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BRIEF REPORT

# Gestational trophoblastic neoplasia associated with a normal pregnancy with no evidence of uterine primary lesion

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**KEYWORDS**
Gestational trophoblastic neoplasia;
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**Abstract** Gestational trophoblastic tumours are neoplasms that derive from trophoblastic tissue; therefore, their occurrence is generally intrauterine. We report the case of a 27-year-old woman with an ovarian tumour that arose during pregnancy. The patient did not have postpartum checkups and came to the clinic after eighteen months, presenting multiple lymphadenopathy predominantly in the cervical region, one of which was biopsied. In the microscopic study, the presence of syncytiotrophoblast-like cells supported the diagnosis of a metastasis of gestational trophoblastic neoplasia. The serum levels of bHCG were found to be elevated. Tomographic and ultrasound images did not show any uterine tumour. Immunohistochemistry allowed us to establish the diagnosis of placental site trophoblastic tumour metastasis.


**PALABRAS CLAVE**
Neoplasia trofoblástica gestacional;
Embarazo;
Trofoblasto intermedio

**Neoplasia trofoblástica gestacional asociada a una gestación normal sin evidencia de lesión uterina primaria**

**Resumen** Los tumores trofoblásticos gestacionales son neoplasias que se derivan del tejido trofoblástico; por lo tanto, su presentación es generalmente intrauterina. Presentamos el caso de una mujer de 27 años con un tumor ovárico que surgió durante la gestación. La paciente no tuvo controles posteriores al parto y acudió a consulta después de 18 meses, presentando múltiples adenopatías de predominio en la región cervical, una de los cuales fue biopsiada; en

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el estudio microscópico, la presencia de células tipo sincitiotrofoblasto apoyó el diagnóstico de una metástasis de neoplasia trofoblástica gestacional. El dosaje sérico de la bHCG se encontró elevado. Las imágenes tomográficas y ecográficas no evidenciaron ninguna tumoración a nivel uterino. La inmunohistoquímica permitió establecer el diagnóstico de metástasis de tumor trofoblástico de sitio placentario.


## Introduction

Gestational trophoblastic tumours are neoplasms derived from intermediate trophoblastic cells, which are usually present in pregnancy as part of the placental, chorionic, and implantation tissues.[1] This group of neoplasms includes gestational choriocarcinoma, placental site trophoblastic tumour, epithelioid trophoblastic tumour, and mixed trophoblastic tumour. The usual presentation of these cases occurs in women of reproductive age with a history of normal, ectopic, or molar pregnancy, who presents with an increase in uterine size, amenorrhea, or vaginal bleeding. In cases with metastasis, the clinical presentation varies depending on the affected organ. There are few cases in which one of these neoplasms has been reported without evidence of a primary uterine lesion.[2] On the other hand, reports of these neoplasms alongside a normal pregnancy have most frequently been associated with cases of gestational choriocarcinoma.

## Case report

A 27-year-old female patient with no significant medical history, G1P1, presented to the clinic 18 months after childbirth, reporting a 2-month history of noticing the appearance of several nodules in her neck that gradually increased in size, associated with an increased abdominal volume. Physical examination revealed left supraclavicular adenopathies, the largest measuring 4 cm × 3 cm, mobile, and stony-hard in consistency. Additionally, an abdominopelvic mass of approximately 17 cm × 12 cm was identified. During further history taking, the patient mentioned that an ovarian cyst had been detected during her prenatal consultations, though she did not specify the month of pregnancy when this occurred. Magnetic resonance imaging (MRI) studies were performed, and she was advised to return after delivery for cystectomy.

The patient had an uncomplicated vaginal delivery, but did not return for further evaluation of the ovarian tumour. During the year following childbirth, she experienced vaginal bleeding unrelated to her menstrual cycle, early satiety, constipation, and weight loss. A review of the MRI images revealed an enlarged uterine cavity due to pregnancy, an anterior body placenta, and a left adnexal cystic tumour measuring 12 cm × 8 cm with a solid nodular component (Fig. 1).

In this new consultation, a computed tomography (CT) scan revealed a large complex cyst measuring 15 cm × 13 cm (Fig. 2), with solid peripheral areas that appeared calcified. Compared to the MRI, there was approximately a 30% increase in the solid area, while the uterus exhibited normal characteristics. Transvaginal ultrasound showed a linear endometrium measuring 2.3 mm in thickness, with an unremarkable myometrium. A biopsy from one of the supraclavicular lymph nodes and microscopy demonstrated

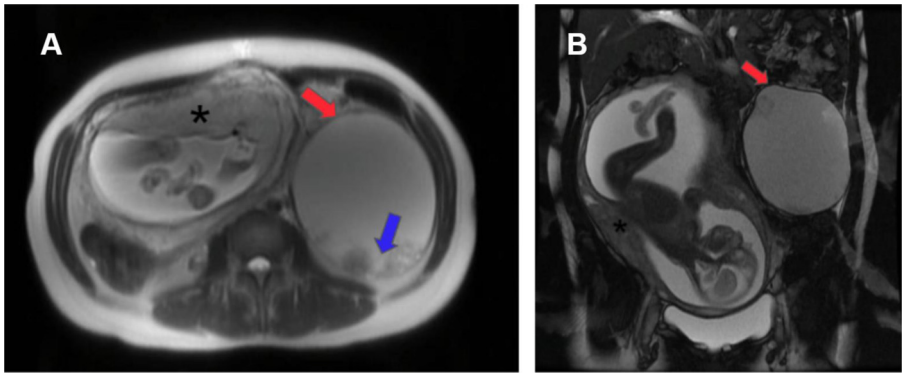


**Figure 1** Abdominal and pelvic MRI on T2-weighted imaging, axial plane (A) and coronal plane (B). Increased uterine cavity size due to pregnancy is observed, with right-sided lateralization due to the presence of a large cystic formation (red arrow) with well-defined borders and a nodular solid component, showing intermediate signal intensity in its posterior aspect (blue arrow), likely originating from the left adnexa. The placenta (*), located anteriorly in the body, shows normal morphology and signal.

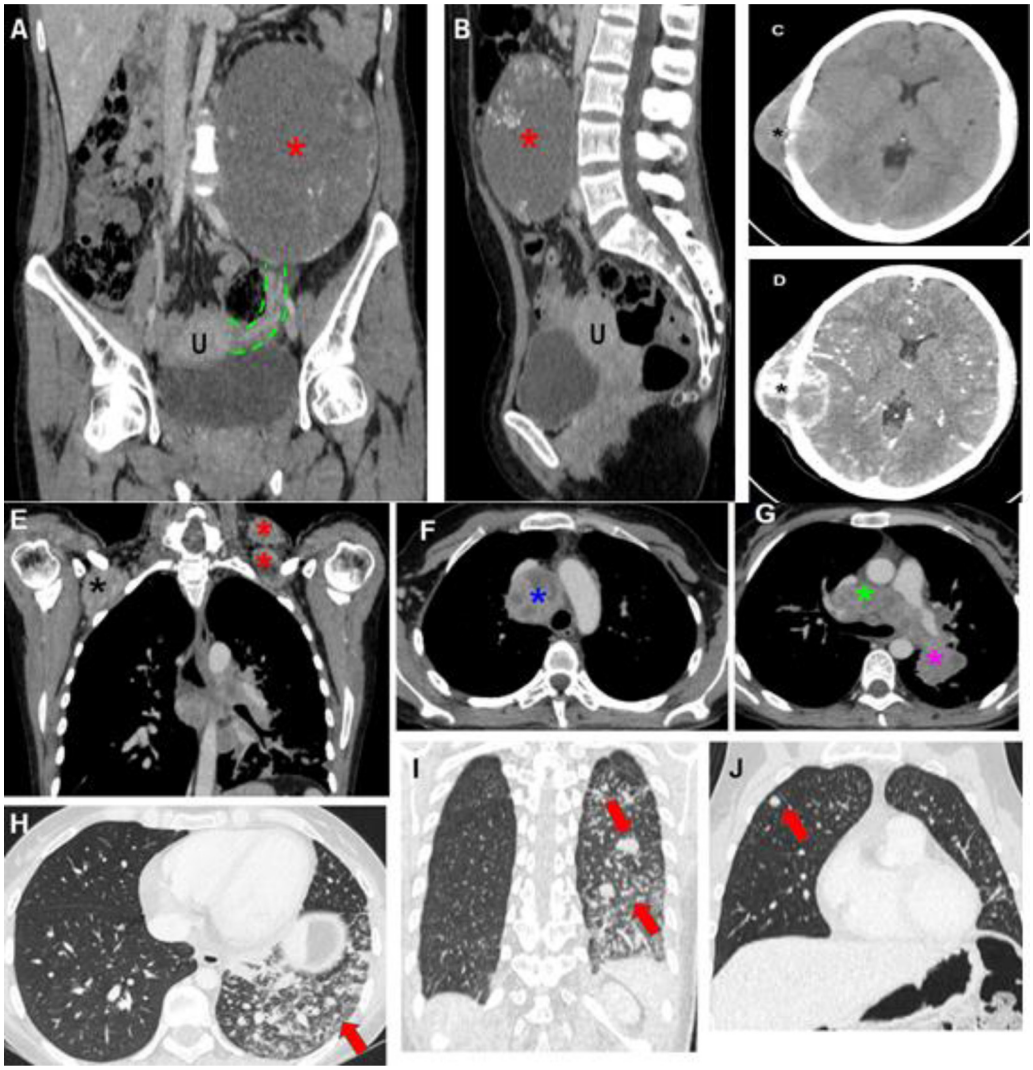


**Figure 2** Abdominal and pelvic CT with contrast, coronal (A) and sagittal section (B). Complex cystic formation (*), dependent on the left adnexa, with the left uterine tube (dotted green lines) communicating with the tumour; the solid component represents 30% of the tumour, and the uterus (U) shows normal morphology and size. Brain CT scan, axial view without and with contrast (C, D), shows a solid lesion (*), with a neoformative appearance, in the right parieto-temporal region, causing bone erosion and compression of brain parenchyma. Chest CT scan with contrast in mediastinal window (E–G) and parenchymal window (H–J), in axial view (F–H) and coronal view (E, I, J), which shows solid nodular lesions with a neoformative appearance in the left supraclavicular (*), right axillary (*), right paratracheal (*), *subcarinal* (*), and left hilar regions (*), as well as multiple solid pulmonary nodes (red arrows).

lymphoid tissue infiltrated by sheets of large, polygonal cells with eosinophilic cytoplasm, hyperchromatic nuclei with irregular borders, and conspicuous nucleoli (Fig. 3). Additionally, areas of necrosis and a few multinucleated giant cells were identified. Immunohistochemistry for HPL, pankeratin, vimentin, and CK8/18 was positive, along with focal positivity for hCG and a Ki-67 index of 25%. Immunohistochemistry was negative for p63, inhibin, PLAP, CD30, AFP, SALL4, HMB45, Melan A, S100, actin, ER, PR, WT1, and E-cadherin. These findings were consistent with metastasis from a placental site trophoblastic tumour (PSTT). The general CT study revealed a metastatic lesion in the cranial vault of the right parietal region, metastatic-appearing lymphadenopathy in the supraclavicular, posterior cervical, mediastinal, and pulmonary hilum regions, as well as multiple nodules in both lung fields and a 1.2 cm metastatic-appearing nodular lymph node in the left breast region (Fig. 2). Blood tests showed elevated bHCG levels up to 2000 mIU/ml.

The patient received chemotherapy, three courses of EMACO, and whole-brain radiotherapy sessions. However, her condition had a torpid progression and she died 5 months after the diagnosis.

## Discussion

Placental site trophoblastic tumour was historically described as a benign trophoblastic tumour known as trophoblastic pseudotumor.[3] However, subsequent studies

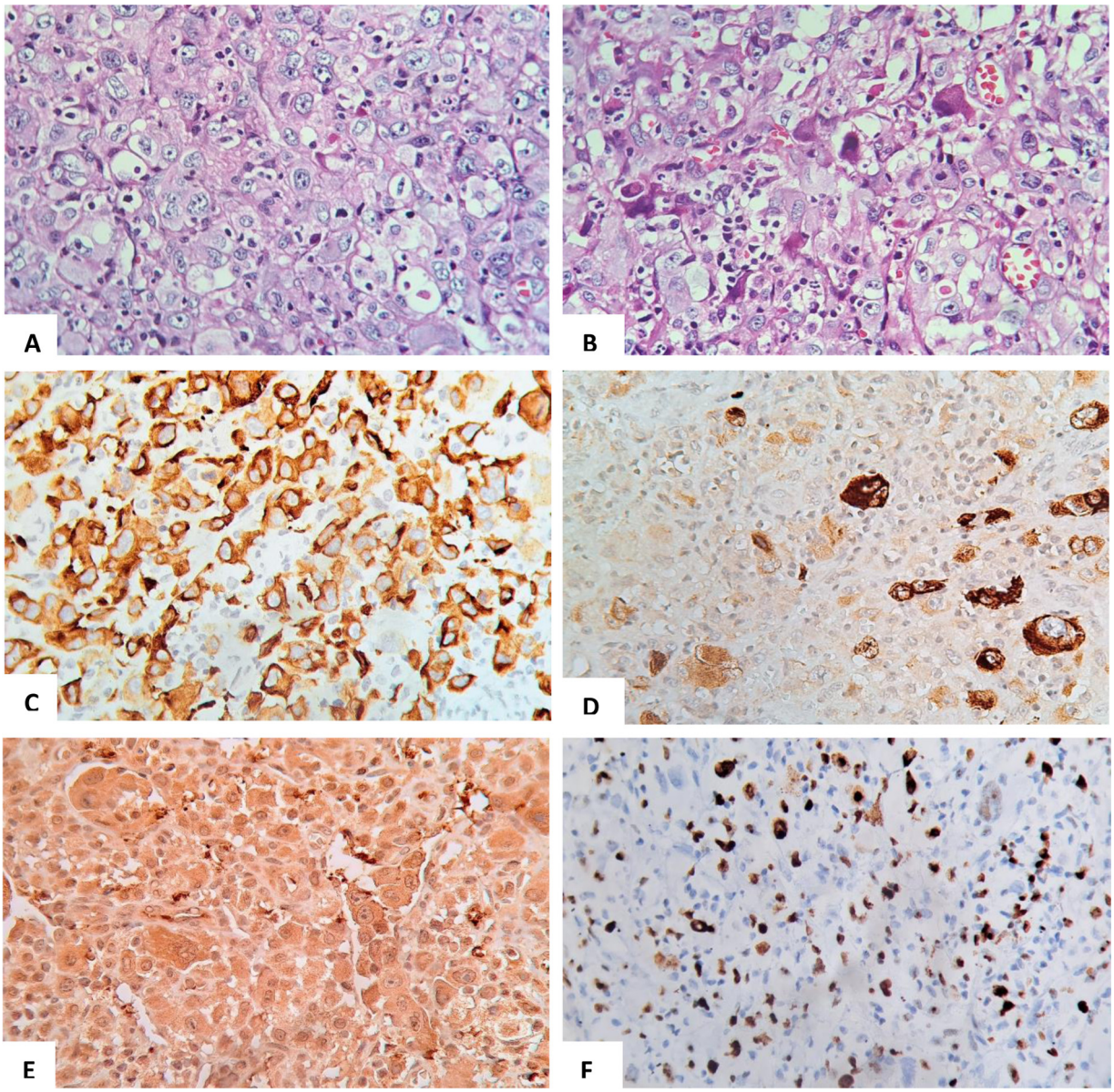


**Figure 3** Microscopy. (A) Photomicrograph showing large cells with abundant eosinophilic cytoplasm, high nuclear grade, and prominent nucleoli (H–E, 100×). (B) The presence of some syncytiotrophoblast-like cells is observed. (C) Relevant immunohistochemistry: positive for pankeratin (cytokeratin). (D) Focal positive hCG. (E) Diffuse positive staining for HPL. (F) Ki67, it was estimated as 30%.

demonstrated its malignant potential. It accounts for 0.25–5% of all trophoblastic tumours.[4] It originates from intermediate trophoblastic cells, which are normally found in distal villi and attach to the endometrium, invading the decidual and spiral arteries to remodel the blood vessels at the placental bed level to provide nutrition to the embryo.[5]

The most frequent location of this neoplasm is within the uterine cavity. However, cases of primary extrauterine presentation have been described, leading to the hypothesis that this neoplasm initially arises in the uterine cavity and may spontaneously regress after early dissemination, leaving no evidence of its intracavitary origin.[6] In this regard, extrauterine presentations can be divided into two groups: those occurring in areas specific to the female genital tract, such as the cervix, vagina, and uterine tube, possibly due to local extension, with regression of the primary intracavitary focus, and those diagnosed in more distant sites such as the lung, liver, and brain, indicating true metastases. Due to their rarity, there are no epidemiological data available on extrauterine presentations. Recurrence and metastasis of this neoplasm occur in 25–30% of patients.[4]

The age range for presentation of this neoplasm is broad, from 20 to 63 years, typically occurring after a pregnancy of any type -normal, ectopic, or molar. The interval between pregnancy and presentation ranges from months to years; however, a presentation after 48 months is considered a poor prognostic factor.[7] Irregular vaginal bleeding is the most commonly reported clinical feature in these cases. Serum

hCG levels usually remain persistently elevated but at low levels.

The macroscopic appearance of primary intrauterine tumours typically manifests as a solid, nodular mass that is circumscribed, with areas of haemorrhage and necrosis, deeply infiltrating the myometrium.[4]

Microscopically, it appears as sheets of large, round or polyhedral cells, generally mononucleated. Scattered binucleated or multinucleated syncytiotrophoblast-like giant cells may also be present.[8] The nucleus is usually pleomorphic with severe atypia and a low mitotic count of 1–2 mitoses/mm$^2$. Vascular invasion is common.

The main differential diagnoses include epithelioid trophoblastic tumour (ETT), undifferentiated carcinoma, squamous cell carcinoma, choriocarcinoma, and leiomyosarcoma. The immunohistochemical markers typically expressed are HPL, pankeratin, CK 18, MUC 4, CD 10, MEL-CAM, GATA 3, and a generally low Ki-67 index, of less than 10%. However, cases with higher values have been reported, so it is recommended to consider a Ki-67 index of less than 30%, especially when making a differential diagnosis from other trophoblastic tumours such as choriocarcinoma.[8] It shows negativity for p63 and may be focally positive for hCG and inhibin.

Histological features associated with poor prognosis include tumour cells with clear cytoplasm, deep myometrial invasion, extensive coagulative necrosis, and a high mitotic count (>2.5 mitoses/mm$^2$).[9] FIGO staging is the most important prognostic factor.

Upon microscopic examination of the present case, the observation of sheets of large cells with abundant eosinophilic cytoplasm infiltrating the lymph node initially raised suspicions of metastasis from squamous carcinoma, epithelioid sarcoma, and melanoma. However, the identification of multinucleated syncytiotrophoblast-like giant cells was pivotal in considering gestational trophoblastic neoplasia among the differential diagnoses. This diagnostic suspicion was reported to the attending physician, who subsequently requested serum bHCG levels. The histomorphology and immunophenotype were consistent with PSTT.

Diagnosing a biopsy in a case like this can be challenging for pathologists, underscoring the critical role of thorough evaluation of histomorphology to suspect this neoplasm. The correlation between microscopic findings and immunohistochemistry with the laboratory values of bHCG and imaging revealing an ovarian tumour without evidence of an intrauterine tumour suggests this case as a primary ovarian PSTT. Such cases are rare, with only a few reported instances,[10] and, in this context, likely developed during pregnancy

## Ethical disclosure

**Protection of persons and animals.** The authors declare that no experiments involving humans or animals were conducted for this research.

**Data confidentiality.** The authors declare that they have adhered to the protocols of their respective institutions regarding the publication of patient data.

**Right to privacy and informed consent.** The authors declare that no patient data appear in this article.

The samples stored at the Anatomical Pathology departments were collected for diagnostic purposes to monitor and promote patient health, not for experimental procedures.

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## Conflict of interest

The authors of this case report declare that they have no conflicts of interest.

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