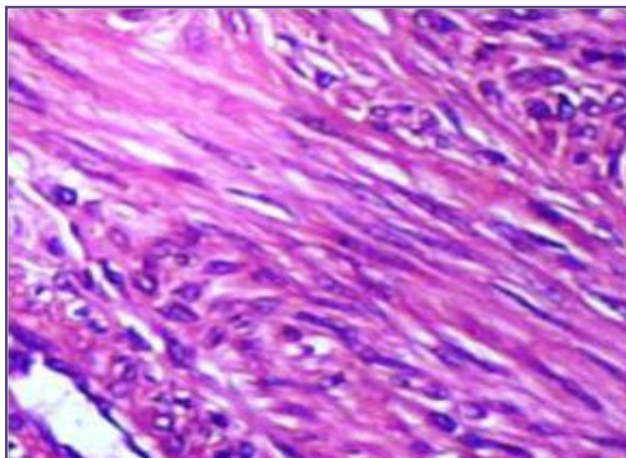


Fig. 2: (H&E, 40X) The tumour showing smooth muscle component with spindle cells arranged in interlacing fascicles.

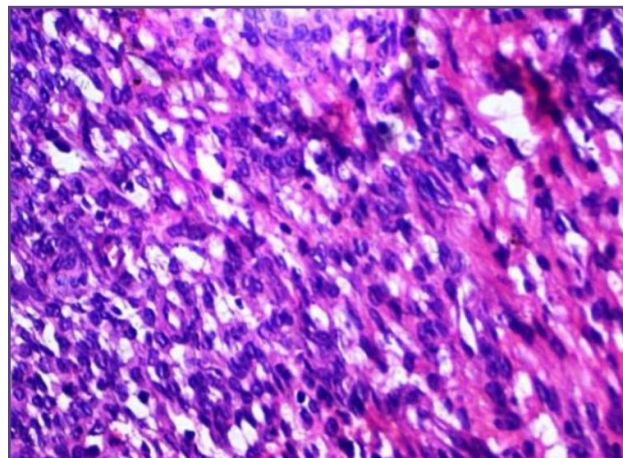


Fig. 3: (H&E, 40X) The tumour, showing the two components- stromal in the top left corner and smooth muscle in the bottom right corner which are merging with each other.

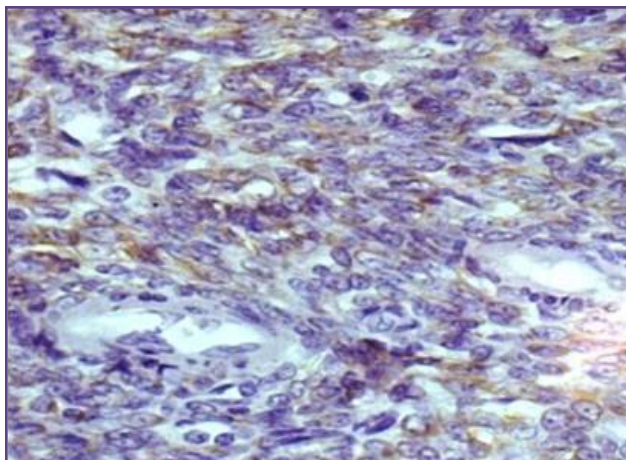


Fig. 4: (CD10, 40X) The tumour cells showed immunopositivity for CD-10 (stromal component).

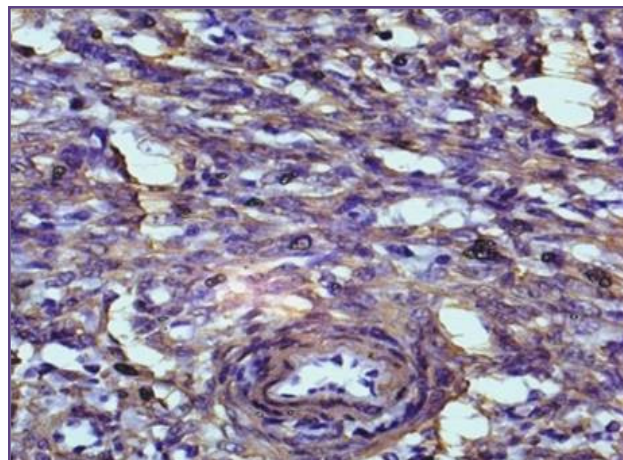


Fig. 5: (SMA, 40X) The tumour cells showed immunopositivity for smooth muscle actin (smooth muscle component).

Discussion

The term “stromomyoma” was proposed by Tang *et al.* [4] to designate a peculiar uterine tumor with ultrastructural characteristics of both endometrial stromal and smooth muscle cells. They opined that these tumours developed due to differentiation of multipotential mesenchymal cells toward myoblasts and stromal cells. They further put forth an alternative explanation that both stromal cells and smooth muscle cells respond to the same stimuli resulting in simultaneous neoplastic proliferation.

However, at present, the diagnosis of a combined tumour is based solely on the presence of significant amounts of both elements as recognized by routine light microscopy. Endometrial stromal tumours (ESTs) have been classified

according to the type of margin as benign (endometrial stromal nodule), having pushing margins and malignant (endometrial stromal sarcoma), having infiltrating margins. [4] Endometrial stromal nodules (ESNs) appear grossly as solitary, sharply circumscribed masses of soft consistency, with the characteristic yellow to orange colour and tend to bulge above the surrounding myometrium. They do not show lymphovascular invasion or invasion into myometrium. Microscopically, these tumours are composed of cells that closely resemble normal proliferative phase endometrial stromal cells, with uniform, small darkly staining round or oval nuclei, finely granular chromatin, occasional mitosis and scant cytoplasm. The stromal nodules are highly vascular, with small arterioles distributed throughout them. Extensive hyalinization is a

common feature in most of these tumours. The prognosis is excellent, with no recurrences.^[10] Focal areas of smooth muscle differentiation are commonly observed in ESTs, but tumours with extensive areas of both smooth muscle and endometrial stromal differentiation are rare. A certain number of mesenchymal uterine tumours show features of both endometrial stromal and smooth muscle differentiation. To establish the diagnosis of mixed endometrial stromal tumour with smooth muscle differentiation, the smooth muscle component should occupy at least 30% of the neoplasm, as seen by haematoxylin and eosin staining.^[9] The smooth muscle component characteristically shows nodules with central hyalinization (starburst pattern) as seen in our cases, which merge with disorganized short fascicles or long mature fascicles of the smooth muscle, a feature which is almost never encountered in conventional smooth muscle tumours.^[2] Behaviourally, these tumours seem to be closer to endometrial stromal than smooth muscle tumour and on the whole, very indolent. Hysterectomy is thus the appropriate therapy and the periphery of the tumour must be thoroughly evaluated to be certain that it is completely circumscribed and non-invasive.

The differential diagnosis of this benign neoplasm includes low-grade endometrial stromal sarcoma (ESS) and highly cellular leiomyoma. Microscopically, the most important single criterion for the diagnosis of ESN is a non infiltrative border of the tumour. Focal irregularities in the form of lobulated or finger like projections into the adjacent myometrium that are not ≥ 3 mm. and are not >3 in number may be seen; which contrasts with the permeative invasion of the myometrium as well as the myometrial vessels seen in low-grade ESS.^[11] From the prognostic point of view, it is extremely important to distinguish between these two tumours, as ESNs do not relapse and low-grade ESSs have a low malignant potential characterized by late recurrences. Hence, extensive sampling of the tumour myometrial interface should be done. This is to evaluate the degree of infiltration of the tumour into the myometrium and to detect vascular invasion, which is extremely important to distinguish the two. Highly cellular leiomyomas are composed of cells with spindle shaped nuclei with a fascicular growth pattern, thick muscular-walled blood vessels, cleft like spaces and show focal merging with the adjacent myometrium.^[9, 12] In our cases, the tumour did not exhibit any of the above mentioned features. Differentiating highly cellular leiomyoma from ESN is important in a curettage or myomectomy specimen, if a spindle cell cannot be classified into that of smooth muscle or stromal cell origin. In cases where the diagnosis is difficult to be established by light microscopy, immunohistochemical analysis may be helpful in arriving at the correct diagnosis,

which is crucial, owing to the differences in treatment and prognosis.^[12] A panel of antibodies including desmin, h-caldesmon, CD10 and inhibin may be very useful in such a scenario, since cellular leiomyomas express h-caldesmon in addition to desmin, while CD10 and inhibin expression is a feature of stromal cells.^[13] Finally, oxytocin receptor, a neurohypophysial peptide which is associated with muscle contraction during labour, stains all conventional leiomyomas and highly cellular leiomyomas as well as leiomyosarcomas, but is not expressed in ESTs.^[14] However, this antibody is not used in daily practice at present. In the above mentioned cases, the characteristic morphological features of the stromal cells and the smooth muscle components were identified by light microscopy. The presence of both the components was confirmed by IHC using CD-10 and SMA for the stromal and smooth muscle components respectively. Further, the gross appearance and well defined non infiltrative microscopic tumour margins emphasized the benign nature of these lesions.

Conclusion

In summary, we have described an uncommon, benign mesenchymal uterine tumour, i.e. ESN with smooth muscle differentiation, which needs to be distinguished from tumours with similar morphological features i.e. low-grade ESS and highly cellular leiomyomas. These cases are being reported because of their rare occurrence and to create awareness amongst pathologists about these lesions regarding their differential diagnosis.

Abbreviations

EST: Endometrial stromal tumour

ESN: Endometrial stromal nodule

ESS: Endometrial stromal sarcoma

H&E: Haematoxylin and eosin

SMA: Smooth muscle actin

Acknowledgements

We would like to thank all the technical staff of pathology department for their co-operation and help.

Funding

None

Competing Interests

None Declared

Reference

1. Moinfar F, Kremser M L, Man Y G, et al. Allelic imbalances in endometrial stromal neoplasms: frequent genetic alterations in the nontumorous

- normal- appearing endometrial and myometrial tissues. *Gynecol Oncol* 2004; 95:662-71.
2. Oliva E, Clement PB, Young RH, et al. Mixed endometrial stromal and smooth muscle tumours of the uterus: a clinicopathologic study of 15 cases. *Am J Surg Pathol* 1998;22:997-1005.
 3. Schammel DP, Silver SA, Tavassoli FA. Combined endometrial stromal/smooth neoplasms of the uterus: a clinicopathological study of 38 cases [abstract]. *Mod Pathol* 1999;12:124A.
 4. Tang C, Toker C, Ances IG. Stromomyoma of the uterus. *Cancer* 1979;43:308-16.
 5. Chang KL, Crabtree GS, Lim-Tan SK, et al. Primary uterine endometrial stromal neoplasms. A clinicopathologic study of 117 cases. *Am J Surg Pathol* 1990;14:415-38.
 6. Evans HL. Endometrial stromal sarcoma and poorly differentiated endometrial sarcoma. *Cancer* 1982;50:2170-82.
 7. Fekete PS, Vellios F. The clinical and histologic spectrum of endometrial stromal neoplasms: a report of 41 cases. *Int J Gynecol Pathol* 1984;3:198-212.
 8. Khalifa MA, Hansen CH, Moore JL, Jr, et al. Endometrial stromal sarcoma with smooth muscle differentiation: recurrence after 17 years: a follow-up report with discussion of the nomenclature. *Int J Gynecol Pathol* 1996;15:171-6.
 9. Clement PB. The pathology of uterine smooth muscle tumours and mixed endometrial stromal-smooth muscle tumours: a selective review with emphasis on recent advances. *Int J Gynecol Pathol* 2000;19(1):39-55.
 10. Tavassoli FA, Norris HJ (1981) Mesenchymal tumours of the uterus. VII. A clinicopathological study of 60 endometrial stromal nodules. *Histopathology* 5:1-10
 11. Baker P, Oliva E. Endometrial stromal tumours of the uterus; a practical approach using conventional morphology and ancillary techniques. *J Clin Pathol*. 2007; 60:235-243.
 12. Oliva E, Young R H, Clement PB, et al. Cellular benign mesenchymal tumours of the uterus. A comparative morphologic and immunohistochemical analysis of 33 highly cellular leiomyomas and six endometrial stromal nodules, two frequently confused tumours. *Am J Surg Pathol* 1995; 19:757-68.
 13. Oliva E, Young RH, Amin MB, et al. An immunohistochemical analysis of endometrial stromal and smooth muscle tumours of the uterus: a study of 54 cases emphasizing the crucial importance of using a panel because of overlap in immunoreactivity for individual antibodies. *Am J Surg Pathol* 2002; 26:403-12.
 14. Loddenkemper C, Mechsner S, Foss H D, et al. Use of oxytocin receptor expression in distinguishing between uterine smooth muscle tumours and endometrial stromal sarcoma. *Am J Surg Pathol* 2003; 27:1458-62.