

## **A tumor-like trophoblastic lesion (placental site nodule)**

### *Tümör benzeri bir trofoblastik lezyon (plasental site nodül)*

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#### **Abstract**

Placental site nodule, developing from intermediate trophoblasts, is a rare benign lesion. Although it is a benign lesion, it is histopathological differential diagnosis from placental site trophoblastic tumor and epithelioid trophoblastic tumor which are aggressive lesions of the intermediate trophoblasts, and non-trophoblastic neoplasms such as squamous cell carcinoma, is important due to its histological appearance. In our report, placental site nodule diagnosed in 33-year-old, female patient who was suffering from intermittent menometrorrhagia and had a diagnostic curettage is presented.

**Keywords:** Placental site nodule, intermediate trophoblasts, abnormal uterine bleeding

#### **Özet**

Plasental bölge nodülü intermediate trofoblastlardan gelişen nadir görülen benign bir lezyondur. Benign bir lezyon olmasına rağmen histolojik görünümü nedeniyle intermediate trofoblastların agresif lezyonları olan plasental bölge neoplastik tümörü ve epitelioid trofoblastik tümör ile skuamöz hücreli karsinom gibi trofoblastik olmayan neoplazilerden histopatolojik ayrımı önemlidir. Bu makalede intermitan menometroraji şikayeti ile başvurup tanısal küretaj yapılan ve plasental bölge nodülü tanısı alan 33 yaşında bir bayan hasta sunulmuştur.

**Anahtar sözcükler:** Plasental bölge nodülü, intermediate trofoblastlar, anormal uterin kanama

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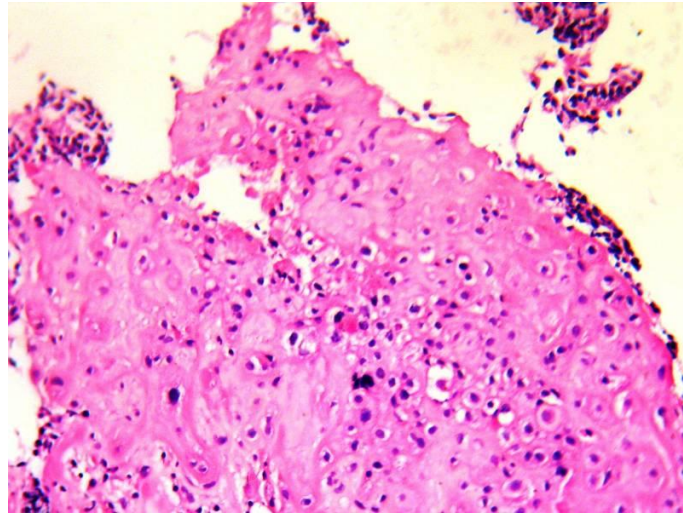
This case was presented as an abstract at National Pathology Congress in Eskisehir

#### **Introduction**

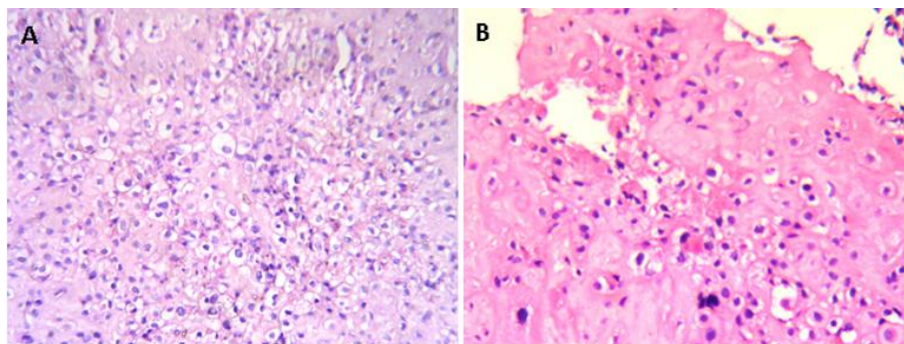
Placental site nodule is a rare benign trophoblastic lesion deriving from implantation type intermediate trophoblasts [1-5]. Although it most frequently occurs at the age of fertility, it is difficult to establish an association with the previous pregnancy because it may clinically emerge a long time after pregnancy [1, 4, 5]. Placental site nodule is often detected with the diagnostic curettages performed in consequence of deviational cervical smear results, abnormal uterine bleeding and menstrual cycle anomalies [1]. Although it is a benign lesion, because of its histomorphological appearance, its differential diagnosis is important from placental site trophoblastic and epithelioid trophoblastic tumors which are aggressive lesions of intermediate trophoblasts as well as non-trophoblastic neoplasm like squamous cell carcinoma [1-3, 6].

## Case report

A 33 years old female patient presented to our clinic with intermittent menometrorrhagia. Her medical history was uneventful with an exception of a caesarian operation that she had three years ago. Her gynecological and general examinations were normal. Her menometrorrhagia complaint started just after caesarean operation and continued intermittently. The uterine size was measured as 75x55x45 mm and the endometrial thickness as 14 mm by transabdominal ultrasonography. Both adnexa were normal in structure and size. She underwent a diagnostic curettage that was applied to the case with a pre-diagnosis of endometrial pathology. Histopathological examination of curettage material revealed well-defined, oval-round eosinophilic-like nodular structures among the endometrial tissue parts exhibiting early proliferative phase findings. Cells with narrow-clear cytoplasm and small nucleus; and with wide eosinophilic cytoplasm, large hyperchromatic nucleus and pleomorphic features were observed in the nodular structures exhibiting intensive hyalinization (Figure 1). These cells formed small groups or single cell strings (Figure 2A and 2B).



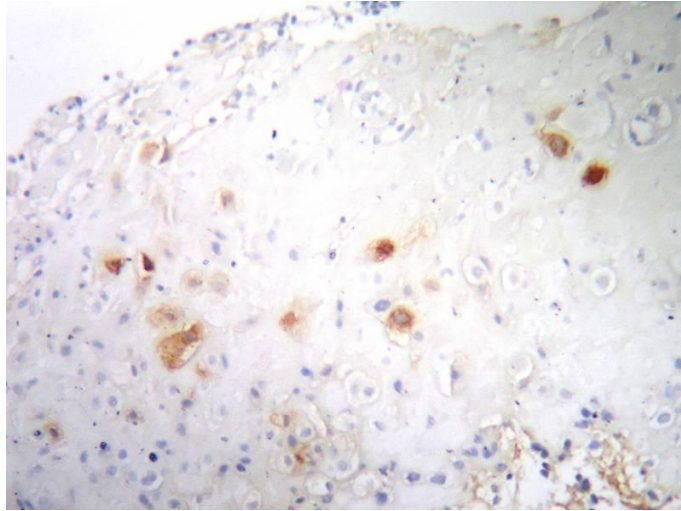
**Figure 1. Intermediate type trophoblastic cell groups observed in the nodular structure with intensive hyalinization (H&Ex 10).**



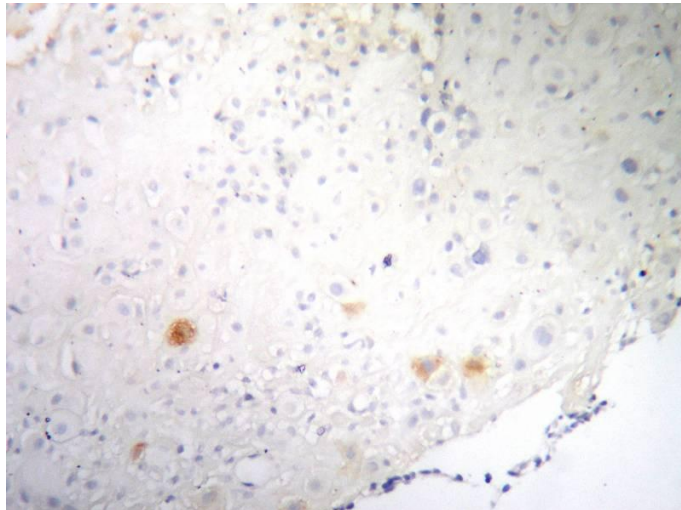
**Figure 2A. Small cells with small nuclei forming small groups and cell string courses (H&Ex20). 2B. Cells with wide eosinophilic cytoplasm, and large hyperchromatic nucleus presents pleomorphic features.**

Decidua and chorionic villus structures were not observed. In histochemical examination focal reaction was observed for PAS Immunohistochemical examination for pancreatin,

human placental lactogen (Figure 3) and placental alkaline phosphatase (Figure 4) revealed a focal positive reaction.



**Figure 3. Focal (+) immune reaction with human placental lactogen (IHCx20).**



**Figure 4. Focal (+) immune reaction with placental alkaline phosphatase (IHCx20).**

Proliferative index of the cells with Ki67 was lower than 1%. With these findings, the diagnosis was placental site nodule. Control curettage was performed a year later and showed that the endometrium was regular in structure and under the influence of progesterone, mid secretion phase findings.

### **Discussion**

Gestational trophoblastic disorders are a wide group of trophoblastic lesions that originate from different subtypes of trophoblastic cells and have variable biological behaviors [1, 7]. The lesions in this spectrum such as placental site nodule or plaque, exaggerated placental site reaction, placental site trophoblastic tumor and epithelioid trophoblastic tumor arise from intermediate type of trophoblasts [2, 7, 8]. Years later, placental nodule site develops from the remnants of placental tissue in uterus which were not exposed to involution, after pregnancy [1]. The period between its diagnosis and the previous pregnancy varies from 1 month to 8 years (the average is 3 years) [4]. They cause abnormal uterine bleedings such as postcoital bleeding, dysmenorrhea, hypermenorrhea, menometrorrhagia, recurrent abortus, abnormal pap smear results, even different clinical

findings such as infertility [1, 4, 8]. The average diagnosis age is 30, and it varies between 20 and 47 [4, 5, 8]. Although there is endometrium involvement in most of the cases [4, 5, 9], involvements of different localizations other than the uterus such as cervix [10], ovary [11] and fallopian tubes [12, 13] have also been reported. Placental site nodule is often microscopic and millimeter-sized [8]. They are microscopically small, single or multiple, round-ovoid, well-defined and quite hyalinized lesions. The cells forming the lesion are small, rich in glycogen, clear or large cells with plenty of eosinophilic cytoplasm. They also show nuclear hyperchromatism, multinucleation and degenerative atypia and mitosis is rare [4, 8] and Ki67 proliferation index is almost low. They have no deciduas and chorionic villous structures [1]. Our case was in reproductive period and she had a normal pregnancy history resulted in a caesarean operation 3 years ago. The patient had a menometrorrhagia complaint lasting for 3 years intermittently. Although exaggerated placental site reaction and placental site nodule are non-neoplastic lesions, placental site trophoblastic tumor and epithelioid trophoblastic tumor are aggressive trophoblastic lesions and have the potential of making local invasion and metastasis [3]. In placental site nodule, since atypical histological appearance can be observed, their differential diagnosis from aggressive lesions of the intermediate trophoblasts and squamous cell carcinoma should be made carefully. Placental site nodule can easily be distinguished from these lesions with its small size and formation of hyaline nodule or nodules whose cellularity are low; not including deciduas and chorionic villus and with a recent pregnancy history. Placental site nodule shows focal positivity with human placental lactogene and human chorionic gonadotropins; and immunoreactivity with placental alkaline phosphatase and cytokeratin [3, 7, 8, 14]. The lesion of our case was observed as two nodular areas with 2 and 3 millimeters size, and hyalinized appearance among the regular structured endometrial tissue parts. The lesion and cells forming the lesion had histomorphologically similar features too. The cells forming the nodule were eosinophilic, with clear cytoplasm in patches, vesicular nuclei, and the borders of cytoplasm were not defined. Decidua or chorion villus structures were not detected among the endometrial tissues. However, because of the fact that minimal atypia was also observed in the cells, Ki67 antibody was studied immunochemically and proliferative index was found less than 1%. Intermediate trophoblastic and syncytiotrophoblastic cells infiltrate myometrium, blood vessel walls by ranging one by one, in the shape of cords and nidus in the reaction of exaggerated placental site, and they often have chorion villus structures [1, 6]. They give strong (+) immunoreactivity with human placental lactogen, but they are not in appearance of epithelioid as placental site trophoblastic tumor is, and they do not form hyalinized nodules like placental site nodule [1, 15]. Placental site trophoblastic tumor infiltrates in muscle fibers and shows vasculotrophism. Multinuclear intermediate trophoblastic cells are observed with round nucleus, wide eosinophilic cytoplasm, in epithelioid looking, but these cells do not constitute hyalinized nodule formation [1, 2]. Squamous cell carcinomas are easily distinguished from placental site nodule with their size, high mitotic index rates and their formation of keratinized cells showing cellular atypia [1, 3]. Decidua should also be considered in the definitive diagnosis of placental site nodule. Decidual cells are separated from placental site nodule consisting clear amphophilic cytoplasm, hyperchromatic cells with their distinct cell membranes, basophilic pale cytoplasm and uniform nucleus. Moreover, decidual cells give negative immunoreactivity with human placental lactogen [1, 3]. While the definitive diagnosis of placental site nodule with benign and malign trophoblastic lesions was done, a large immune panel was also applied although the patient had typical clinic presentation and histomorphological findings. Positive immunoexpression was obtained with human placental lactogen and human chorionic gonadotropins, and the diagnosis of placental site nodule was established by low presence of Ki67 proliferative index.

Although placental site nodule is a rare trophoblastic lesion, when there is presence of an association with a previous pregnancy; it is an entity of which diagnosis can easily be

established by the help of its well-defined histomorphological features and immune profile. Despite the fact that it is a benign lesion, it should be absolutely kept in mind that it is a lesion that requires differential diagnosis from placental site trophoblastic tumor and epitheloid trophoblastic tumor which are the aggressive lesions of intermediate trophoblasts because of their histological appearances that show atypia as well.

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