



# Endometrial Stromal Nodule with Intense Decidual Changes. Findings during Delivery of the Placenta

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## Case Report

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## Abstract

**Background:** Endometrial stromal nodules involving the placental membranes are exceptionally rare. Only two cases have been described in the literature. We report a new case of endometrial stromal nodule with intense decidual changes as an incidental finding during delivery of the placenta.

**Case:** A 31-years-old female patient with no history of interest presented after a normal term delivery, a 3.5 x 2.6 x 1cm well circumscribed nodule independent of the placenta and not attached to it. The tumor was asymptomatic and was not identified ultrasonographically. Microscopically, the neoplastic nodule was composed of spindle and epithelioid cells with extensive eosinophilic cytoplasm with a decidualized appearance without associated glands, except for minimal epithelial remnants in the periphery. Characteristic features of endometrial stromal tumor were identified, such as CD10, WT-1, and progesterone receptor positivity, and an expanding noninfiltrating linear pushing rim. There were also pregnancy-related changes, such as decidualization and myxoid change. The lesion was considered a endometrial stromal nodule with an unusual morphology and increased proliferation rate due to the hormonal stimuli of pregnancy.

**Conclusion:** We report a rare case of an incidental endometrial stromal nodule during delivery of the placenta, representing only the third such case reported in the world literature. In all likelihood, this neoplasm originated from the decidua of the free membranes.

**Keywords:** Endometrial Stromal Tumor; Endometrial Stromal Nodule; Placenta

**Abbreviations:** ESTs: Endometrial Stromal Tumors; WHO: World Health Organization; ESN: Endometrial Stromal Nodule; LG-ESS: Low-Grade Endometrial Stromal Sarcoma; HG-ESS: High-Grade Endometrial Stromal Sarcoma; UUS: Undifferentiated Uterine Sarcoma.

## Introduction

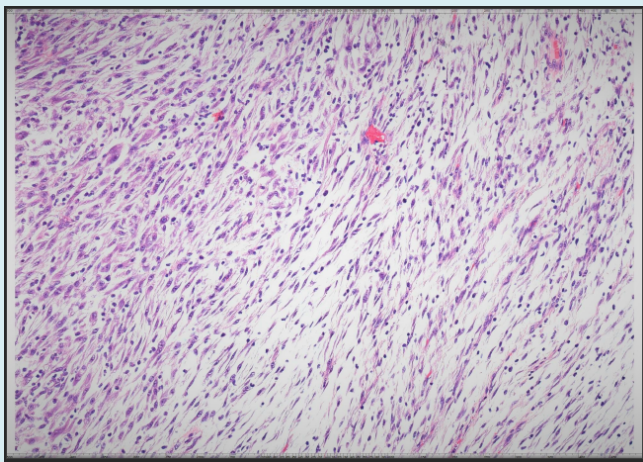
Endometrial stromal tumors (ESTs) are uncommon uterine tumours responsible for less than 10% of uterine mesenchymal neoplasms and less than 2% of all uterine

neoplasms [1]. The last classification of the World Health Organization (WHO) in 2020 sub-categorized ESTs into four groups: Endometrial Stromal Nodule (ESN), Low-Grade Endometrial Stromal Sarcoma (LG-ESS), High-Grade Endometrial Stromal Sarcoma (HG-ESS), and Undifferentiated Uterine Sarcoma (UUS) [2]. The endometrial stromal nodule (ESN) is a benign tumor characterized by a well-delineated, expansive margin and composed of cells resembling endometrial stroma in the proliferative phase with minimal or absent myometrial invasion (<3 mm and <3 bulges) and no vascular invasion [3]. Very few cases of endometrial

stromal nodules involving the placenta have been described. Given the rarity of these tumors and the scarcity of reports in the literature regarding the clinical management and final evolution of these cases. We report a new case of endometrial stromal nodule with intense decidual changes found during delivery of the placenta.

## Case Report

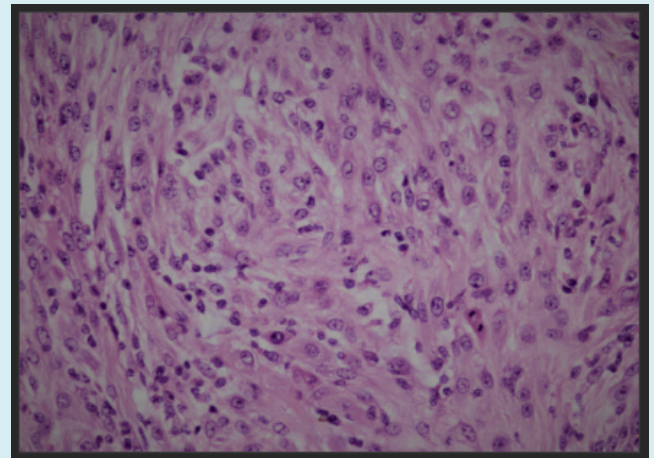
A 31-year-old woman, primigravida, had an unremarkable previous clinical history. The ultrasounds controls without incidences. The pregnancy was uneventful, and at the 39th week, a healthy male baby weighing 3270 g was delivered spontaneously. During the expulsion of the placenta, a 3 cm well-defined whitish ovoid nodule was identified, apparently independent of the placental membranes. Clinically it was thought to correspond either to a expelling of the placental tissue. The placental expulsion that followed was unremarkable with no unusual bleeding. We received for histological study a nodular tumor that macroscopically measured 3.5 x 2.6 x 1 cm, was oval, somewhat flattened, well demarcated, unencapsulated, grayish-brown in color. The cut surface presented a fleshy, whitish appearance with an elastic consistency. It was completely included for histological study. Microscopically, the nodule was composed of spindle and epithelioid cells with extensive eosinophilic cytoplasm with a decidualized appearance without associated glands, except for minimal epithelial remnants in the periphery. The cells showed varied architecture with more compact epithelioid areas alternating with spindle-shaped, storiform areas and very loose edematous-myxoid foci (Figure 1).



**Figure 1:** Microscopic image showing decidual tumor cells with abundant plump eosinophilic cytoplasm and focal myxoid changes. HE 20x.

Foci of ischemic necrosis were identified. The nuclei were rounded or ovoid, of medium-large size with a small

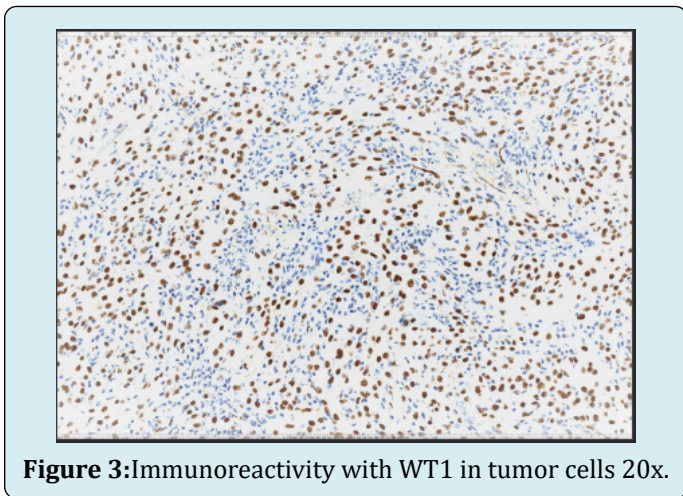
nucleolus and nuclear grooves, sometimes showing a vesicular appearance with a nucleolus. The proliferative activity was 5/7 mitoses per 10 HPF (Figure 2) in the most active areas (interpreted in the gestational context). There was a slight accompanying mixed inflammatory component and a rich vascular network (CD-34) of very small caliber and homogeneously distributed. In the periphery, remains of myometrium and decidua were identified with isolated intermediate trophoblast cells.



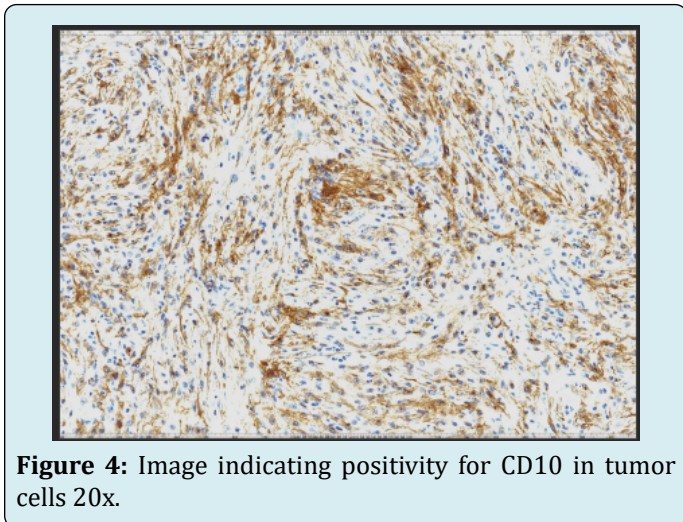
**Figure 2:** Decidualized cells and a figure of mitosis 20x.

Immunohistochemistry revealed strong positivity for WT-1 (Figure 3), CD-10 (Figure 4), and progesterone (Figure 5). B-catenin was diffuse but weakly positive. The minimal epithelial remnants in the periphery were positive with CK8/18 and EMA. The proliferative activity (Ki-67) was moderate with around 20% (Figure 6), although it must be interpreted in the context of a pregnancy with a strong hormonal environment. Focal staining with estrogen and GATA-3. Cells were negative with muscle markers such as desmin, actin, calponin and caldesmon. Negativity with trophoblastic markers: PLAP, human placental lactogen, p63, p40 and human chorionic gonadotropin. ALK, inhibin, HMB-45 and Melan-A were also negative. This is a very unusual lesion with a decidualized appearance due to gestational changes. The lesion was in close contact with the decidua (remnants are observed in the periphery) with minimal surface myometrium. It is a decidualized cell lesion with endometrial stromal phenotype (WT-1, CD-10, and progesterone positive) without accompanying glands. A wide differential diagnosis was made, ruling out, among other lesions, muscle tumors (negative for desmin, actin, calponin and caldesmon), trophoblastic tumor, especially that of the placental bed (negative with PLAP, human placental lactogen, p63, p40 and chorionic gonadotropin), PECOMA (negative with HMB-45 and Melan-A) and inflammatory my fibroblastic tumor (negative with ALK, actin and desmin). For all these reasons, it was interpreted as ESN with intense

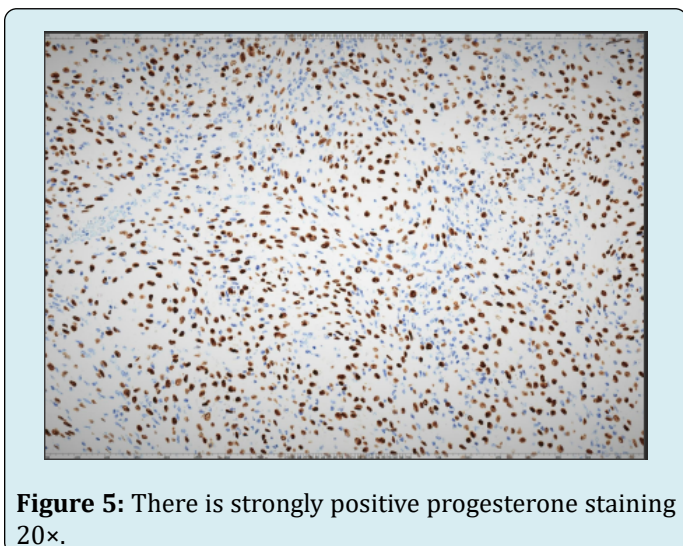
gestational decidual changes. Clinical and ultra-sonographic follow-up of the patient, latest at 12 months after delivery, revealed no abnormalities in the uterine cavity.



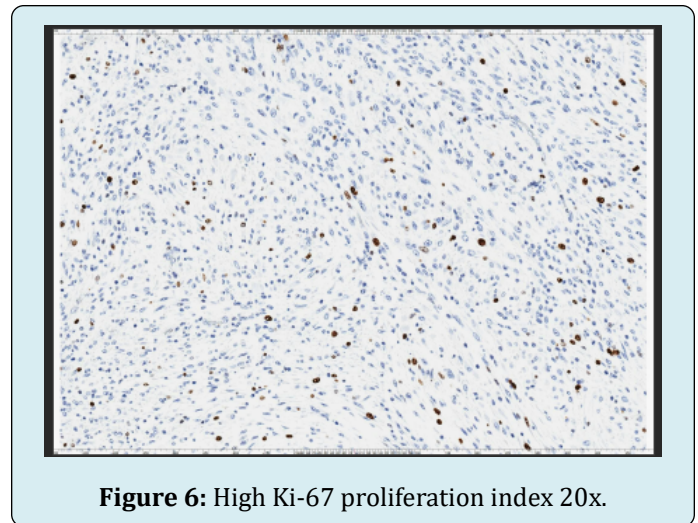
**Figure 3:**Immunoreactivity with WT1 in tumor cells 20x.



**Figure 4:** Image indicating positivity for CD10 in tumor cells 20x.



**Figure 5:** There is strongly positive progesterone staining 20x.



**Figure 6:** High Ki-67 proliferation index 20x.

## Discussion

Neoplasms within the placental membranes are exceptionally rare. A few cases of leiomyomas have been described. Rare individual reports of endometrial stromal nodule and low grade endometrial stromal sarcoma have also been describe [4,5] (Table 1). Endometrial Stromal Nodules, which are considered a clinically benign tumors. They occur much more commonly in the corpus than in the cervix. They are frequently polypoid with protrusion into the uterine cavity but may be intra-myometrial (ranging up to 10 cm). They typically are well circumscribed and show a uniform tan to yellow, soft cut surface. Cyst formation as well as ischemic-type necrosis and hemorrhage may be seen. They are characterized microscopically by a well-circumscribed, pushing border; however, small irregularities present as lobulated or finger-like projections (<3 in number and <3 mm) into adjacent myometrium may occur [3,6]. The neoplastic cells of ESNs resemble proliferative phase endometrial stroma, being composed of cells with uniform round to ovoid nuclei that have scant to moderate amounts of amphiphilic to eosinophilic cytoplasm. These cells appear to whorl around the prominent vascular component, which resembles the spiral arterioles of non-neoplastic endometrium. The vessels are typically evenly spaced and uniform in caliber throughout the neoplasm; however, occasionally large, thick-walled vessels may be present, although this is usually only a focal finding identified in only a minority of cases. ESNs can show variant morphology, most commonly smooth muscle differentiation, but unusual forms of differentiation including skeletal muscle may occur. Immunohistochemistry for vimentin, CD 10, and actions as well as WT1, ER, and PR are typically positive (rarely tumors may be CD 10 negative). Desmin and h-caldesmon are positive in areas of smooth muscle differentiation although occasionally areas of conventional stromal differentiation may be desmin positive, and if so, typically it shows a

perinuclear cytoplasmic pattern of staining. Over 70% of tumors are positive for androgen receptors [7], and some investigators have shown nuclear  $\beta$ -catenin positivity [8]. Variable degree of keratin expression may be seen [9]. Areas of sex cord differentiation may be positive for inhibin, calretinin, CD99, melan A, and WT1 [10]. Histologically, ESN and LG-ESS are distinguished by the presence of stromal invasion. LG-ESS shows invasive patterns, whereas ESN does not. ESN has an expansive but noninfiltrative border that often compresses the surrounding myometrium and endometrium [11]. In the majority of cases, the distinction between an ESN

and low-grade endometrial stromal sarcoma (LGESS) cannot be made with certainty in a curettage/biopsy specimen as the margin of the tumor usually cannot be assessed well or completely. In these cases, the diagnosis of 'endometrial stromal neoplasia' should be rendered with a note stating that the distinction between a nodule and a sarcoma cannot be made. Recent studies have shown that ESN and LG-ESS share common genetic alterations. As in LG-ESS, JAZF1-SUZ12 fusion is the most common rearrangement in ESN, estimated to be present in 65% of ESN cases [12].

Author	Year	Age	Size (cm)	Gross Findings	Microscopic	IHC
Karpf, et al. [4]	2007	28	5	well circumscribed nodule	Non-infiltrative pushing border. Decidualization and myxoid change	Vimentin, CD10, PR positive. Ki67 about 40%
Heller, et al. [5]	2018	31	3.7x2,2x1.4	well circumscribed nodule	Non-infiltrative pushing border	Vimentin, CD10, PR positive. CD31 focal
Present case	2023	31	3.5x2.6x1	well circumscribed nodule	Non-infiltrative pushing border. Decidualization and myxoid change	Vimentin, CD10, PR, WT-1 and B-catenin positive. Ki67 about 20%

**Table 1:** Previous reports of endometrial stromal nodules in the placenta. IHC: Immunohistochemistry, CM: centimeter.

The diagnosis of endometrial stromal nodule was based on both its benign clinical behavior (no evidence of recurrence after a period of 12 months) and its pathologic features, which revealed a well circumscribed nodule with an expansive, non-infiltrative growth pattern, features characteristic of endometrial stromal tumors, such as CD10, progesterone receptor positivity, and plexiform vascularity. The diagnosis of leiomyoma was discarded owing to negativity for smooth muscle markers. Endometrial stromal tumors show a high histopathologic variability and indeed in this case the morphology was not entirely characteristic of ESN since there were focal degenerative myxoid and decidualized areas. These were interpreted as pregnancy-related changes. The variable but strong reactivity for CD10 may also be related to gestational stromal differentiation in which the usual endometrial stromal CD10 staining is known to be patchy or diminished. Uterine mesenchymal tumors continue to be a challenge to diagnose due to their non-specific clinical presentation, often non-distinctive gross appearance, varied (and many times overlapping) morphologic appearance, and unsuspected pitfalls in immunohistochemical expression. In the present case, the nodular tumor was entirely situated within the endometrial decidualized tissue; the expulsion of the placenta during delivery ensured the complete expulsion of the tumor attached to it, therefore proving curative, as confirmed by subsequent negative controls of the uterine cavity and the absence of any abnormal postpartum or puerperal bleeding. However, advised close follow-up with ultrasound control.

The pathologist must be aware that this lesion might involve the placenta in order to correctly identify it.

### Author Contribution

The project was conceived by JPGT. The manuscript was written by RSO, with revision and intellectual input from AAR, and JPGT. Pathology slides and images were produced and annotated by RSO. Consent from the patient was obtained by AAR. All authors have read and approved the manuscript.

### Ethics Approval and Consent to Participate

The patient has consented to the submission of the case report for submission to the journal.

### Acknowledgment

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This study received no external funding.

### Conflict of Interest

The authors declare no conflict of interest.

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