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Abstract: Glioblastoma multiforme is one of the most rapidly progressing cerebral tumors and the most aggressive one in our neurosurgical experience. We present the case of a 45 year old patient with very aggressive type of tumor who had come to our service for the following: intense headache, confusion, right hemiparesis installed approximately one month before. IRM scan shows up the presence of a large tumoral mass without a precise border in the left temporal-parietal region which had extended all the way down to the thalamus. The planned intervention used 5-aminolevulinic acid (5-ALA) for the precise removal of the tumor mass, suboptimal because of the risk of lesioning the motor tracts – indicated by the intraoperative electrophysiological monitoring. After surgery the outcome was good with the partial regression of the motor deficit, but only after 3 weeks due to the unexpected tumor growth the neurological status started to decay and even worsened. The patient underwent surgery again with the partial remission of the symptoms although following imagistic controls showed up fast tumor growth once more. He was recommended to oncology service for the beginning of radiotherapy. We consider the evolution and invasion of this tumor in only a 3 weeks period being impressive.

Key words: glioblastoma multiforme, 5-aminolevulinic acid (5-ALA), recurrent disease, re-operation

Background

Glioblastoma multiforme is one of the most rapidly growing cerebral tumors and the most aggressive one in our neurosurgical experience. It is a glial cell tumor, a glioma and it originates in the support cells of the brain –

glial cells or in their precursors. Unfortunately, it is the most common primary brain tumor occurring during adulthood (20%), and the most frequent glial cell tumor – 51% of all gliomas (1). The confirmation of a glioblastoma by histological diagnosis is a

devastating condition, and it certainly represents a turn point in our patients' journey. American Brain Association indicates an average survival rate of 14 months, less than 10% of all the patients managing to survive more than 5 years with all the current available therapeutic methods (2). We can tell without a doubt, it's quite aggressive, for example, one of the worst and well known tumors for their high malignancy rate –the small cell lung carcinoma – has a median survival rate of 20 months and 20% of the patients are still alive after 5 years (3). The term of multiforme suggests that GBM are complex tumors with various aspects in grossly, microscopy and in various types of imaging methods, with complex clinical manifestations, complex genetic patterns, and, of course, various growing behavior.

The current standard treatment include a radical surgical resection followed by radio- and chemotherapy. The important thing for us as surgeons and what matters above all else is what we can surgically do to improve the patient's survival rate and his quality of life. There are many studies that emphasized the importance of the gross total resection (GTR) in the treatment of these aggressive tumors. GTR may be considered as a valuable independent prognostic factor for our patients survival, and a GTR of 98% or more of the tumor volume, as it can be appreciated on MRI enhanced images, is considered mandatory for a better evolution and prognosis (4, 5, 6). Other important prognostic factors are patient age and performance status (7). Despite improved surgical techniques, therapies and radiotherapies, prognosis for this type of pathology remains very poor: most patients die within 12–18 months from diagnosis (8).

In order to improve the extent of the

resection we use 5-aminolevulinic acid (5-ALA)-induced fluorescence to guide our procedure and, of course, the intraoperative neuromonitoring for the safety of our resection.

Case presentation

We present a 45 year-old man which was admitted in December 2016 to the Emergency Clinical Hospital “Prof. Dr. N Oblu”, Iasi; for about a month he had been suffering from intense headache, confusion, and loss of strength of the right arm and leg. A CT and MRI scan showed the presence of a tumor in the temporal-parietal region of the left hemisphere with thalamic extension (Figure 1)

We performed a tumor excision using 5-aminolevulinic acid (5-ALA), and electrophysiological monitoring of the motor cortex and tracts - with favorable outcome after surgery and progressive remission of the previously installed motor deficit. He attended neuromotor rehabilitation treatment. The resection was less than desired -subtotal - because of the MEP-s which indicates the vicinity of the motor tracts.

After 3 weeks from the procedure, before attending any oncological complementary treatment, he came to the Emergency Department of our hospital with motor aphasia, right hemiplegia and sleepiness which had occurred 3 days before. CT scan with contrast shows up unexpected large tumor growth and invasion and hydrocephalus due to the Monro and Sylvius aqueduct compression (Figure 3). The patient was reoperated on the next day. Postoperative evolution was favorable with partial remission of the motor deficit and aphasia, and the patient was addressed to the oncological department in 2 weeks for radiotherapy and temozolomide treatment.

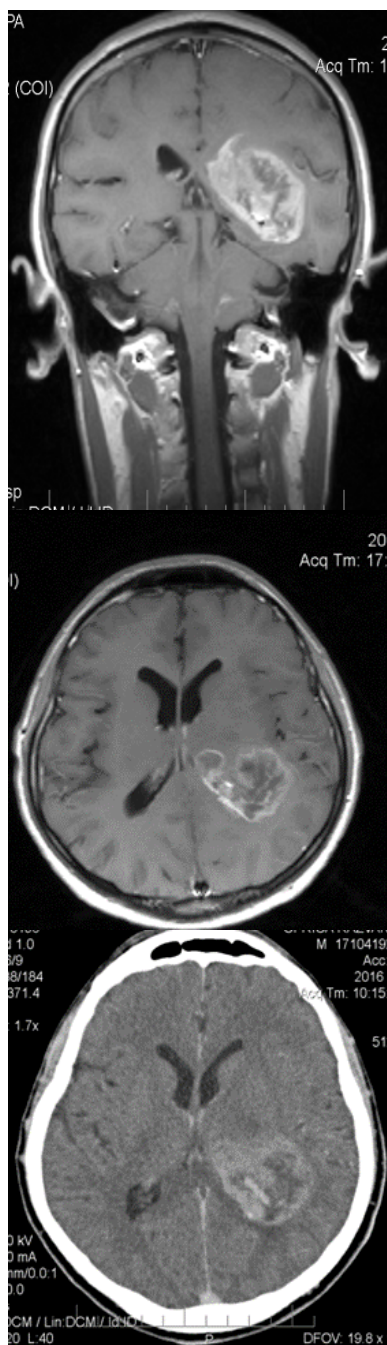


Figure 1 - a) CT scan- axial section b) MRI scan - axial and coronal sections- image preoperative – glioblastoma involving the left thalamus

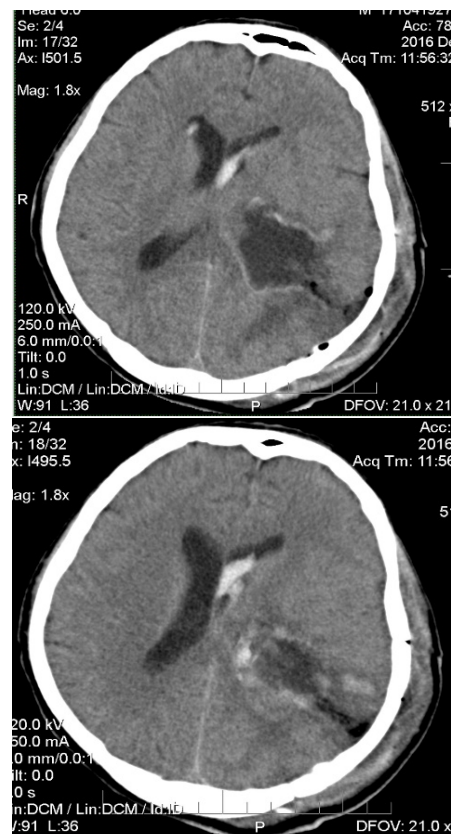


Figure 2 - Enhanced CT scan first day after surgery – small tumoral remnant in thalamus [1]



Figure 3 - CT with IVC showing the large, precocious, invasive tumor evolution

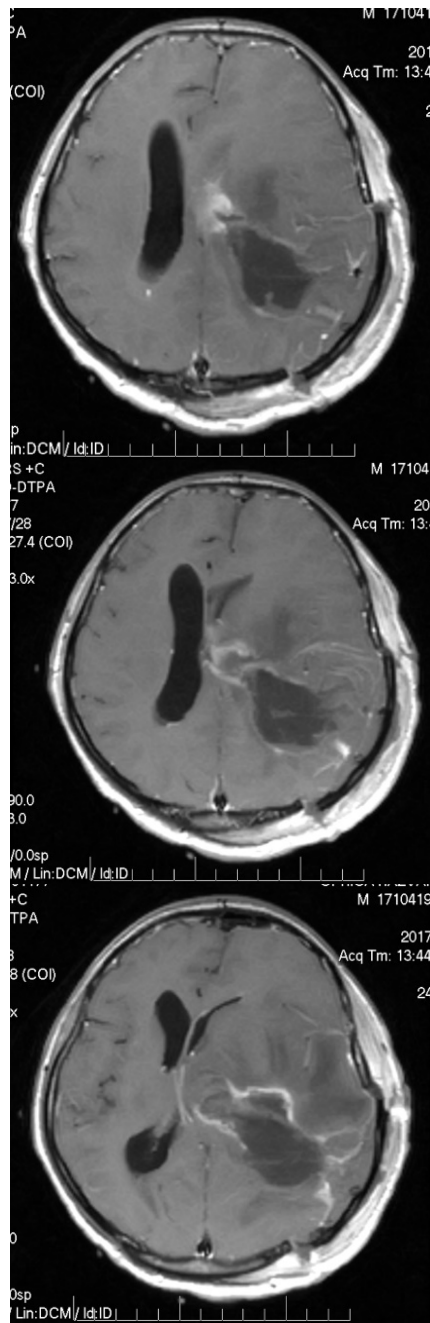


Figure 4 - MRI post-op [2]



Figure 5 - Ct post radiotherapy simulation

Discussion

The aggressively character of glioblastomas was described for the first time since 1926, when Bailey and Cushing described some unusual rapidly growing forms of astrocytic tumors (9). There are many studies now which emphasize the importance of molecular and genetic abnormalities in the behavior of a particular type of glioblastoma. Even some GBM may be histologically identical, they are molecularly distinct, and this individuality influence their evolution, but, of course, may require a specific tailored treatment (10). We believe that our patient had one of this very

aggressive type of tumor, the evolution and invasion in only a 3 weeks period being impressive.

The use of substances like 5-Aminolevulinic acid hydrochloride (11), which mark and thus make tumoral tissue easier to identify during an operation, have improved surgery for cerebral gliomas; in fact they allow for a more thorough excision (12), but increased the risk for postoperative complications like neurological deficit, so the using of intraoperative neuromonitoring is mandatory in order to decrease this potential risk. We experienced that in our case, finally we were not able to resect all the amount of tumor revealed by 5-ALA intraoperative visualization because of the electric imperative risk signs for motor deficit. In fact the initial motor deficit increased after the surgery but with good recovery, that may indicate the value of the electrophysiology in stopping us in time, but also it indicates that the use of the 5-ALA may be risky in the absence of experience and carefully monitoring.

Repeat surgery may play a role in debulking the tumor, providing symptom relief, and differentiating tumor recurrence from pseudo-progression or radiation necrosis (grade of recommendation: B). However, before surgical intervention, it is essential to clearly define treatment goals and the effect on prognosis and quality of life for the patient (13). Studies have shown that GBM recurrence most often occurs in the form of a local continuous growth within 2 to 3 cm from the border of the original lesion. Choucair, et al. reported that more than 90% of patients with glioma showed recurrence at the original tumor location and that multiple lesions

developed in 5% after treatment (14).

We emphasize the importance of performing oncology treatment. An important part of a high-grade glioma treatment is radiotherapy. In typical situations, patients begin radiation treatments within 2 to 4 weeks after tumor resection (15). Our patient has not started radiotherapy after the first intervention, which probably caused tumor growth.

Conclusion

Unfortunately, despite all intensive studies, surgical and oncological advances, GBM remains the cerebral tumors with the worst prognosis. Between these bad tumors, there are some cases with even quicker evolution and extensive invasion. What make them behave like is a subject for many molecular and genetic studies. The use of 5-ALA and intraoperative neuromonitoring may help the extension of a safety resection. The precocity of radio-chemotherapy treatment is mandatory, especially in aggressive cases.

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