

## **Multiple Cerebral Infarctions Revealing Metastatic Choriocarcinoma**

**Aasmi H\*, Khattab H, Sikkal A, El Otmani H, Rafai MA and El Moutawakil B**

*Department of Neurology, University of Hassan II Casablanca, Casablanca, Morocco*

**\*Corresponding author:** Aasmi H, Department of Neurology, University of Hassan II Casablanca, Casablanca, Morocco

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### **Abstract**

**Introduction:** Choriocarcinoma is a highly malignant trophoblastic neoplasia with a propensity for early metastasis, particularly to the lungs, liver, vagina, and Central Nervous System (CNS). The latter, a rare manifestation, can sometimes be the initial clinical presentation.

**Observation:** We report the case of a 44-year-old female who presented with proportional and total left hemiplegia and lateral hemianopsia. Brain imaging revealed multiple bilateral ischemic strokes the different vascular territories. The D-dimer level was elevated to 510 ng/mL, and the serum human chorionic gonadotropin ( $\beta$ -hCG) level was  $>1,000$  IU/mL. Metastatic choriocarcinoma was diagnosed, and chemotherapy was initiated.

**Conclusion:** Cancer-related coagulopathy, micro tumor emboli, or both could be implicated in the pathogenesis of cerebral infarctions. In such a scenario, serum measurement of  $\beta$ -hCG should be included in the panel of tumor markers in cases of ischemic stroke in young women.

**Keywords:** Choriocarcinoma; Stroke; Gestational trophoblastic disease; Metastases

### **Introduction**

Choriocarcinoma is a clinical manifestation within the spectrum of Gestational Trophoblastic Disease (GTD), which is a highly malignant form that can rapidly spread through the bloodstream to the lungs, vagina, liver, kidneys, ovaries, and brain. Approximately 20% of choriocarcinoma patients experience central nervous system (CNS) involvement, with clinical presentations including intracranial hypertension, intracerebral hemorrhage, and stroke [1,2]. We report a case of metastatic choriocarcinoma that was incidentally discovered during the evaluation of a patient who presented with multiple bilateral strokes.

### **Case Report**

A 44-year-old woman presented, with a history of miscarriage in 2019 and uninvestigated uterine bleeding since October 2022. She was admitted in December 2022, because of left hemiplegia with facial palsy and language disturbances. These symptoms were preceded by behavioral changes, characterized by agitation and incoherent speech, developing progressively over the preceding month. Physical examination revealed confusion and left-sided hemiplegia. Brain Magnetic Resonance Imaging (MRI) revealed multiple bilateral ischemic strokes involving the carotid and vertebrobasilar territories (**Figure 1**). Owing to clinical worsening on the second day of hospitaliza-

tion, a cerebral CT scan showed a new ischemic stroke of the right middle cerebral artery (**Figure 2**).

The Electrocardiography and transthoracic echocardiography revealed no abnormalities. Transesophageal echocardiography could not be performed because of agitation. The hemogram, sedimentation rate, electrolytes, and renal, hepatic, and thyroid functions were normal. LDL cholesterol level was 1.52 g/L, and D-dimer levels were elevated at 510 ng/L.

Lumbar puncture could not be performed because of the mass effect observed in the control imaging. The multiple nature of the strokes suggests an embolic origin. Given the history of uterine bleeding, tumor-related causes were considered. Among the indicated tumor markers,  $\beta$ -hCG levels were elevated ( $>15,000$  mIU/mL with a normal range  $<100$  mIU/mL), increasing to 44,574 mIU/mL after 5 days. Thoraco-abdominopelvic Computed Tomography (CT) revealed the presence of a hypodense and heterodense endoluminal content at the level of both the left lower lobar artery and the left lower pulmonary vein without involvement in other locations.

The combination of this radiological appearance and the elevation of  $\beta$ -HCG in a young female patient strongly suggested gestational trophoblastic disease.

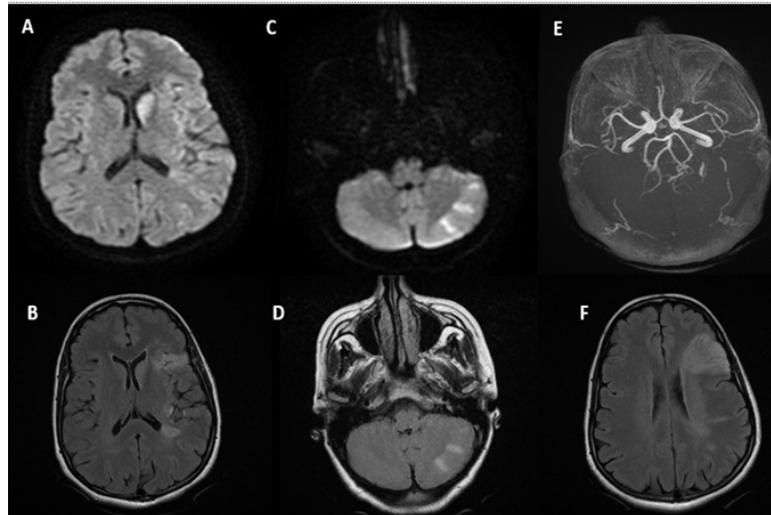


Figure 1: Brain MRI showing multiple ischemic strokes in different territories (A, B, C, D, F) with normal arterial MR angiography (E).



Figure 2: Brain CT scan revealing a new contralateral ischemic stroke: Right Sylvian ischemic stroke with mass effect.

Curative anticoagulation with low molecular weight heparin (LMWH) was initiated before transferring the patient to the oncology department for further management.

Meanwhile, the  $\beta$ -hCG levels continued to increase (66,019 mIU/mL). The clinical course was marked by the emergence of cerebral metastases, and the patient died one month after the vascular event (Figure 3, 4).

## Discussion

Strokes are common in cases of cancer, occurring in 15% of patients and significantly worsen their prognosis [3]. The frequency of ischemic stroke is comparable to that of cerebral hemorrhage [4]. Strokes can occur either following the initial cancer diagnosis [5] or preceding the diagnosis of the cancerous condition, as described in our case [6]. The first major autopsy study, conducted in 1985 by Graus et al. demonstrated that the most common complication of the central nervous system in cancer patients was metastasis, followed by cerebral infarction and hemorrhage [7]. It has also been reported that patients experiencing stroke during active cancer are typically younger, and cryptogenic strokes are more severe and more frequent [3].

The time interval between cancer diagnosis and stroke varies widely and depends on the cancer type. In fact, solid tumors

tend to develop strokes later than malignant hematologic conditions [8]. Graus et al. described the primary clinical presentation of strokes in cancer patients as more resembling diffuse encephalopathy rather than a typical sudden-onset with focal deficits [7]. Our patient also exhibited features of encephalopathy, characterized by psychiatric disturbances and a confusional state, well before acute stroke presentation. This could be attributed to the diverse mechanisms of stroke in patients with a cancerous condition, which may be directly related to cancer or caused by its complications, such as coagulation disorders, infections, leptomeningeal extension, or therapeutic interventions (eg. Chemotherapy and radiotherapy...) [7,9].

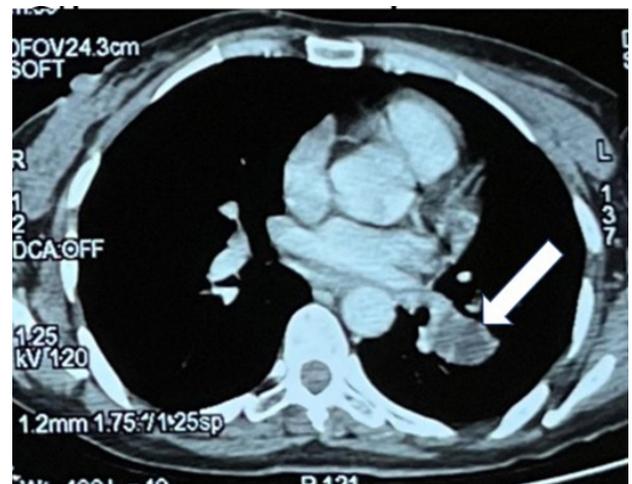


Figure 3: Thoracic CT scan revealing a transcissural process at the level of the left lower lobar artery.

Generally, cancer-associated ischemic strokes are described as affecting multiple vascular territories [3,10,11], accompanied by elevated D-dimer levels and a pro-inflammatory component such as low hematocrit and elevated CRP levels [12-15], as well as fibrin degradation products [12-14] a tumor marker can further support the diagnosis [16].

The management of cancer-associated stroke depends on the event type. For ischemic stroke, intravenous thrombolysis may be considered, with a wide indication for anticoagulants. Additionally, hemorrhage and cerebral venous thrombosis are managed according to established protocols [9].

In addition to cardiovascular origins, whenever faced with multiple lesions.

Despite the generally favorable prognosis of choriocarcinoma

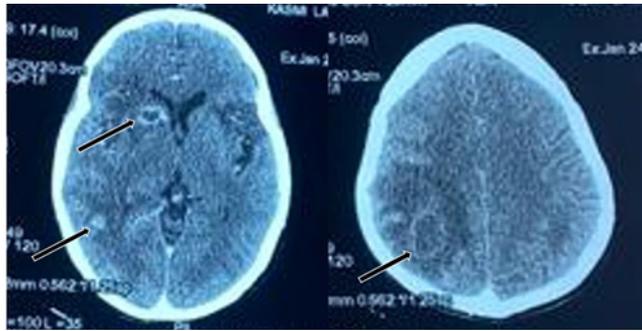


Figure 4: Brain CT with contrast injection showing multiple brain metastases.

owing due to its chemosensitivity, the comorbidity with a vascular event darkens the prognosis and increases the mortality rate [3].

In our case, choriocarcinoma as a tumor entity, was characterized by its high metastatic potential and chemosensitivity. Its diagnosis is primarily based on biological markers, specifically plasma  $\beta$ -hCG levels [17,18]. This condition develops rapidly and metastasizes to the lungs and liver and less frequently to cerebral blood vessels, causing thrombosis or more commonly, the formation of a neoplastic aneurysm, leading to ischemic strokes or intraparenchymal hemorrhage, respectively [5,19,20].

This clinical vignette adds to the various observations in the literature highlighting the association between cancer and stroke, emphasizing the importance of considering neoplastic pathology.

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