Metastatic Intracranial Choriocarcinoma in the Absence of a Primary Lesion: A Case Report

Steven-Andrés Piña-Ballantyne[1] Eunice-Jazmín Espinosa-Aguilar[2]
Ana-Laura Calderón-Garcidueñas[1] Rebeca de Jesus Ramos-Sánchez[3]

[1] Department of Neuropathology, Instituto Nacional de Neurología y Neurocirugía Manuel Velasco Suárez, Mexico City, Mexico
[2] Internal Medicine Department, Clínica-Hospital Mérida, Yucatán, Mexico
[3] Department of Neuroradiology, Instituto Nacional de Neurología y Neurocirugía Manuel Velasco Suárez, Mexico City, Mexico

Address for correspondence Ana-Laura Calderón-Garcidueñas, PhD, MD, Department of Neuropathology, Instituto Nacional de Neurología y Neurocirugía, Av Insurgentes Sur 3877, La Fama, Tlalpan, 14269 Ciudad de México, CDMX (e-mail: ana.calderon@innn.edu.mx).

Asian J Neurosurg 2025;20:155–159.

Abstract

Intracranial choriocarcinoma is a rare and aggressive neoplasm characterized by the proliferation of trophoblastic tissue. Although choriocarcinoma most commonly arises in the uterus as a component of gestational trophoblastic neoplasia, instances of intracranial choriocarcinoma are exceptionally uncommon. We report a case of intracranial choriocarcinoma without any evidence of a tumor elsewhere. A 25-year-old woman presented with a history of 1 month of evolution with right frontal hemicranial headache, followed by visual disturbances, otalgia, and diplopia. On neurological examination, she was conscious, cooperative, and well-oriented; a grade 1 bilateral papilledema, left homonymous hemianopsia, and sixth cranial nerve paresis, with diplopia, were detected. Neuroimaging showed a right parieto-occipital lesion with features mimicking an atypical meningioma. After surgical resection, a diagnosis of choriocarcinoma was issued. Primary intracranial choriocarcinomas are typically located in the sellar and pineal regions. The occurrence of this tumor within the occipital lobe suggested metastasis; however, a primary tumor in the thoracic or abdominal organs was not observed and a delayed metastasis was considered. This case highlights the diagnostic challenges associated with intracranial choriocarcinoma.

Keywords
- intracranial choriocarcinoma
- parieto-occipital lobes
- woman
- left homonymous hemianopsia
- delayed metastasis

Introduction

Primary intracranial germ cell tumors (PIGCTs) comprise 1% of all primary brain tumors in adults.[1]

When an intracranial choriocarcinoma is documented, its location points to a primary or metastatic origin. Primary intracranial germ cell tumors (PIGCTs), including choriocarcinoma, comprise 1% of all primary brain tumors in adults,[1] and the most frequent sites are the pineal and sellar regions.[2] Locations outside these areas suggest metastatic disease. In cases of metastatic lesions, there are two possibilities, gestational choriocarcinoma or choriocarcinoma not associated with pregnancy.[3]

Gestational trophoblastic neoplasias (GTN) are a group of malignant tumors arising from trophoblastic cells (choriocarcinoma, invasive mole, placental site trophoblastic tumor,

article published online
October 10, 2024

DOI https://doi.org/10.1055/s-0044-1791712.
ISSN 2248-9614.

Thieme Medical and Scientific Publishers Pvt. Ltd., A-12, 2nd Floor, Sector 2, Noida-201301 UP, India

and epithelioid trophoblastic tumor). In this group, incidence of metastasis is between 3 and 21.4%.[3] Usually, in 90% of cases, brain metastasis is part of a disseminated tumor. However, in the 11.3% of the cases, brain metastasis is the only evidence of systemic disease.[4]

We present a case of a young woman with headache, ocular symptoms, and a right occipitoparietal lobe lesion with dural attachment, with no evidence of a primary lesion elsewhere. Choriocarcinoma was confirmed by histological analysis.

Case Report

A 25-year-old married woman with a history of three pregnancies and three children (5-year-old girl, 2-year-old boy, and 6-month-old baby) was referred for evaluation. No abnormal transvaginal bleeding was reported after the last pregnancy. The patient started a month before admission, with pulsating right hemicranial headache (frontal predominance), accompanied by nausea, vomiting, sonophobia, and photophobia. After a week, scotomas appeared in the left eye and 3 days later, intense bilateral otalgia, hyperthermia, and diaphoresis were added. She visited the emergency department of her local hospital, and a diagnosis of urinary tract infection was issued. Analgesics and antibiotics were prescribed, and the patient's condition was partially resolved. However, visual disturbances persisted, the headache worsened, and diplopia was added. Then, the patient was referred to our institute for further studies. Upon arrival, general examination was normal. The patient was conscious, and well-oriented. Grade I bilateral papilledema and left homonymous hemianopsia were documented. Also, she had a bilateral sixth cranial nerve paresis with diplopia.

Complete blood count, blood chemistry, clotting times, and serum electrolytes were normal. Cranial computed tomography (CT) scan showed an extra-axial heterogeneous right parieto-occipital lobes lesion with intense perilesional edema; the lesion was attached to the internal table of the diploe with secondary hyperostosis (►**Fig. 1**). Magnetic resonance imaging revealed dural insertion; therefore, an atypical meningioma was suspected. Dexamethasone 8 mg every 8 hours intravenously was initiated. The patient underwent a right occipitoparietal craniotomy with excision of the lesion. Upon dural opening, a darked-reddish parietal lesion with hard consistency was observed at the level of the extra-axial right precuneus; the lesion was regularly vascularized with a cleavage plane. An opaque-reddish ovoid tissue ($72 \times 45 \times 40$ mm), hemorrhagic when cut, was sent for histopathological study.

The tumor was composed of blood lakes delimited by two types of cells; some were cubic with a round, central nucleus (cytotrophoblast); and others were large, multinucleated (syncytiotrophoblast). Extensive areas of necrosis and hemorrhage were present. Although no mitotic activity was observed, Ki67 staining was positive in 90% of the neoplastic cells. The cells stained intensely with antibodies against

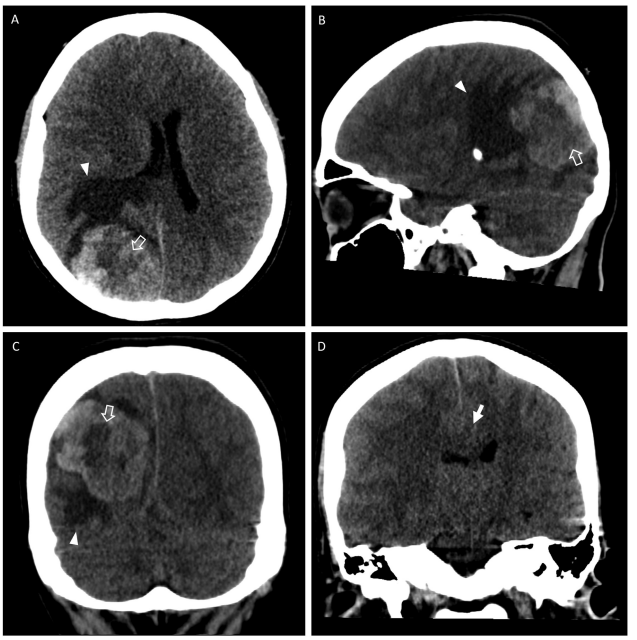

Fig. 1 Noncontrast cranial computed tomography: (**A**) axial, (**B**) sagittal, and (**C**, **D**) coronal. The right occipitoparietal lobes show a supratentorial, intra-axial, corticosubcortical lesion with partially defined and lobulated margins. It is heterogeneous, predominantly hyperdense (64 UH), with a low-density center that could suggest necrosis (hollow arrows). Vasogenic perilesional edema was associated (arrowheads) with narrowing of adjacent sulcus, right displacement of the midline, and right subfalcine hernia (white arrow).

chorionic gonadotropin and β-catenin, confirming the diagnosis of choriocarcinoma (►**Fig. 2**).

After the surgery, the patient referred loss of vision and complex visual hallucinations that consisted of seeing people and animals, which caused her a lot of anxiety. Neuro-ophthalmological examination showed simple bilateral conjunctival hyperemia, a bilateral visual acuity of 20/50, and abnormal eye mobility with endotropia at 30 prismatic diopters, and severe (+++) limitation of bilateral abduction, at the primary gaze position. A left homonymous hemianopia with macular damage was documented. Fundus examination showed papillae effacement, and hemorrhagic exudates. The macula showed waxy exudates. A final diagnosis of bilateral grade II acute papilledema with macular edema and bilateral VI cranial nerve paresis and a left homonymous hemianopsia in relation to right occipital lesion was issued.

The postsurgical imaging study showed residual tumor (►**Fig. 3**). Based on the diagnosis of choriocarcinoma and its location, a metastasis was suspected, and the patient was extensively searched for a primary lesion. Full-body CT did not reveal any abnormalities (►**Fig. 4**). The patient was referred immediately to an oncology institute for an integral treatment. There, a positron emission tomography-computed tomography (images not available) showed sclerosis in the right iliac artery; however, no areas of hypermetabolism were observed in relation to a primary site or other metastatic sites. Patient did not return for her oncological treatment to that institution.

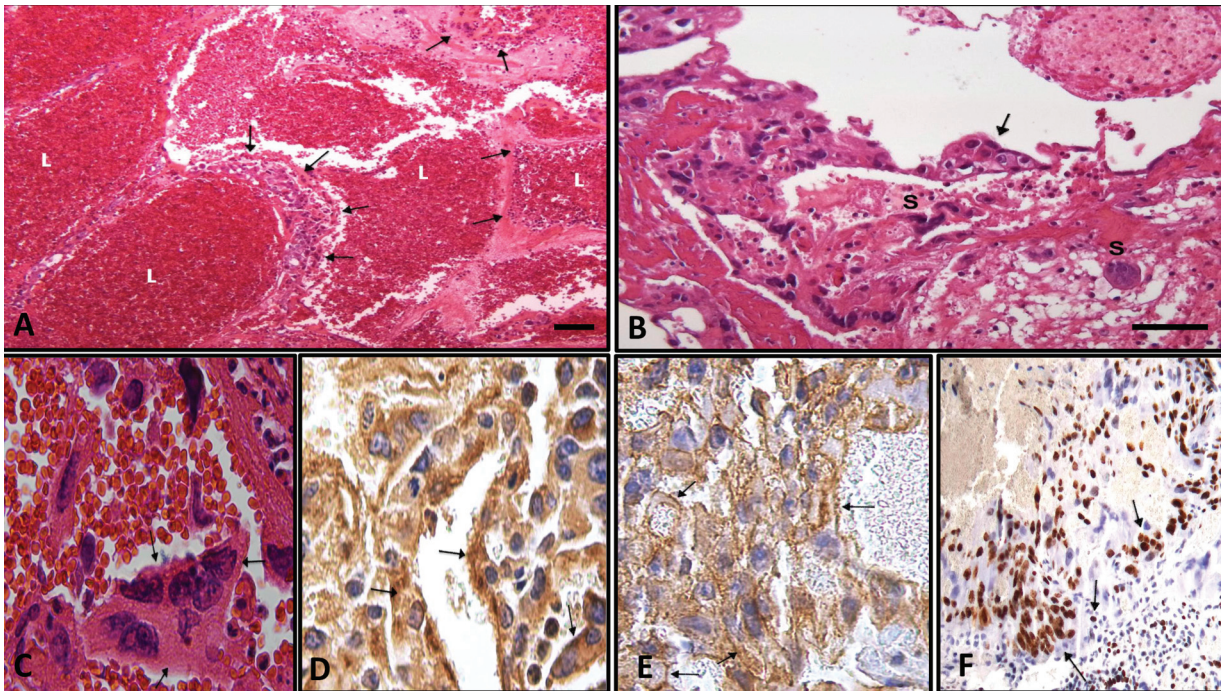

Fig. 2 (**A**) The tumor was composed of blood lakes (L), surrounded by at least two types of cells (arrows; hematoxylin and eosin [H&E]), 50X. (**B**) Cubic cells with a single nucleus (arrow), cytotrophoblast type, and large multinucleated cells (S) syncytiotrophoblast type, were observed. H&E 100X. (**C**) Detail of syncytiotrophoblast. H&E, 400X. Immunohistochemistry: (**D**) Chorionic gonadotropin, with cytoplasmic staining in syncytiotrophoblast. (**E**) Beta-catenin with membranous staining in the cytotrophoblast. (**F**) Ki67, nuclear staining in 80% of neoplastic cells (arrows).

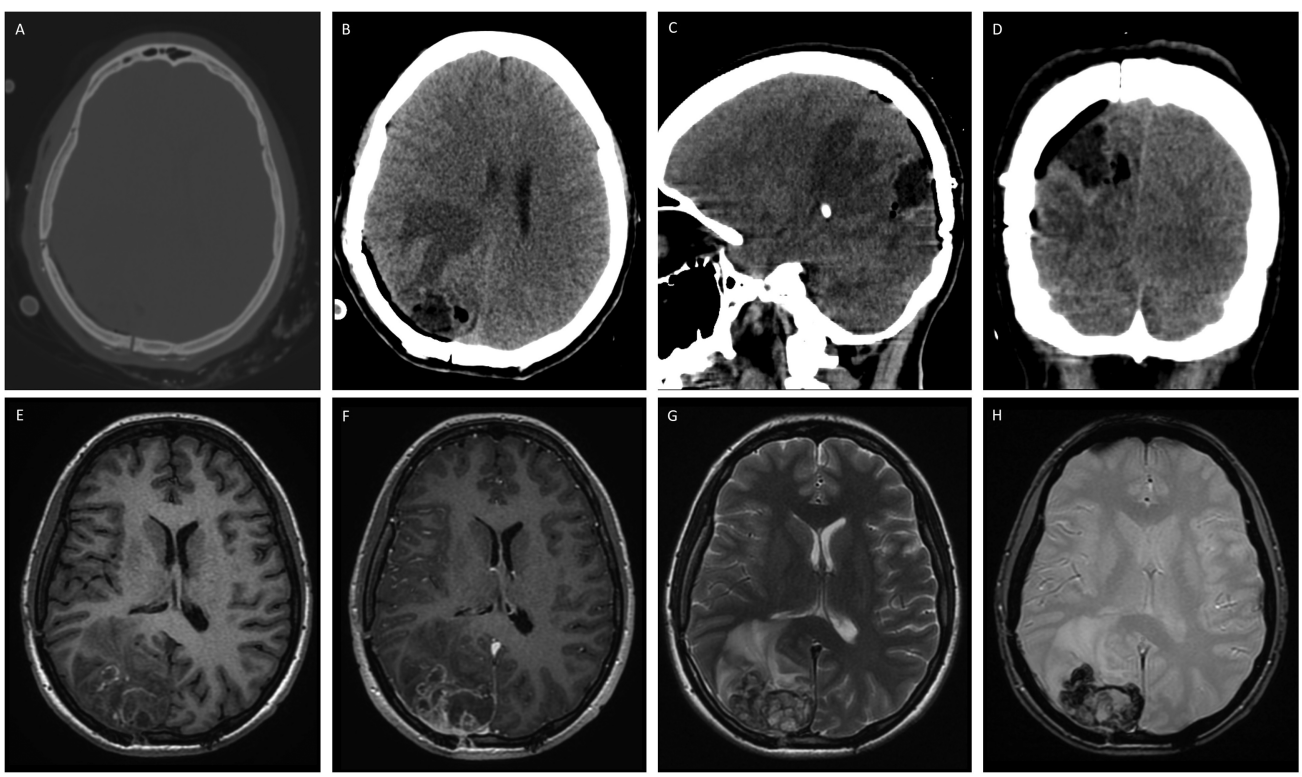

Fig. 3 Postsurgical noncontrast cranial computed tomography. Bone window (**A**) with postoperative changes due to right occipitoparietal craniotomy. Axial (**B**), sagittal (**C**), and coronal (**D**) with right occipitoparietal surgical cavity, pneumocephalus, and hyperdense margins that could correspond to postsurgical hemorrhage or residual tumor. Contrast-enhanced magnetic resonance imaging 2 months after surgery. Axial T1-weighted imaging (T1WI) (**E**), contrast-enhanced T1WI (**F**), T2WI (**G**), and susceptibility-weighted imaging (SWI; **H**) with heterogeneous residual tumor, which has hyperintense areas on T1, hypointensity on T2 and SWI corresponding to hemorrhage; heterogeneous enhancement was observed. Adjacent vasogenic edema persists, causing displacement of the right lateral ventricle.

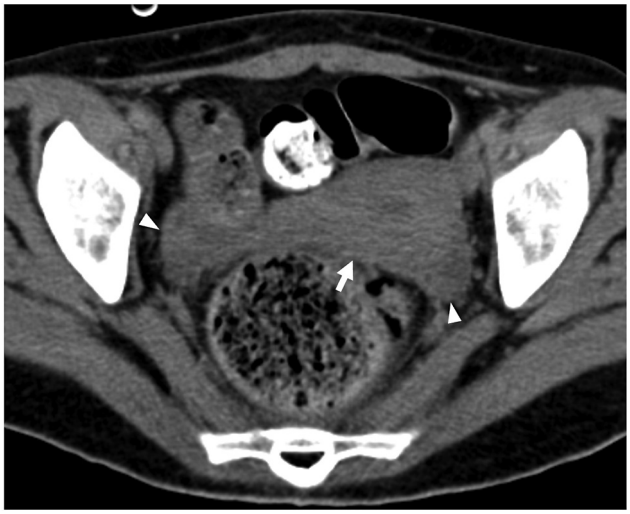

Fig. 4 Contrast-enhanced abdominal computed tomography. The uterus (white arrow) and both ovaries (arrowheads) are normal. No pelvic masses were observed.

Discussion

Choriocarcinoma is a highly vascular trophoblastic tumor. Trophoblast cells undergo differentiation into cytotrophoblast (mononuclear) and syncytiotrophoblast (multinuclear). Typically, choriocarcinoma develops within a gestational event, but nongestational-choriocarcinoma arises from germ cells in gonadal or extragonadal locations, such as the mediastinum, retroperitoneum, or pineal gland.[5]

In the case presented, owing to the location, the dural insertion, and the intra-tumoral necrosis, an atypical meningioma was considered at admission.[6] However, with the histopathological diagnosis and the location of the tumor, a search for a primary tumor outside the central nervous system began. It is known that choriocarcinoma spreads through lymphatic route (retroperitoneal lymph node system) and by hematogenous via. The most affected organs include the lungs, liver, and brain (especially frontal lobes).[7] After ruling out a primary lesion, delayed metastasis was suspected due to the location and the relatively recent pregnancy and birth. The patient did not report any gynecological problems during pregnancy or postpartum. There are studies of choriocarcinoma following term pregnancy, but patients present generally, persistent vaginal bleeding,[8] with a maximum of 19 weeks delay from onset of symptoms to treatment.[9] The presentation of choriocarcinoma after a molar pregnancy is something that most physicians are familiar with, however, after a full-term pregnancy and apparently a normal postpartum period is an exceptional event.[10] In fact, gestational choriocarcinoma occurs after molar pregnancies (50%), term pregnancies (25%), and other gestational events (35%).[11] However, there are few reported cases in the same situation of our case. A 22-year-old woman presented with left parietal metastasis, seizure syndrome, and intracranial hypertension. The histopathological diagnosis was choriocarcinoma and after resection, the β-human chorionic gonadotrophin (β-HGC) hormone levels were 20,000 IU. The patient had had a normal pregnancy and delivery 2 years previously and at the time of surgery she had no gynecological abnormalities, nor was a primary lesion found.[12]

In our case, the diagnosis of choriocarcinoma was confirmed at the oncology hospital, but after her initial visit and the completion of extension studies, the patient no longer returned to that institution and we do not know her subsequent evolution. However, although brain metastases imply stage IV disease, in the case of gestational choriocarcinoma, the chances of survival, with appropriate treatment, are good.[13] In a French series of 21 patients with GTN and brain metastasis, three (14%) patients died within 1 month due to cerebral hemorrhage, three (14%) patients died 1 month after starting treatment, and the total 5-year survival was 70%.[13]

The term GTN includes pathologies such as invasive mole, choriocarcinoma, placental site trophoblastic tumor, epithelioid trophoblastic tumor, and atypical placental site nodule. One case in 40,000 pregnancies will present with choriocarcinoma, while this tumor is expected in 1 in 40 hydatidiform moles. The diagnosis of GTN is based on serum levels of (β-HGC) and this marker is basic to evaluate response to treatment.[14]

Treatment of GTN depends on its classification. Using the International Federation of Gynecology and Obstetrics (FIGO) classification, the patient corresponded to stage IV (GTN extending to all other metastatic sites). According to the modified World Health Organization (WHO) prognostic index score, she had a high score (>6). For those low-risk GTN (FIGO/WHO score <6) a medical treatment with one of two single-agent drugs, methotrexate (MTX, methotrexate with folinic acid, 8-day and MTX 5-day regimen) or actinomycin-D, is recommended, obtaining complete remission between 81.8 and 83.5% in the low-risk group. Multiagent therapy is used for high-risk patients. EMA-CO regimen (etoposide, methotrexate, actinomycin D, cyclophosphamide, vincristine) is recommended, with a complete response in 71 to 78% of cases and long-term survival rates of 85 to 94%.[14] In high- and low-risk groups, chemotherapy should be continued for at least two to three consolidation courses after the first hCG normalization. In the other hand, immunotherapy is indicated in drug-resistant disease.[14]

Choriocarcinoma is a very chemosensitive tumor; however, hysterectomy in low-risk patients is indicated if the patient is satisfied with the number of children, in chemoresistant disease, or in cases with severe vaginal hemorrhage.[15]

In the case of brain metastases and diagnosis of choriocarcinoma, systemic therapy is the frontline treatment; radiotherapy is considered for resistant/recurrent disease or in clinical trials. Surgery is indicated to relieve intracranial pressure and bleeding.[16]

Finally, knowledge of the genetics of gestational choriocarcinoma may provide new diagnostic and treatment strategies in the future. This tumor is characterized by overexpression of epidermal growth factor receptor, TP53 and *MDM2* proto-oncogene[17] and aberrations of methylation pattern (hypermethylation is strongly associated with gene downregulation).[18]

Conclusion

Although rare, gestational choriocarcinoma can manifest as a late or delayed metastasis, after a normal delivery, without gynecological alterations during or after pregnancy.

Authors' Contributions

S.A.P.B. and E.J.E.A. collected data and wrote the first draft of the manuscript with support from A.L.C.G. A.L.C.G. diagnosed the tumor and conceived the case report, supervised, and contributed to the final version of the manuscript. R.J.R.S. contributed to the interpretation of the neuroimages and analysis of the data. All authors provided critical feedback and helped shape the research, analysis, and manuscript.

Ethical Approval

The study was conducted according to the principles established in the Declaration of Helsinki.

Funding

None.

Conflict of Interest

None declared.

Acknowledgments

Our deep gratitude to Noemi Gelista-Herrera, Israel Torres-Ramirez de Arellano, and Brenda Peralta-Rodriguez for their wonderful support in histology and immunohistochemistry.

References

1 Levin VA, Giglio P, Kyritsis AP. The management of gliomas, medulloblastoma, CNS germ cell tumors, and carcinomas metastatic to the CNS. In: Cavalli F, Hansen H, Kaye S, eds. Textbook of Medical Oncology. Martin Dunitz, London, England2005: 415–430

2 Lv XF, Qiu YW, Zhang XL, et al. Primary intracranial choriocarcinoma: MR imaging findings. AJNR Am J Neuroradiol [8003708]. 2010;31(10):1994–1998. Accessed March 18, 2024 at: https://www.ajnr.org/content/31/10/1994

3 Xiao C, Yang J, Zhao J, et al. Management and prognosis of patients with brain metastasis from gestational trophoblastic neoplasia: a 24-year experience in Peking union medical college hospital. BMC Cancer 2015;15:318

4 Piura E, Piura B. Brain metastases from gestational trophoblastic neoplasia: review of pertinent literature. Eur J Gynaecol Oncol 2014;35(04):359–367

5 Cheung AN, Zhang HJ, Xue WC, Siu MK. Pathogenesis of choriocarcinoma: clinical, genetic and stem cell perspectives. Future Oncol 2009;5(02):217–231

6 Salah F, Tabbarah A, ALArab Y N, et al. Can CT and MRI features differentiate benign from malignant meningiomas? Clin Radiol 2019;74(11):898.e15–898.e23

7 Ngan HYS, Seckl MJ, Berkowitz RS, et al. Diagnosis and management of gestational trophoblastic disease: 2021 update. Int J Gynaecol Obstet 2021;155(suppl 1, suppl 1):86–93

8 Miller JM Jr, Surwit EA, Hammond CB. Choriocarcinoma following term pregnancy. Obstet Gynecol 1979;53(02):207–212

9 Nugent D, Hassadia A, Everard J, Hancock BW, Tidy JA. Postpartum choriocarcinoma presentation, management and survival. J Reprod Med 2006;51(10):819–824

10 Yousefi Z, Mottaghi M, Rezaei A, Ghasemian S. Abnormal presentation of choriocarcinoma and literature review. Iran J Cancer Prev 2016;9(02):e4389

11 Bogani G, Ray-Coquard I, Mutch D, et al. Gestational choriocarcinoma. Int J Gynecol Cancer 2023;33(10):1504–1514

12 Sharma M, Velho V, Binayake R, Tiwari C. Primary intracranial choriocarcinoma presenting as a ring-enhancing lesion: a case report and review of literature. Asian J Neurosurg 2017;12(01): 85–88

13 Gavanier D, Leport H, Massardier J, et al. Gestational trophoblastic neoplasia with brain metastasis at initial presentation: a retrospective study. Int J Clin Oncol 2019;24(02):153–160

14 Lukinovic N, Malovrh EP, Takac I, Sobocan M, Knez J. Advances in diagnostics and management of gestational trophoblastic disease. Radiol Oncol 2022;56(04):430–439

15 Piątek S, Szczęsny N, Szymusik I, et al. Fertility-sparing treatment in gestational choriocarcinoma: evaluating oncological and obstetrical outcomes in young patients. Med Sci Monit 2023;29:e942078

16 Tsai J, Vellayappan B, Venur V, et al. The optimal management of brain metastases from gestational trophoblastic neoplasia. Expert Rev Anticancer Ther 2022;22(03):307–315

17 Di Fiore R, Suleiman S, Felix A, et al. An overview of the role of long non-coding RNAs in human choriocarcinoma. Int J Mol Sci 2021; 22(12):6506

18 Szabolcsi Z, Demeter A, Kiraly P, et al. Epigenetic dysregulation of trophoblastic gene expression in gestational trophoblastic disease. Biomedicines 2021;9(12):1935

