Secondary glioblastoma with abdominal metastasis: Case report

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ABSTRACT

Extracranial glioblastoma (GB) metastasis is an uncommon entity, rarely described in the literature, representing 0.2% of cases of GB. Several theories have been proposed to explain the extracranial dissemination of GB, such as surgical interventions, ventriculoperitoneal shunt, and radiation therapy. We present a case of a 15-year-old adolescent girl, with an initial diagnosis of low-grade glioma and later transformation to a high-grade glioma. In the final phase of the disease, the patient presented with distention and abdominal pain, secondary to peritoneal compromise of GB metastasis. The use of new therapies has increased survival times, leading to a rise in the probability of developing extracranial metastasis.

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Introduction

Glioblastoma (GB) accounts for 15% of all primary brain tumors. It has a poor prognosis with a 5-year survival rate of 4.7%. The cause of death is usually due to tumoral intracranial compromise, rather than metastasis. Only 0.2% of patients with GB develop extracranial metastasis with a 2-year median time of presentation [1].

It is believed that GB metastasis is very unlikely because of the presence of the blood-brain barrier, the absence of brain lymphatic system, and poor prognosis. However, treatment improvements, such as complete surgical resection and concomitant radiotherapy-chemotherapy, have increased the survival time, therefore increasing the probability of extracranial dissemination [2].

Regarding the physiopathology leading to extracranial metastasis, several hypotheses have been proposed, including direct access to the dural vessels during surgical interventions, invasion of the dura mater and bone, and migration through the ventriculoperitoneal shunt [2]. Another aspect that must be taken into consideration is the count of circulating tumoral cells, which are an extravasation of GB cells to vascular space, originating from hematogenous dissemination and implantation of GB on extracranial areas. The presence of tumoral circulant cells has been detected in 20% of GB cases; however, not all patients develop metastases [3]. Additionally, it has been proposed that there are enzymatic factors that predispose to...
extracranial spreading: gelatinase A and B are proteolytic enzymes that degrade the extracellular matrix of the central nervous system, promoting spreading; these enzymes also degrade the basal membrane of the blood vessels [4]. Forsyth et al. found higher expression of the active form of these enzymes in GB with extraneural metastasis [5,6].

A significant theory is the generation of radiation-induced glial cell sarcomatous metaplasia, which develops extracellular matrix proteins associated with vascular and hematogenous invasion. Several molecular characteristics have also been found, such as P53 mutations, gene PTEN, P16 deletion, and MDM2 and CDK4 amplifications [7].

We present the case of a 15-year-old adolescent girl with an initial diagnosis of low-grade glioma, which subsequently transformed to a high-grade glioma, with later development of abdominal metastasis.

Case presentation

A 15-year-old adolescent girl presented to our institution with a 1-month history of a mild global headache, more predominantly in the mornings. Her physical examination was unremarkable with no neurologic findings. A brain magnetic resonance imaging (MRI) was performed, revealing a mass localized on the right basal ganglia, predominantly in the thalamus, associated with midline deviation and perilesional...
edema; no restricted diffusion was found; and a low-grade glioma was considered (Fig. 1). An open biopsy was done, and an increase in the intracranial pressure in the hydrocephalus, along with an obstruction of the third ventricle due to the lesion, was found. Pathologic examination revealed an unspecified mesencephalic tumor with no necrosis, inflammation, or increased cell proliferation, and no malignant features were observed. Hence, conservative management was decided.

A year later, the patient presented with severe headache and vomiting. A brain computed tomography (CT) scan revealed acute hydrocephalus, and the patient required a ventriculoperitoneal shunt. Subsequently, a stereotactic biopsy was performed, and the pathology showed a low-grade astrocytoma. Given the localization and depth of the lesion, conformational radiotherapy was begun. The patient had good treatment tolerance and continued clinical and imaging follow-up.

Two years later, a follow-up brain MRI revealed a tumor growing on the posterior aspect of the thalamus with an extension toward the right temporal lobe. Stereotoxic radiosurgery was performed using a fractionated technique, and the histopathology results confirmed the same type of tumor detected 2 years ago.

A year after the radiosurgery, the patient started experiencing moderate epigastric abdominal pain; the patient was assessed by gastroenterology, and the pain was thought to be due to a possible chronic gastritis. A month later, the patient presented to the emergency department with neurologic impairment, left hemiparesis, and a severe headache. Brain MRI revealed a basal ganglia tumor, with evidence of necrosis and extension to the ventricle. A stereotactic biopsy was taken, and pathology confirmed a GB (Fig. 2). Treatment was initiated only with temozolomide; radiotherapy was ruled out because of the high risk of radiotherapy toxicity because of the previous radiosurgery.

One week later, the patient was admitted with severe abdominal pain, fever, and abdominal distention. An abdominal CT revealed multiple nodular lesions on the posterior wall of the uterus, the lateral wall of the rectum, the II hepatic segment, the right kidney, and the peritoneal layers (Fig. 3). According to the immunohistochemistry and pathology results, nodular lesions biopsy results was secondary to GB. Taking into account the patient’s poor prognosis, she was remitted to palliative care. One month later, the patient presented with an intense headache, agitation, abdominal pain, and distention. Two days later, the patient succumbed to the disease.

Discussion

Lun et al. performed a literature review, finding a total of 88 reported cases of GB extracranial metastases [8]. Previous studies
had described an average detection time of extracranial metastasis of 8.5 months and a time to death of 1.5 months [9]. In the current case, the metastasis detection time was 1.5 months with a time to death of 1 month. The extracranial compromise could be frequently ignored because of the fast progression of the disease, the low frequency of GB metastasis, and the nonspecific clinical presentation of disease.

It is important to note that this case is a secondary GB, which is more frequent in young patients, such as ours. It is known that the transformation of a low-grade glioma to a high-grade glioma takes up to 50-55 months and, in this case, the transformation took 58 months [9]. We believe that this prolonged time could have generated the appropriate conditions for the development of metastasis.

The most frequent areas affected by GB metastasis are the lungs (59%), lymphatic nodes (51%), bone (30%), and liver (20%) [9]. In this case, there was peritoneal metastasis with a compromise of the liver and other abdominal organs. The medical literature notes that the clinical presentation in such cases is abdominal distention, ascites, pain, and a palpable mass, which is similar to our case; nevertheless, we did not associate the abdominal symptoms with GB [9].

According to the imaging guidelines for extracranial glioblastoma published in 2014 by the Journal of Neuro-Oncology, the evaluation of patients with suspected abdominal metastasis of GB must be undertaken via an abdominal CT scan and fluorodeoxyglucose-positron emission tomography. These studies will reveal a mass with irregular and poorly defined borders, and a hypermetabolism will be evident on the fluorodeoxyglucose-positron emission tomography [4]. In our case, a CT scan was used, revealing multiple nodular lesions with soft tissue density localized in the liver, right kidney, and uterus.

So far, there is no established treatment regime for GB metastasis, and the actual therapies are not effective. In this case, our patient underwent chemotherapy with no response or improvement, leaving palliative care as the only last resort [10].

We performed a research in PubMed, looking for other cases of secondary GB with extracranial metastasis, and we found several cases of primary GB and a few for secondary GBs. Zhen et al. reported a case of a 25-year-old man with diagnosis of diffuse astrocytoma (grade II) that recurred 1 year later with a diagnosis of GB; later, the man presented with right cervical lymph node metastases [11]. Additionally Cervio et al. reported a case of a patient with oligodendroastrocytoma, which developed over a period of 12 years to malignant progression to GB followed by multiple cytologically confirmed bone metastases [12]. Dawar et al. found 5 cases of secondary gliosarcoma arising from GB with extracranial metastasis [13].

In conclusion, this case revealed several factors that potentially predisposed the patient to develop an extracranial metastasis of GB. The 4 surgical interventions, including the biopsies, the ventriculoperitoneal shunt, the double radiation therapy, and the prolonged period for the evolution of the disease, are circumstances that could explain the tumoral cell dissemination to the abdominal cavity. The present study supports the previous theories reported by literature regarding the development of GB extracranial metastasis. However, further research, with a higher level of evidence, is necessary to clarify the physiopathology and management of this rare entity.

Fig. 3 – Abdominal computed tomography scan with contrast, revealing multiple metastatic lesions that compromise the right kidney (A), the peritoneum (B-D), and the posterior uterine wall and the lateral rectal wall (E). Asterisks (*) mark metastasis lesions.
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