

HEMORRHAGIC CEREBRAL METASTASIS AS A FIRST MANIFESTATION OF A HEPATOCELLULAR CARCINOMA

CASE REPORT

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ABSTRACT - We report herein a rare instance in which a patient presented with a hemorrhagic cerebral metastasis as the initial manifestation of a hepatocellular carcinoma (HCC). A few cases of cerebral metastasis from HCC have been reported in the literature, mainly from eastern countries. This is the first report from South America of a cerebral metastasis from hepatocellular carcinoma.

KEY WORDS: hepatocellular carcinoma, metastases, brain, hemorrhage.

Metástase cerebral hemorrágica como manifestação inicial de um carcinoma hepatocelular: relato de caso

RESUMO - Relatamos o caso de um paciente que teve como primeira manifestação de um carcinoma hepatocelular uma metástase cerebral hemorrágica, evento raro na literatura. Os poucos casos de metástase cerebral por carcinoma hepatocelular foram relatados em países do Oriente, onde o tumor é mais comum. Este é o primeiro relato de metástase cerebral de carcinoma hepatocelular da América do Sul.

PALAVRAS-CHAVE: carcinoma hepatocelular, metástase cerebral, hemorragia.

The epidemiology of hepatocellular carcinoma (HCC) in the world is according to geographic location. It is unusual in Western countries (incidence of 5/100.000) but commoner in Orient and Africa (20-150/100.000)^{1,2}. Cerebral metastases are rare, in all regions, being a postmortem finding in the majority of cases.

We report herein a rare instance in which a patient presented with a hemorrhagic cerebral metastasis as the initial manifestation of a HCC.

CASE REPORT

A 43-year-old white right handed man was referred to the Hospital São Paulo Neurologic Emergency Room, with a 12-hour history of a right hemiparesis of acute onset. He also complained of a 9 Kg weight loss during the last 8 months. The patient had had a moderate alcohol consumption since the age of 17 years and underwent a cardiac surgery 27 years before admission for a correction of a Fallot's tetralogy. Physical examination revealed hepatomegaly and a continued panfocal heart murmur grade IV. The neurologic examination showed a right hemiparesis, predominantly in the superior limb, sparing the face, with a partial ipsilateral loss of pain and temperature. Fundoscopic examination was normal. There was neither aphasia nor mental status alteration. Initial

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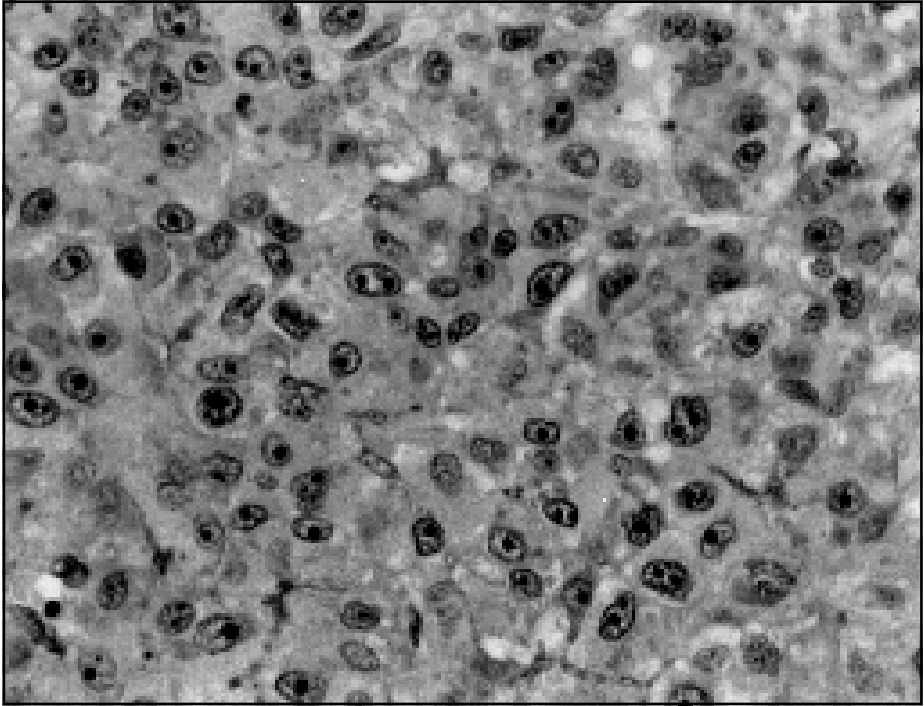


Fig 1. Photomicrography showing a metastatic carcinoma with a trabecular and solid pattern and the neoplastic cells were positive for carcinoembryonic antigen with a canalicular staining pattern. CEA, 160x.

laboratory results showed elevated liver enzymes and a slight decrease in the hematocrit and hemoglobin count. CT cranial scan revealed an intracerebral hemorrhage in the left parietal region, without midline shift. A large hepatic mass with necrotic areas was found in the abdominal CT scan, and there were signs of metastatic nodules in the pulmonary CT scan. Upon the evacuation of the cerebral hematoma, a single mass suggestive of metastasis was found and completely resected. The cerebral specimen disclosed a metastatic carcinoma suggestive of hepatocellular carcinoma (Fig 1). A liver biopsy was performed and confirmed hepatocellular carcinoma. After surgery, the patient recovered completely from the neurologic deficit. Whole brain radiotherapy was started without complications and hepatic embolization was performed to treat the liver tumor. One month later, the patient developed ascites and a progressive dyspnea. He died 16 weeks after the diagnosis. No autopsy was performed.

Methods

Light microscopy. Tissue samples were fixed in 10% formalin and embedded in paraffin. Sections (5 mm thick) were stained with hematoxylin and eosin.

Immunohistochemistry. Immunoperoxidase studies of paraffin sections were performed using a standardized avidin-biotin method. Antibodies tested included cytokeratin (AE1/AE3; 1:200, DAKO), S-100 protein (1:500, DAKO), carcinoembryonic antigen (CEA; 1:400, DAKO), thyroglobulin (1:400, DAKO) and alpha-fetoprotein (AFP; 1:450, DAKO).

Results

Histologic and Immunohistochemical findings. The cerebral specimen disclosed a metastatic carcinoma with a trabecular and solid pattern. The neoplastic cells were polygonal with vesicular nuclei and prominent nucleoli. The cytoplasm was finely granular. The neoplastic cells were positive for CEA, with a canalicular staining pattern (Fig 1), and for cytokeratin. Staining for S-100 protein, thyroglobulin and alpha-fetoprotein were negative.

DISCUSSION

Spontaneous hemorrhage occurs in primary and secondary tumors of the brain. For primary tumors, it is more likely to be found in angioma, angioblastoma, neuroepithelial cyst, pituitary adenoma, gliomas, and medulloblastoma³. For metastatic intracranial tumors, bronchogenic carcinoma, choriocarcinoma, malignant melanoma, renal cell carcinoma, thyroid carcinoma, germinoma and prostatic adenocarcinoma are the most common histologic types. Hemorrhage into malignant neoplasms accounts for 10% of all spontaneous intracranial hematomas⁴, and 5 to 10% of patients with cerebral metastasis may present with acute neurologic symptoms caused by hemorrhage into the tumor or cerebral infarction⁵.

The mechanisms of hemorrhage in brain tumors are multifactorial. Factors as invasion of the vascular wall by the tumor cells, degeneration and hemorrhagic infarction, rapid tumor growth, and high grade of malignancy have all been proposed as bleeding pathogenesis¹.

The incidence of brain metastatic hemorrhage has been reported to be about 40% for melanoma, 70% for renal cell carcinoma, and 50% for choriocarcinoma⁶. For HCC the incidence varies from 65% to 87.5%, and for brain metastases larger than 2 cm, attention should be paid for future bleeding⁷.

Autopsies of patients with hepatocellular carcinoma revealed a high incidence of both pulmonary and lymphatic metastasis, but no cerebral metastasis were found in 60 cases studied by Patton and Horn⁸. Posner did not find metastasis from HCC in the Memorial Sloan-Kettering Cancer Center series⁹. Primary manifestation of hepatocellular carcinoma as metastatic disease accounts for only 0-5% in most series. The Liver Cancer Study Group of Japan reported that cerebral metastases were discovered in only 11 of 501 (2.2%) autopsied HCC cases¹⁰. The poor prognosis of HCC and the low affinity of the HCC cells for the brain may explain why HCC is unlikely to cause cerebral metastases⁷.

A few cases of cerebral metastasis from HCC have been reported in the literature, mainly from eastern countries^{1,3,7,11-15}. There is one report of a patient from the U.S. who presented a retro-orbital metastasis¹⁶. In 16 patients studied by Murakami et al.⁷, the CNS metastasis was the first manifestation of the hepatic disease in only 5 patients, as it was in our patient.

The epidemiology of HCC in Brazil is uncertain. In North and South America the incidence is less than 5/100000². This is the first report from South America of a cerebral metastasis from hepatocellular carcinoma.

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