Clinical Case Report

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Brain metastasis of choriocarcinoma presenting as multiple intracranial hematomas

A case report

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Abstract

Rationale: Choriocarcinoma is the most malignant type of gestational trophoblastic neoplasia. Brain metastasis is the main cause of death and disability in choriocarc- inoma patients. Brain metastasis of choriocarcinoma easily invades the vessel wall to form microaneurysms, so we have reason to believe that multiple intracerebral hemorrhage is related to neoplastic intracranial microaneurysms.

Patient concerns: We report a rare case of brain metastasis of choriocarcinoma that caused six hemorrhages in four lesions within 50 days and anterior cerebral artery aneurysm.

Diagnoses: We diagnosed multiple intracerebral hematoma, choriocarcinoma and intracranial aneurysms.

Interventions: Evacuation of hematoma by craniotomy.

Outcomes: The patient finally asked to terminate the treatment and was discharged. One month later, the patient died of upper gastrointestinal bleeding.

Lessons: more than 20 cases of oncotic aneurysm from choriocarcinoma have been reported in the English literature, but few had multiple hematomas. Therefore, this case is unique. Brain metastasis of choriocarcinoma should be considered when patients experience unexplained cerebral hemorrhage, especially repeated intracranial hemorrhage in women of childbearing age. Early and intensive treatment can help achieve a better prognosis and avoid a fatal outcome. Multiple intracranial hematomas are related to neoplastic intracranial microaneurysms.

Abbreviations: CT = computed tomography, HCG = human chorionic gonadotrophinin.

Keywords: brain metastasis, choriocarcinoma, intracerebral hemorrhages, multiple, neoplastic aneurysm

1. Introduction

Choriocarcinoma is the most malignant type of gestational trophoblastic neoplasia. Gestational choriocarcinoma may follow any type of pregnancy: 50% of choriocarcinomas are preceded by hydatidiform moles, 25% by abortion, 23% by normal pregnancy, and 2% by ectopic pregnancy.[1,2] Choriocarcinomas grow rapidly and can metastasize to the lung and liver, and less frequently to the brain; cerebral metastasis occurs in 10% to 20% of patients.[3] Local signs and intracranial hypertension are the most common symptoms of cerebral metastasis, and surgical treatment is often used for patients with high intracranial pressure. Brain metastasis is the main cause of death and disability in choriocarcinoma patients. If the metastatic tumor is disrupted during the growth process, tumor hemorrhage, invasion of the surrounding brain tissue, intracranial hematoma, or subarachnoid hemorrhage may occur, which can be life-threatening.[4,5] However, there are few reports of multiple cerebral hemorrhages, and effective treatments are lacking.[6] Here, we report a case of brain metastasis of choriocarcinoma that caused multiple cerebral hemorrhages. We observed 6 hemorrhages in 4 lesions within 50 days. This is the first report of this high frequency of bleeding.

2. Case report

An 18-year-old woman, 2-0-1-1, had experienced irregular vaginal bleeding over the course of 6 months and was admitted to the hospital with confusion for 4 hours. After admission, the patient continued to be confused and experienced frequent vomiting. Her pupils were round and of equal size, with sensitivity to light. She complained of a stabbing pain in the neck, and the muscle strength of the extremities was grade V. Head computed tomography (CT) showed multiple hemorrhages in the right temporal-parietal lobe and occipital lobe, right temporal-parietal hematomas, ventricle compression, and midline shift (Fig. 1). As the patient was young and the bleeding site was atypical, cerebrovascular malformation could not be excluded. After preoperative examination, evacuation of the hematoma in the temporal-parietal lobe and decompressive craniotomy was performed under general anesthesia. During the surgery, the intracranial hematoma was removed. We did not observe vascular malformation. Because intraoperative intracranial pressure was high, we removed the patient's skull. No special treatment was provided as the volume of the posterior occipital

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DW and HS have contributed equally to this work.

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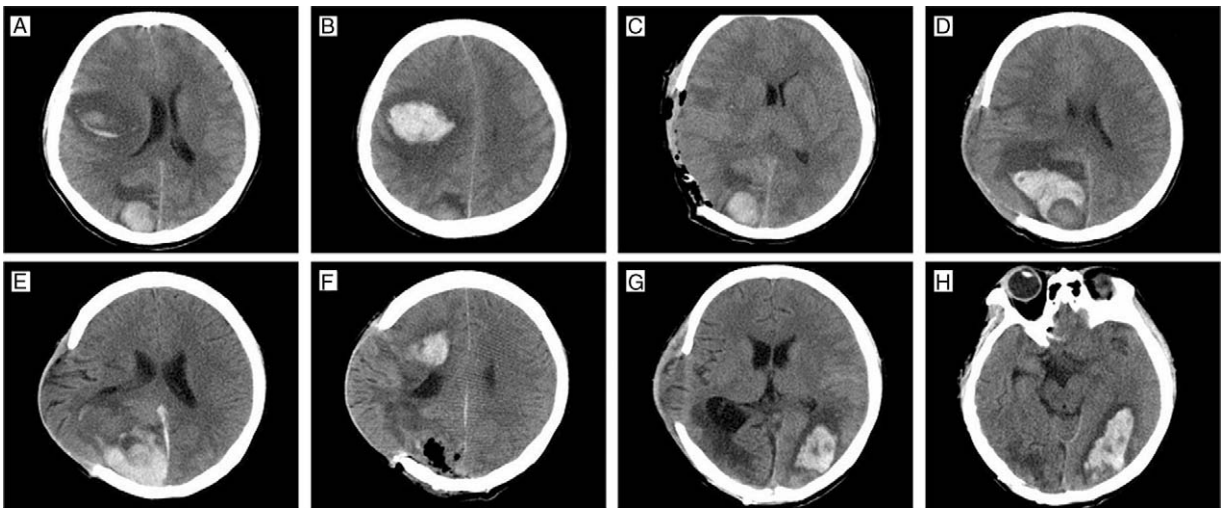

Figure 1. (A, B) Head CT showing multiple hemorrhages in the right temporal-parietal lobe and occipital lobe, right temporal-parietal hematomas, ventricle compression, and midline shift. (C) Postoperative axial CT scan showing the frontal and parietal hematomas were removed and occipital hematoma retained. (D) Rebleeding of the occipital lobe 1week after the operation. (E) Third bleeding on the right occipital lobe 25 days after the first operation. (F) Head CT after the second operation showing a fresh hematoma in the right frontal lobe. (G) Head CT 12 days after the second operation showing a fresh hematoma in the left occipital lobe. (H) Head CT 15 days after the second operation showing enlargement of the left occipital hematoma. CT = computed tomography,

hematoma was small. Postoperatively, the patient had a clear mind and was able to speak fluently. The extremities were normal, and she could eat and communicate normally. Irregular vaginal bleeding was still seen, and no abnormality was found by gynecologic ultrasound. One week after the surgery, the patient experienced frequent vomiting and severe headache. CT showed an increased right occipital hematoma, right hemisphere swelling, and high pressure at the decompression window. Based on the patient's symptoms and CT examination, dehydration and conventional therapy were performed. Follow-up CT examinations showed that the occipital hematoma was in the absorption period, and her symptoms improved. To determine the cause of bleeding, we performed digital subtraction angiography that indicated abnormal vessels in the right occipital lobe, which later proved to be the blood vessel of the tumor, and an anterior cerebral artery aneurysm (Fig. 2). Pulmonary CT showed an occupying lesion in the chest without a clear nature. Abdomen CT, pelvic ultrasound examination, including uterus, uterine appendages, vagina showed no occupying lesion, Twenty-five days after the surgery, recurrence of the intracranial hypertension was seen. Head CT showed bleeding in the right occipital lobe, with a hematoma over 30 mL. Conventional medication was unable to relieve the symptoms of intracranial hypertension. Hence, we performed craniotomy to remove the hematoma.

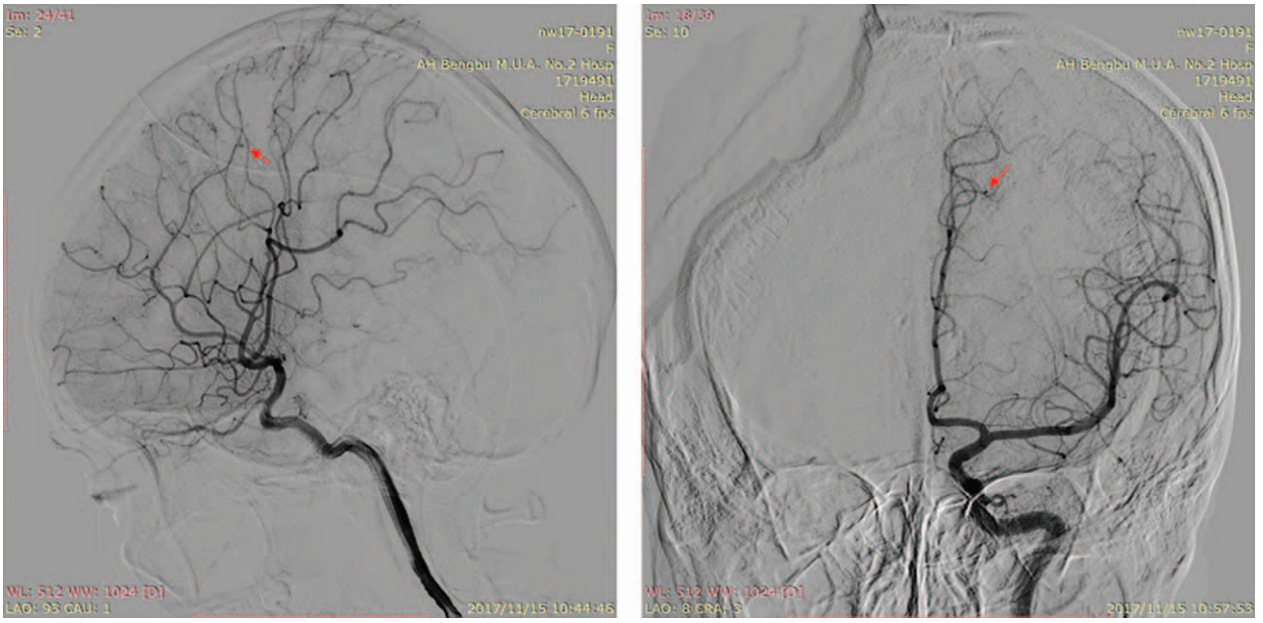

Figure 2. Cerebral angiograms showing anterior cerebral arterymicroaneurysms (arrows).

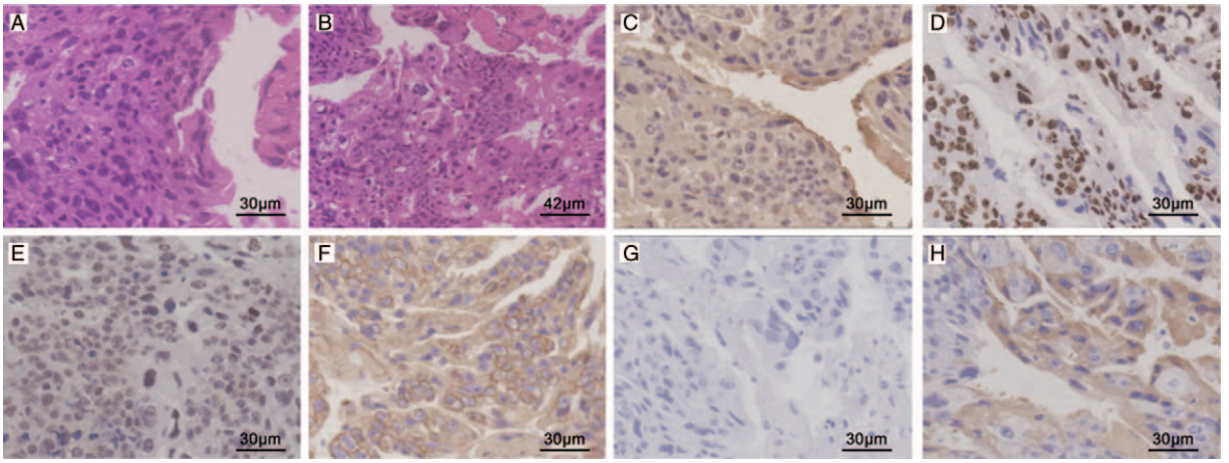

Figure 3. Histopathologic staining of the lesion resected during the second craniotomy. (A, B) Hematoxylin-eosin stain showing atypical cells with mitotic figures and prominent nucleoli consistent with choriocarcinoma (magnification, ×200 and ×100). (C) HCG immunostaining showing hormone secretion by tumor cells (magnification, ×200). Immunohistochemical staining demonstrating neoplastic cells with (D) a Ki-67labeling index of 90% (magnification, ×200); (E) positive immunoreactivity for PLAP (magnification, ×200); (F) positive immunoreactivity for CK (magnification, ×200); (G) negative immunoreactivity for GFAP (magnification, ×200); and (H) positive immunoreactivity for inhibin (magnification, ×200). CK = cytokeratin, GFAP = glial fibrillary acidic protein, HCG = human chorionic gonadotrophinin, PLAP = placental alkaline phosphatase.

During the surgery, a purple and red goiter with rich blood transport was resected for pathological examination. Based on the previous medical history, we considered it a choriocarcinoma. Postoperative head CT showed a fresh hematoma in the right frontal lobe. Based on the hematoma volume, we performed conventional therapy. The pathological report suggested brain and lung metastases of choriocarcinoma with total human chorionic gonadotropin (THCG) > 1000 mIU/mL. Histological examination of the hematoma was compatible with a diagnosis of choriocarcinoma. The specimens showed several atypical pleomorphic trophoblastic cells on a necrotic background and some scattered trophoblasts in the hematoma and invading the vessel wall. Immunohistochemistry revealed positive staining for human chorionic gonadotrophin (HCG) the tumor cells, as well as neoplastic cells with a Ki-67 labeling index of 90%, positive immunoreactivity for placental alkaline phosphatase, cytokeratin, and inhibin, and negative immunoreactivity for glial fibrillary acidic protein (GFAP) (Fig. 3). However, the endometrial biopsy specimen showed no evidence of chorionic villi, trophoblasts, or decidual reaction. Twelve days after pathological diagnosis, the intracranial hypertension symptoms recurred, accompanied by decline in vision (only light sensation). Head CT showed a fresh hematoma in the left occipital lobe, with a small hematoma volume. We chose conventional therapy, and head CT after 3 days indicated an enlarged hematoma. The patient had a clear mind, and conventional therapy was administered. Head magnetic resonance imaging (MRI) was then performed because we believed that the multiple bleeding sites were caused by brain metastasis of choriocarcinoma and no metastases were seen in other organs (Fig. 4). Five days later, the patient asked to terminate the treatment and was discharged. One month later, the patient died of upper gastrointestinal bleeding. The patient and patient's family consented to publication of the case.

3. Discussion

Choriocarcinoma develops from trophoblastic cells and is a highly malignant tumor. Metastatic choriocarcinoma must be treated as soon as possible because this tumor has a tendency to rapidly grow and haematogenous spread. Treatment of metastatic choriocarcinoma using chemotherapy and/or radiotherapy produces long-term survival rates of as high as 80%. Despite the important improvements in treatment, patients affected by cerebral metastasis and oncotic aneurysms still have a poor prognosis.[7,8] Because trophoblastic cells are highly proliferating and can replace vascular endothelial cells to form the vascular endothelial layer, they can easily invade the maternal blood and result in distant metastasis. Most deaths in choriocarcinoma patients are due to brain metastasis. The neoplastic cells form emboli that are trapped in the cerebral circulation and metastasis develops. These metastases have a predilection to invade the vessel wall, and this can result in a hemorrhage within the tumor mass or the development of a fusiform cerebral aneurysm that may rupture, resulting in an intracerebral or subarachnoid hemorrhage.[1,9–11] Histological examination of the aneurysms, in this case, showed occlusion of the vessels by tumor cell emboli, proliferation of the tumor cells into the vessel walls, and rupture of the internal elastic lamina. Single or multiple aneurysms can be seen in choriocarcinoma. However, there are comparatively few cases in which the presence of aneurysms has been proven angiographically or histologically.[12] There are 2 mechanisms for neoplastic aneurysm formation. After tumor embolization in the distal cerebral vessels, focal destruction of the intima, internal elastic lamina, and media layers may cause a true neoplastic aneurysm. Alternatively, lodging of the tumor embolus in the vasa vasorum and involvement of the internal elastic lamina may lead to aneurysm formation in the final stage.[13]

Here, we reported a rare case of brain metastasis of choriocarcinoma that caused multiple cerebral hemorrhages. Thus far, more than 20 cases of oncotic aneurysms from choriocarcinoma and only 6 cases of multiple intracranial hematomas have been reported in the English literature.[6] This case is unique, because we observed 6 instances of hemorrhage in 4 lesions within 50 days; this high volume of bleeding has not been previously reported. The patient had a medical history of irregular vaginal bleeding. However, she did not seek treatment

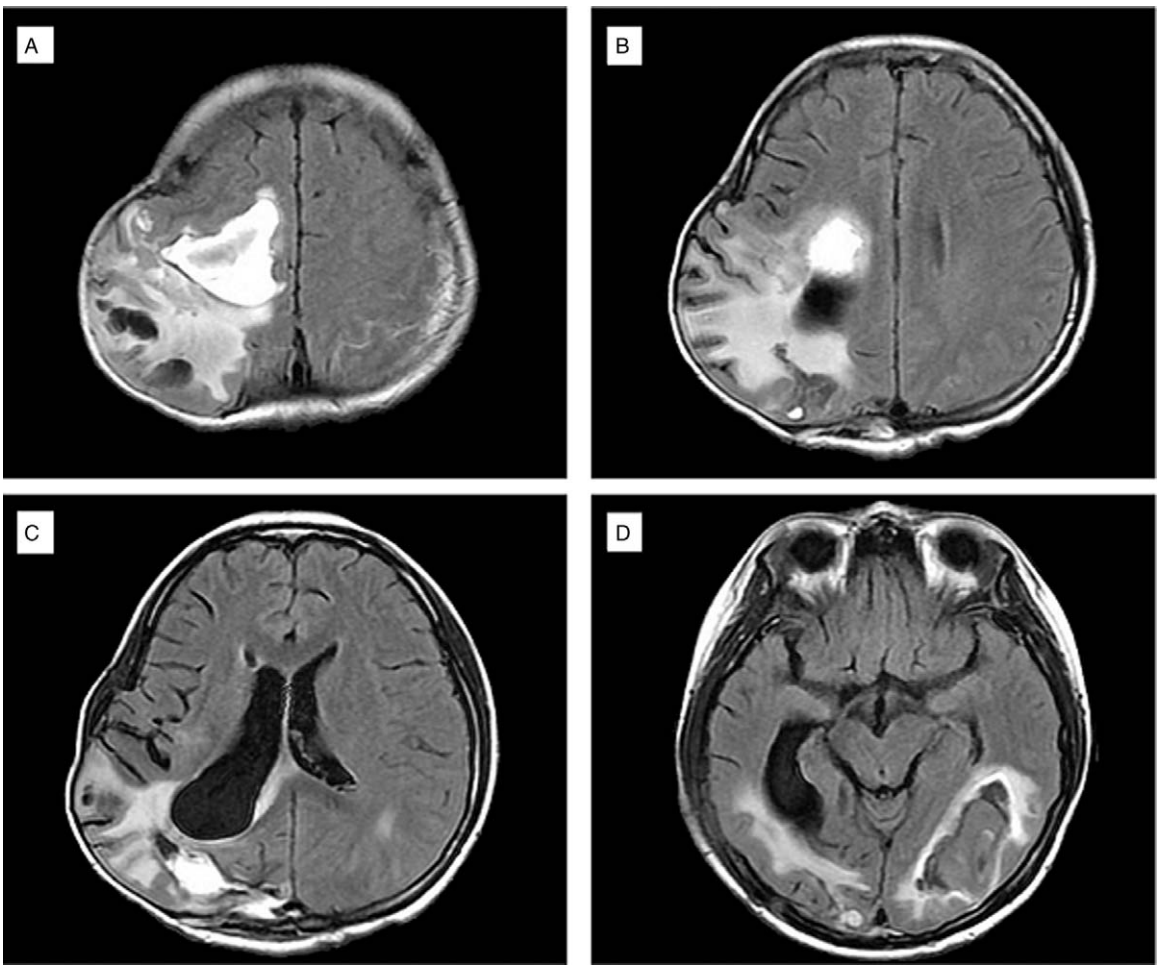

Figure 4. After 6 instances of hemorrhage in 4 lesions, head magnetic resonance imaging showed multiple intracerebral hemorrhage.

until she developed lobar hemorrhage caused by brain metastasis. We originally considered occult vascular malformation and anterior cerebral artery aneurysm because the only hematoma change was observed in the imaging examinations. However, the final pathological diagnosis was brain metastasis of choriocarcinoma, which caused multiple instances of bleeding in a short time. This case highlights blood vessel invasion of brain metastasis of choriocarcinoma. The aneurysm was located at the end of the anterior cerebral artery, so we believe the patient had neoplastic intracranial microaneurysms. We have reason to believe that multiple intracerebral hemorrhage is related to neoplastic intracranial microaneurysms, and, regardless of the lesion size, they may lead to fatal intracranial hemorrhage. Brain metastasis of choriocarcinoma and cerebral hemorrhage should be considered when patients experience unexplained cerebral hemorrhage, especially repeated intracranial hemorrhage in women of childbearing age. HCG testing and other gynecological examinations need to be carried out immediately.

When central nervous system metastases of choriocarcinoma are suspected, HCG levels can be measured in the cerebrospinal fluid to exclude cerebral involvement if CT scans of the brain are normal. If diagnosed with choriocarcinoma, all patients should undergo a careful metastatic workup, including the following:

(1) chest radiography or CT,
(2) CT of the abdomen and pelvis, and
(3) CT or MRI of the head.[6]

When the pelvic examination and chest radiographic findings are negative, metastatic involvement of other sites is uncommon.[14] The treatment must be initiated as possible and not delayed by a surgical treatment. Surgeons should also try to remove intracerebral choriocarcinoma as completely as possible during the first operation. Early and intensive treatment can help achieve a better prognosis and avoid a fatal outcome.

The limitation of this study is that, although other causes of hemorrhage have been excluded, it was impossible to obtain pathological diagnostic support in the bleeding sites because of surgical limitations. Additionally, we did not find the primary lesion.

4. Conclusions

Brain metastasis of choriocarcinoma should be considered when patients experience unexplained cerebral hemorrhage, especially repeated intracranial hemorrhage in women of childbearing age. Early and intensive treatment can help achieve a better prognosis and avoid a fatal outcome. Multiple intracranial hematomas are related to neoplastic intracranial microaneurysms.

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