

## An Endometrial Stromal Tumor with Extensive Smooth Muscle Differentiation, Collagenous Rosettes and Focal Fibromyxoid Change: Case Report and Diagnostic Pitfalls

### Yaygın Düz Kas Farklılaşması, Kollajen Rozetler ve Fokal Fibromiksoid Değişiklikler İçeren Bir Endometriyal Stromal Tümör: Olgu Sunumu ve Tanısal Tuzaklar

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#### ÖZ

Endometriyal stromal tümörler (EST'ler) uterin mezenkimal tümörler içerisinde 2. sıklıkta görülür ve endometrial stromal nodül (ESN) bu grup içerisindeki benign neoplazmıdır. ESN, düz kas diferansiyasyonu, epitelyal paternler veya fibromiksoid stroma içerebilir, bu da ayırıcı tanıyı zorlaştırır. Burada, yaygın düz kas farklılaşması ve fokal miksoid alanlar içeren nadir bir ESN olgusu sunulmaktadır. Makroskopik olarak, tümör intramural, iyi sınırlı ve kistikti. Histolojik olarak, tümör selüler alanlar, miksoid odaklar içermekteydi ve yaygın kollajen rozet formasyonları oluşuyordu. İmmünohistokimyasal olarak, tümör hücreleri B-katenin ve WT-1 için yaygın pozitif; CD56, düz kas belirteçleri, epitelyal belirteçler ve CD10 için fokal pozitif. Düz kas farklılaşması ve kollajenöz rozetler içeren ESN, intrakaviter ve intramural uterin mezenkimal tümörlerin ayırıcı tanısında düşünülmelidir. ESN'de fibromiksoid stroma ve yaygın düz kas farklılaşması tanımlanmıştır. ESN'nin bu morfolojik varyantının bilinmesi doğru tümör sınıflandırması için önemlidir.

**Anahtar Kelimeler:** endometrial stromal nodül; düz kas farklılaşması; kollajen rozetler

#### ABSTRACT

Endometrial stromal tumors (ESTs) are the second most common type of uterine mesenchymal tumors and endometrial stromal nodule (ESN) is a benign neoplasm within this category. ESNs can exhibit smooth muscle differentiation, epithelial patterns, or fibromyxoid stroma, which can complicate differential diagnosis. In this report, we present a rare case of ESN with featuring extensive smooth muscle differentiation and focal myxoid areas. Grossly, the tumor was intramural, well-circumscribed, and cystic. Histologically, the tumor consisted of cellular areas, myxoid areas, and extensive collagen roset formation. Immunohistochemical analysis showed that, the tumor cells were diffusely positive for B-catenin and WT-1, focally positive for CD56, smooth muscle marker, CAM5.2, PanCK and CD10. ESN with smooth muscle differentiation and collagenous rosettes should be considered in the differential diagnosis of intracavitary and intramural uterine mesenchymal tumors. Both fibromyxoid stroma and extensive smooth muscle differentiation have been documented in ESNs. Recognizing this morphologic variant of ESN is crucial for accurate tumor classification.

**Keywords:** collagen roset; endometrial stromal nodule; smooth muscle differentiation

Received: 20.02.2025; Accepted: 26.05.2025

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**How to cite:** Kıvrak H, Kadan E, Altahhan V, Özdemir Ö, Bozdoğan Ö. An endometrial stromal tumor with extensive smooth muscle differentiation, collagenous rosettes and focal fibromyxoid change: case report and diagnostic pitfalls. Ahi Evran Med J. 2025;9(3):403-407. DOI: 10.46332/aemj.1644066

## INTRODUCTION

Tumors originating from the stroma of the endometrium are the second most common tumors of the uterus after smooth muscle tumors and include 3 entities: endometrial stromal nodule (ESN), low-grade endometrial stromal sarcoma (LG-ESS) and high-grade endometrial stromal sarcoma (HG-ESS).<sup>1</sup> Accurate diagnosis of endometrial stromal lesions is critical for patient treatments and prognosis. However, differential diagnoses can be challenging due to overlapping morphological features-such as smooth muscle differentiation and epithelial patterns-as well as immunohistochemical characteristics.

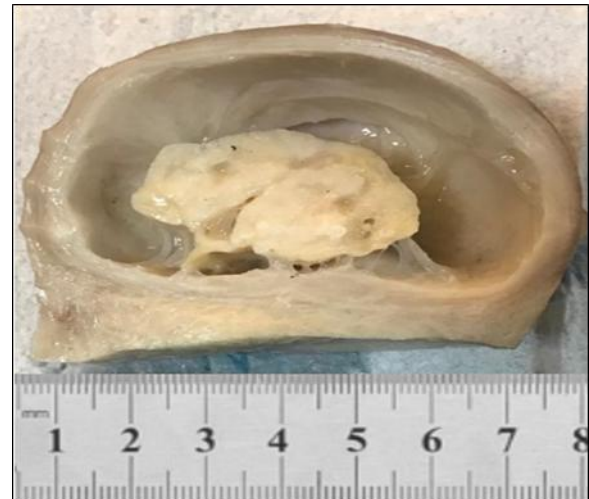
Both ESNs and LG-ESSs, exhibit uniform small tumor cells that have scant cytoplasm and oval nuclei, which tend to whorl around arterioles.

The distinction between the two is primarily based on the presence of myometrial infiltration and/or lymphovascular invasion. In cases where there is smooth muscle differentiation, it often leads to a characteristic starburst pattern of collagen formation.<sup>2</sup> Smooth muscle differentiation can sometimes be misinterpreted as myometrial invasion, resulting in a false diagnosis of LG-ESS when it is actually an ESN. Collagen rosettes are also a common finding in Low grade fibromyxoid sarcoma (LG-FMS), although uterine LG-FMS are extremely rare. We herein present a rare case of ESN with extensive smooth muscle differentiation and focal fibromyxoid areas.

## CASE REPORT

A 48-year-old premenopausal patient (gravidity 2, parity 2) was referred to the Department of Obstetrics and Gynecology with the complaint of heavy menstrual bleeding

and pelvic pain. Pelvic examination indicated no palpable mass, but a mobile, smooth, and enlarged uterus. Multiple uterine masses were found ultrasonographically. The serum levels of CA-125 and CA 19-9 are 23 and 12.9, respectively. With these findings, the patient was operated with a prediagnosis of myoma uteri. A total abdominal hysterectomy was performed. A well-defined tumor was present in the myometrium measuring 7x5x4 cm, without extending into the surrounding tissue. The tumor was clearly demarcated from the adjacent myometrium (Figure 1).

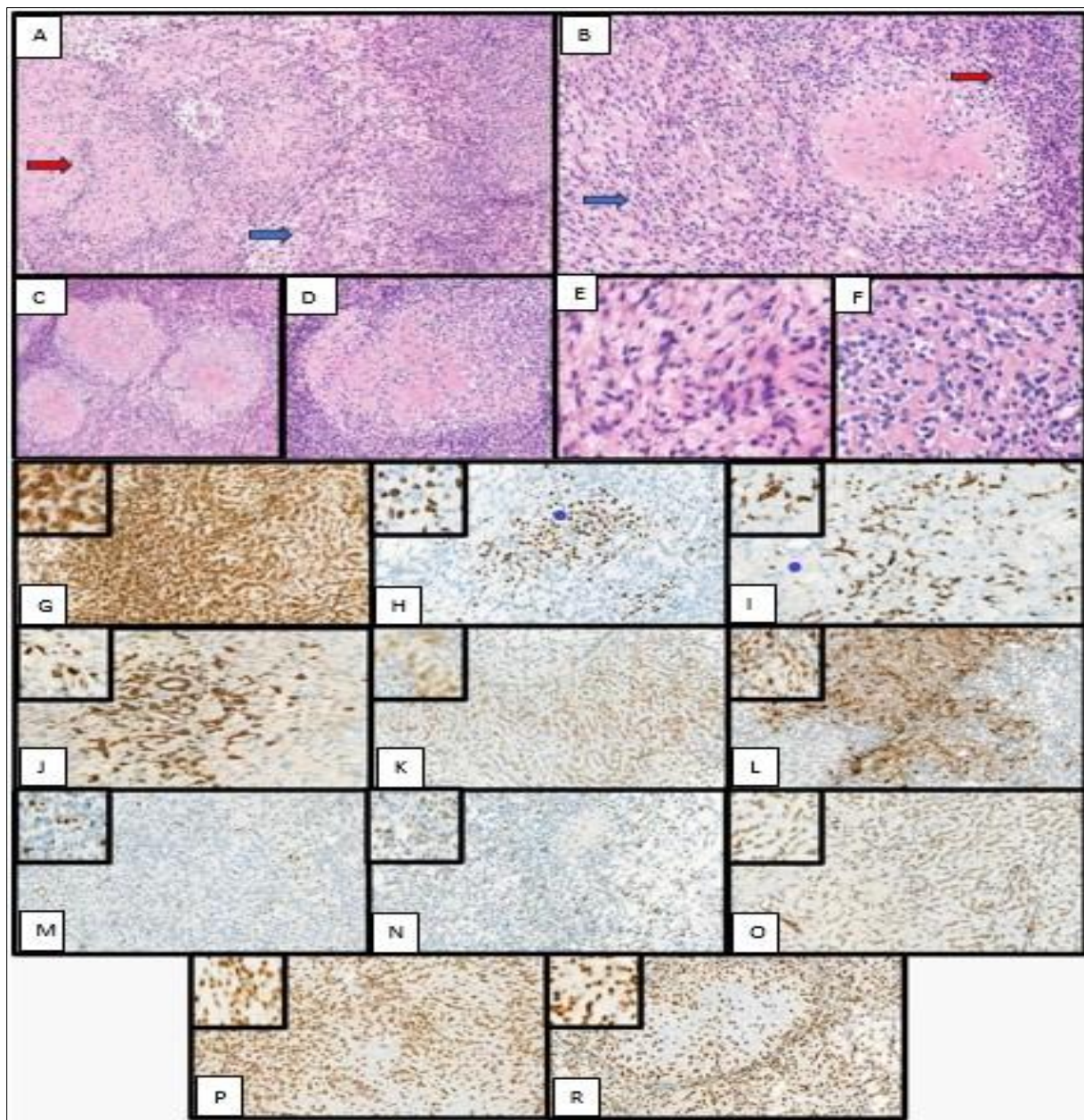


**Figure 1.** Macroscopically, the intracystic mass was observed to undergo cystic and hydropic degeneration in focal area and the cut surface appeared fleshy and gelatinous.

Microscopic examination revealed that the intramural nodule exhibiting cystic degeneration was identified as a uterine mesenchymal tumor with areas of focal hydropic changes. The tumor comprised both cellular and hypocellular and focal myxoid areas (Figure 2A). In cellular areas, the neoplastic cells separated by varying amounts of intercellular collagen. Tumoral cells exhibited both spindle and epithelioid morphologies (Figure 2B,2E,2F). Extensive smooth muscle differentiation was identified. A starburst pattern similar to ‘Collagenous nodules’ seen in LG-FMS were frequently observed in areas where smooth

muscle differentiation was identified (Figure 2C, 2D). In hypocellular areas, tumor cells were dispersed throughout edematous stroma. Focal myxoid changes were present (Figure 2A). Tumoral cells are oval-round nuclei with inconspicuous nucleoli, finely granular chromatin, and scanty cytoplasm. One mitosis was identified in 10 HPF. In a focal area, small cells very similar to those in normal endometrial stroma were observed. No atypical mitosis, necrosis or lymphatic, vascular or myometrial invasion

was observed in the tumor which was completely sampled in relation to the surrounding myometrium. Immunohistochemical examination revealed that tumoral cells expressed diffuse cytoplasmic B-catenin, diffuse nuclear WT-1, ER and PR; focal cytoplasmic SMA, Desmin, H-Caldesmon, CAM5.2, PanCK, CD56 and CD10 (Figure 2G-2R). Proliferative activity was determined as 1% with Ki67. MUC4 was negative.



**Figure 2.** A. Myxoid areas (blue arrow) and more fibrotic collagenized areas (red arrow) are seen together (50x) B. Tumoral cells were observed in spindle morphology (blue arrow) in myxoid areas and epithelioid morphology (red arrow) in fibrotic areas. (200x); C-D.Starburst pattern (C: 50x, D: 100X); E-F.Spindle and epithelioid tumor cells (200x). G-R. B-Catenin, Desmin, Caldesmon, SMA, CD10, CD56, Calretinin, PanCK, WT-1, ER, PR expression in tumor cells respectively.

Formalin-fixed paraffin-embedded (FFPE) blocks were used for RNA isolation. The target regions were amplified using the RNA-based Archer® FusionPlex Sarcoma v2" kit and sequenced on the Illumina NextSeq platform. In the NGS analysis performed with a 63-gene panel including the JAZF1 and BCOR genes. However, no fusion was detected in any gene in the panel. Written informed consent was obtained from the patient.

## DISCUSSION

ESN which is the circumscribed benign neoplastic proliferations of endometrial stromal cells, has been known for many years but the literature on these lesions is scanty. Despite the large case series of endometrial stromal tumors in the literature, these studies include very few ESNs. The vast majority of ESN cases in the literature are case reports.<sup>3</sup> Smooth muscle differentiation, fibromyxoid changes, sex-cord like differentiation, endometrioid glands and rhabdoid or epitheloid morphology can all be observed in all endometrial stromal lesions.<sup>1</sup> While smooth muscle differentiation is a well-known characteristic of LG-ESTs, it is also frequently detected in ESNs.<sup>4</sup> The differentiation mentioned rarely results in a pattern known as

the starburst pattern or collagen rosettes. This pattern is characterized by nodules containing collagen bundles that radiate towards the periphery, with a distinct area of hyalinization in the center. Studies observing the starburst pattern in endometrial stromal tumors are summarized in Table 1. Furthermore, if the pathologist has not personally examined the gross specimen, assessment of the "true" margin of an ESN is can be difficult in cases with smooth muscle differentiation, leading to a misdiagnosis of an LG-ESS.<sup>5</sup> LGFMS and other soft tissue tumors, in which a starburst pattern or collagen rosettes are typically observed, are extremely rare in the uterine body. However, in cases which the starburst pattern is common and fibromyxoid stroma was observed, LG-FMS should be included in the differential diagnosis and MUC4 which is typically positive in LG-FMS, should be added to the immunohistochemical panel.<sup>6</sup> Awareness of this morphologic variant of ESN is crucial for accurate tumor classification and for distinguishing it from tumors with similar morphology that may originate from the myometrium or endometrial stroma.

**Table 1.** Literature in which starburst pattern/collagen rosettes were detected in ESTs. (\*: The number of cases in which collagen rosettes were observed is not mentioned in this literature).

Author	Year	Number of cases in the study (Number of cases with starburst pattern )	Paper
Evans H et al*	1982	18	Endometrial Stromal Sarcoma and Poorly Differentiated Endometrial Sarcoma
Dionigi A et al	2002	50 (9)	Endometrial Stromal Nodules and Endometrial Stromal Tumors With Limited Infiltration
Oliva E et al*	2007	10	High Frequency of JAZF1-JJAZ1 Gene Fusion in Endometrial Stromal Tumors With Smooth Muscle Differentiation by Interphase FISH Detection
Alaoui FA et al.	2011	1	Endometrial stromal nodule: Report of a case.
Cady F.M et al	2014	1	Endometrial Stromal Sarcoma With Hyalinizing Giant Rosettes and Separate Leiomyoma With Palisading Nuclei in the Same Uterus
Kokohaare E et al	2018	1	Endometrial Stromal Sarcoma With Hyalinizing Giant Rosettes, Mimicking Low-Grade Fibromyxoid Sarcoma
Genç ŞÖ et al	2021	1	Endometrial Stromal Nodule: A Case Report

**Conflict of Interests**

The authors declare that there is not any conflict of interest regarding the publication of this manuscript.

**Ethics Committee Permission**

Informed consent was obtained from the patient.

**Authors' Contributions**

Concept/Design: HK, EK, VA, ÖÖ, ÖB. Data Collection and Processing: HK, EK, VA, ÖÖ, ÖB. Data analysis and interpretation: HK, EK, VA, ÖÖ, ÖB. Literature Search: HK, EK, VA, ÖÖ, ÖB. Drafting manuscript: HK, EK, VA, ÖÖ, ÖB. Critical revision of the manuscript: HK, EK, VA, ÖÖ, ÖB. Supervision: ÖÖ, ÖB.

**REFERENCES**

1. Höhn AK, Brambs CE, Hiller GGR, May D, Schmoeckel E, Horn LC. 2020 WHO classification of female genital tumors. *Geburtshilfe Frauenheilkd.* 2021;81(10):1145-1153
2. Kolson Kokohaare E, Strauss DC, Jones RL, Thway K. Endometrial Stromal Sarcoma With Hyalinizing Giant Rosettes, Mimicking Low-Grade Fibromyxoid Sarcoma. *Int J Surg Pathol.* 2018;26(6):525-527.
3. Fdili Alaoui FZ, Chaara H, Bouguern H et al. Endometrial stromal nodule: report of a case. *Case Rep Med.* 2011;2011(1):260647.
4. Dionigi A, Oliva E, Clement PB et al. Endometrial stromal nodules and endometrial stromal tumors with limited infiltration: a clinicopathologic study of 50 cases. *Am J Surg Pathol.* 2002;26(5):567-581.
5. Lloreta J, Prat J. Endometrial stromal nodule with smooth and skeletal muscle components simulating stromal sarcoma. *Int J Gynecol Pathol.* 1992;11(4): 293-298.
6. Mohamed M, Fisher C, Thway K. Low-grade fibromyxoid sarcoma: Clinical, morphologic and genetic features. *Ann Diagn Pathol.* 2017;28:60-67.