Case Report

Histology of a cerebral hemorrhage: AVM as a seat of a metastatic choriocarcinoma

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A B S T R A C T

Introduction: There are published cases of cerebral hemorrhage secondary to vascular alterations caused by choriocarcinoma metastases. However, it is extremely rare to find this type of bleeding secondary to an association of such a metastasis with a brain arteriovenous malformation (AVM).

Clinical case: We present the case of a 19-year-old male who came to the Emergency Department complaining of intense headache of abrupt onset. His physical examination revealed a striking increase in size of the right testicle of tumoral origin. Chest X-ray evidenced metastasis to the lungs and a brain CT showed a frontal hemorrhage of probably metastatic origin. The latter eventually progressed to cause the death of the patient. Pathology of the brain hematoma disclosed a choriocarcinoma within the brain AVM nidus.

Conclusions: The case presented is an extremely rare confluence of choriocarcinoma brain metastasis within an AVM. The hemorrhagic onset could have been secondary to bleeding from either of the two histological components of the subjacent mixed pathological lesion.

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Histología de un hematoma cerebral: MAV como asiento de una metástasis de coriocarcinoma

R E S U M E N

Introducción: Aunque se han descrito casos de hemorragia cerebral secundaria a anomalías vasculares inducidas por metástasis de coriocarcinomas, es excepcional el que una hemorragia cerebral se deba a una asociación de malformación arteriovenosa con metástasis de coriocarcinoma.

Caso clínico: Presentamos el caso de un paciente varón de 19 años que acudió a urgencias por cefalea brusca, intensa. Su exploración física demostró un tumor testicular de gran tamaño que probablemente había originado una masa de tipo coriocarcinoma que había causado la hemorragia cerebral. Se evidenció metástasis pulmonar de coriocarcinoma e imágenes de tomografía computarizada que demuestran una malformación arteriovenosa cerebral con hemorragia de probable etiología metastática. El paciente falleció días después de la llegada a urgencias.

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Introduction

Metastatic tumors are known causes of brain hemorrhages, particularly, the metastases of choriocarcinoma which hemorrhage in a high percentage of cases. Cases of cerebral hemorrhages secondary to vascular alterations induced by metastatic choriocarcinomas have been published, mostly secondary to the presence of oncotic aneurysms originated by embolic fragments of tumor. These emboli damage the vessel wall and promote the formation of aneurysms or pseudoaneurysms, which can be observed pathologically in the tissue samples obtained by evacuating the hematoma. However, it is exceptional to find a brain hemorrhage secondary to a metastases embedded on a pre-existing arteriovenous malformation, and even more if considering a choriocarcinoma.

Clinical case

We present the case of a 19-year-old male, with no known clinical history of interest, admitted into the emergency department because of abrupt onset of severe frontal headache with associated vegetative courtship. In addition, he referred presenting dry cough for weeks. Clinical examination evidenced no neurological deficits but on general inspection there was a marked increase in the size of the right testicle up to 20 cm of diameter. The testicle tumor was of hard consistency, not painful to palpation and had no skin or scrotal alterations. There was also a 2–3 cm dermal nodule located in the left scapular region. The chest X-ray evidenced a pattern of “loose balloon” suggestive of metastases to both lung fields (Fig. 1). Brain CT revealed a 5 cm × 4 cm hyperdense lesion in the right frontal lobe, with associated vasogenic edema causing mass effect and midline shift, suggestive of hemorrhage secondary to brain metastases (Fig. 2). The patient thus had an admission suspicion diagnosis of testicle neoplasm with skin, lung and brain metastases.

The tumor of the testicle was immediately biopsied and chemotherapy was planned in view of the pathological results. The sample consisted of a mixed germ cell tumor: 90% endodermal sinus tumor, 5% choriocarcinoma and 5% teratoma. Seventy-two hours after the surgery, while the patient was about to receive the first cycle of chemotherapy, he suddenly presented a marked neurological deterioration with decrease of the level of consciousness to GCS = 4, as well as pupil-
frontal craniotomy although bilateral mydriasis had already appeared. After surgery no neurological improvement was achieved, and the patient finally died. The pathological anatomy of the brain hematoma surgically evacuated evidenced an arteriovenous malformation associated to the presence of a germinal mixed tumor with choriocarcinoma histology predominance (Fig. 4).

**Discussion**

Our patient’s brain hematoma pathological diagnosis corresponded to a metastatic testicular tumor with predominantly choriocarcinoma histology sitting on the nidus of a brain arteriovenous malformation.

Testicular tumors have an incidence of approximately 5/100,000 population and constitute 5% of the genitourinary malignancies in humans. They are usually diagnosed in patients aged 20–40 years old. Thanks to aggressive oncological treatment, prognosis has improved in recent decades. Its etiology can be multifactorial, with influence of genetic and acquired factors. Their histology is usually mixed, showing teratoma, endodermal sinus tumor, and choriocarcinoma cell lines. Metastases tend to differ from the primary tumor pathology, generally expressing the more malignant histological variant. The spread can either be via lymphatic (except choriocarcinoma) or hematogenous (in the case of the nonseminoma testicular tumors), affecting mainly lung, liver and brain.

Another type of primary tumor that can metastasize in a similar way is the gestational choriocarcinoma, a malignant neoplasm originated in gestational trophoblast.

Both types of choriocarcinomas, non-gestational and gestational, metastasize to the brain in 10–20% of cases.

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**Fig. 3** – Cranial CT corresponding to neurological deterioration, showing frontal rebleeding.

Parenchymal rebleeding, with increase in the size of the hemorrhage and of the midline displacement (Fig. 3).

The patient was immediately transferred to neurosurgery and the brain hematoma was evacuated through a frontal craniotomy although bilateral mydriasis had already appeared. After surgery no neurological improvement was achieved, and the patient finally died. The pathological anatomy of the brain hematoma surgically evacuated evidenced an arteriovenous malformation associated to the presence of a germinal mixed tumor with choriocarcinoma histology predominance (Fig. 4).

**Fig. 4** – Histology of the surgical specimen (brain hematoma): (a) HE 4×, giant cells with granular, pink, amphophilic cytoplasm. Cytokeratin, CD30, PLAP positive. (b) HE 20×, solid patterns. Primitive epithelial type cells with minimal features of differentiation. High grade features of large, epithelioid, anaplastic cells with prominent nucleoli; indistinct cell borders. (c) HE 10× AVM. Thick-walled irregular blood vessels of arterial and venous types with intervening brain tissue. (d) HE 20×, features of AVM.
Intraparenchymal brain hemorrhage secondary to metastatic choriocarcinoma tumor, occur in up to 60% of these metastases. In the literature we have found reports of 25 cases of subarachnoid or intraparenchymal hemorrhages due to rupture of oncotic aneurysms secondary to choriocarcinomas. Neoplastic or oncotic aneurysms are rare, generally related to embolization from cardiac myxoma, bronchogenic carcinoma or choriocarcinoma. Most are located on the branches of the middle cerebral artery, with partial destruction of the vessel wall leading to rupture and bleeding. The mechanism of aneurysm formation is tumor embolus producing rupture of the vessel’s wall, followed by recanalization and dilatation of the wall.

Also, three cases of spontaneous subdural hematoma as the initial manifestation of the metastatic tumor, and even some cases of bleeding from arteriovenous fistula secondary to metastatic injury sitting on another primary tumor have been reported.

Scardigli et al. described a case of brainstem hemorrhage in a patient diagnosed of lung cancer, whose histological study of the extracted biopsy sample evidenced an arteriovenous malformation associated with metastatic cells. Shrestha et al. published another similar case, this time from a right parietal intraparenchymatous hemorrhage evacuated in a 22-year-old patient. The histology of the sample revealed the presence of cells suggestive of metastatic choriocarcinoma, which had been masked by the presence of an arteriographically diagnosed arteriovenous malformation.

It has been realized that the more frequent dissemination of a testicular germ-cell tumor is to lung and brain, so it is strongly recommended to perform brain imaging to all patients presenting with this type of primary tumor and lung involvement. Early detection of brain metastases may improve the prognosis of the patient by removing them, which improves neurological condition when affected but also reduces the high risk of bleeding from such metastases.

Our case is exceptional because of the pathologically demonstration of a metastatic choriocarcinoma sitting on a brain AVM, clinically manifested by bleeding which could have originated from any of the lesions.

Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.neucir.2014.08.001.

REFERENCES