Role of Preoperative Functional Brain MRI and Awake Craniotomy in Surgeries for Gliomas in Eloquent Areas

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Introduction

GLIOMAS make up ~30% of all brain and central nervous system tumors and 80% of all malignant brain tumors) and one of leading cause of cancer-related death in general population. Glioblastoma carries the worst prognosis, while low grade gliomas have the best chance for survival [1].

Unfortunately, gliomas are often located in regions of the brain defined as "eloquent" areas, meaning damage to these areas can create permanent neurological deficit. The role of radical surgery in the management of glial-type brain tumors is still controversial. It has been demonstrated that radical or subtotal resection correlates positively with prolongation of survival and longer time to progression. So neurosurgeons aim to achieve maximal surgical resection of these tumors whenever feasible [2].

Functional MRI is the most commonly used tool for pre-operative visualization of the motor, sensory, language and visual functional organization of patient brain. Because of its noninvasive nature and widespread availability, it has helped in revolutionizing cognitive neuroscience, and it has shed new light on the cerebral representation of function [3].

Awake craniotomy allows maximal tumor resection with minimizing the risk of permanent post operative neurological deficits [4].

Patients and Methods

This is a prospective study of 12 patients suffering from gliomas in eloquent areas managed in the period between January, 2013 and January 2015 in the Neurosurgery Department at Cairo University Hospitals.
The rationale of this work was to evaluate the different treatment modalities and the variable outcomes of surgical excision of gliomas in eloquent areas of the brain using of pre-operative functional MRI-brain and awake craniotomy.

Inclusion criteria:
- Gliomas in eloquent areas.
- Age above 12 years.
- Both sexes.
- Fully conscious and well oriented.

Exclusion criteria:
- Gliomas in non-eloquent areas.
- Patient with disturbed conscious level.
- Pediatric age group.
- Patients with communication difficulties.
- Patients with extreme anxiety.
- Morbid obesity.
- Patients with COPD, complicated airway, end organ affection in the form of hepatic, cardiovascular, or renal impairment.

Pre-operative patient evaluation:

History:
Personal history included; name, age, sex, occupation, residence, marital status an, associated medical disorders such as diabetes and hypertension, and special habits of medical importance.

The presenting complaint was the most single distressing complaint to the patient, in addition to other complaints included in the patient's symptoms.

Present history included evaluation and analysis of the patient's symptomatology regarding the onset, course and duration, in addition to analysis of other neurological symptoms in focus.

Neurological symptoms included; symptoms of increased intracranial tension as headache, vomiting, motor, sensory or speech affection, seizures and behavioral changes.

Past history included analysis of history of previous surgeries, medications received, previous irradiation.

Examination:

Complete general examination including: The patient's vital signs, height, weight, head, neck, chest and abdomen were performed for all patients.

A fully detailed and thorough neurological examination that included examination of the conscious level, cognitive functions, handedness, speech dominance, speech, cranial nerves, motor and sensory functions, was performed for all patients.

Investigations:
Routine laboratory investigations including CBC, blood sugar, liver and kidney functions, PT, PC, INR, serum sodium and potassium were performed.

Radiological investigations included pre-operative CT scan (without and with contrast) and MRI (T1 W, T2W, and T1 W with contrast) were done for all patients. In addition pre operative functional MRI brain and tractography imaging techniques were done for odd number patients.

Management:

Pre-operative management:
All patients were loaded with phenytoin; 15mg/kg IV, followed by maintenance dose of 6mg/kg/day until surgery.

All Patients were given Dexamethazone 24mg/day started one day pre-operatively with strict blood sugar monitoring and hyperglycemic control.

Patients who had evident lower limb weakness rendering them not ambulant, were closely monitored for proper hydration and were given prophylactic dose of short acting anticoagulants (fractionated low molecular-weight Heparin); 40 units/day. These anticoagulants were stopped 12 hours before surgery.

Patients who had history of, or turned out “on examination or by investigations”, to have medical disorders such diabetes or hypertension, were subjected to proper assessment and were given the proper corresponding medications.

All patients were given 1 gm of a third generation cephalosporin 6 hours before surgery (after performing an intra-dermal sensitivity test) and after induction of anesthesia.

Operative management:

Awake craniotomies were performed in all patients; Anesthesia for awake craniotomy was conscious sedation technique.

Surgical findings included tumor composition, consistency, extension, adhesion compression or infiltration of the eloquent areas and proximity to the major intra-cerebral vessels mostly carotid artery bifurcation, MCA and its branches.
During removal of the tumor we will continuously test motor and speech function, and if anything changed, we stopped removal of the tumor.

*Surgical removal was categorized into:* Total resection. Subtotal resection, tumor debulking and open biopsy. All tissue specimens obtained during tumor resection were sent for histopathological examination.

**Postoperative management:**

All patients were kept in an intensive care unit for the first postoperative 24 hours, and then they were transferred to the regular patients’ ward.

All patients were subjected to a complete and detailed postoperative neurological clinical evaluation comprising level of consciousness, cognitive functions, speech, cranial nerves, motor and sensory functions.

All patients had a postoperative control CT scan then follow-up MRI brain with and without contrast that helped in evaluating and confirming the extent of tumor resection according to the classification method reported by Berger et al. [5]: total resection if there was no residual signal abnormality, subtotal resection if there was <1 cm³ residue, and tumor debulking or partial resection if there was >10 cm³ residue.

Patients were kept in the hospital until they were stable enough for discharge. Before discharge, patients were referred to the oncology department to adjuvant radio or chemotherapy according to their histopathology results and according to the oncology department protocols. Patients having dysphasia were also referred for speech therapy.

**Follow-up and outcome:** All patients were followed up at intervals of 1 month whenever possible as some patients didn’t show at their scheduled follow-up dates.

Follow-up included detailed neurological examination to evaluate the neurological deficits that the patients already had, and to detect any new neurological deficits the patients developed during the follow-up period.

The outcome of patients was graded according to the patients’ clinical and functional status in the last follow-up visit they showed up at. The outcome was graded into 4 groups according to the classification of Berger et al. [5]:

- **Excellent:** Patients were considered to have an excellent outcome if they had total or subtotal resection of the tumor without the occurrence of new neurological deficits or permanent complications.
- **Good:** Patients were considered to have a good outcome if they had total or subtotal resection of the tumor with the occurrence of transient new neurological deficits or transient deterioration of pre-existing neurological deficits, provided that they were able to perform their daily activities without or with minor assistance.
- **Fair:** Patients were considered to have a fair outcome if they had only debulking of the tumor or had new neurological deficits or deterioration of their pre-existing neurological deficits rendering them dependant on others in performing their daily activities.
- **Poor:** Patients were considered to have a poor outcome if they had deterioration of their pre-existing neurological deficits and/or new neurological deficits, to the extent that they were not able to perform their daily activities without major and complete assistance, totally bed ridden, comatose requiring hospitalization or eventually died.

**Results**

There were 8 males (67%) and 4 females (33%). The median age of presentation in this study was 38 years.

In this study the main presentation of patients was headache (100%), followed by seizures in 6 patients (50%), followed by contra-lateral motor weakness in 4 patients (33%), and followed by dysphasia in 2 patients (17%).

In this study the most commonly involved lobe was the frontal lobe where it was involved in 6 patients (50%), followed by the temporal lobe in 4 patients (33%), followed by the parietal lobe in 2 patients (17%).

*FMRI criteria of the lesions:* In 5 patients (42%) the tumor was infiltrating eloquent cortical or subcortical areas (infiltration of motor area in 3 patients and infiltration of Broca’s area in 2 patients), While in 7 patients (58%) the tumor was displacing the eloquent areas.

We achieved gross total resection in 8 patients (67%), tumor debulking in two patients (17%), and subtotal resection in two patients (17%). Post-operatively, 1 patient (8%) had transient new onset motor weakness, out of the 4 patients presented with pre-operatively motor weakness, two patients (50%) had further deterioration of motor power. Regarding speech, one patient (8%) had new onset
expressive. Out of the two patients (8%) that originally presented with dysphasia, one patient (50%) had further deterioration of speech up to global aphasia, and was permanent.

Out of the patients eight patients had excellent outcomes (67%), two patients (17%) had good outcomes, one patient (8%) had a fair outcome, and 1 patient (8%) had a poor outcome.

A 27 years old male presented with headache 4 months prior to admission and seizures 3 months prior to admission in the form of partial complex. On examination, the patient had he had normal general and neurological examination. MRI brain showed a left frontal parafalcine mass. Functional MRI brain revealed that: There’s well cortical presentation of primary motor areas of Rt hand and Rt foot at the lateral and medial aspects of the left precentral gyrus respectively with distance from the tumor 1.5cm for the area of cortical representation of the Rt hand while 0 distance for the area of cortical representation of the Rt foot. The patient was operated upon under awake craniotomy. Tumor resection was stopped once the patient started to have some Rt foot motor weakness problems. This was followed by proper hemostasis and closure in anatomical layers. On histopathology, the tumor turned out to be Astrocytoma GII. Patient was transferred to Oncology Department and chemotherapy was given.

Discussion

In our study, we operated upon 12 patients; 8 males (67%) and 4 females (33%), where the male : female ratio was 2:1 compared to; 2:1 in Feigl et al. [6] study, 1.4:1 in González-Darder et al. [7] study and 0.77:1 in Lubrano et al. [8] study.

The median age of presentation in this study was 38 years with the youngest patient 17 years old and the oldest 60 years old. In Feigl et al. [6] study the age ranged from 27 to 76 years with a median age of 55 years. In González-Darder et al. [7] study the median age was 54 years. In Lubrano et al. [8] study, the age ranged from 13 to 78 years.

Out of the 12 patients included in our study, 6 patients (50%) presented with focal neurological deficit compared to; 72% in Feigl et al. [6] study, 29.4% in González-Darder et al. [7] study, and 37.5% in Lubrano et al. [8] study.

Regarding anatomical distribution, the incidence of gliomas was higher in the left hemisphere in
our study as well as in the other reported studies, where in our study 9 patients (75%) had left-sided lesions compared to 94% in Feigl et al. [6] study, 64.7% in González-Darder et al. [7] study and all of the 16 patients included in Lubrano et al. [8] study.

It was noticeable that gliomas most commonly affect the frontal lobe followed by the temporal lobe where in our study, 6 patients (50%) had frontal lesions compared to; 66% in Feigl et al. [6] study, 70% in González-Darder et al. [7] study, and all of the 16 patients included in Lubrano et al. [8] study. Similarly, among our patients, 4 patients (33%) had temporal lobe involvement compared to; 16% in Feigl et al. [6] study, and 24% in González-Darder et al. [7] study.

In our study, pre-operative Functional MRI brain and awake craniotomy was performed in all patients (100%).

On the other hand, awake craniotomy was performed as a standard technique in all the patients included in the studies Lubrano et al. [8], none of the patients in Feigl et al. [6] study, none of the patients in González-Darder et al. [7] study, while pre-operative functional MRI brain was performed as a standard technique in all the patients included in the studies of Feigl et al., [6] and González-Darder et al. [7] (combined with intra-operative cortical and subcortical mapping and stimulation).

Regarding the extent of surgical procedure according to the classification of Berger et al. [8]:

In our study; two patients had tumor debulking (17%), compared to; 35.3% in González-Darder et al. [7] study (multimodal navigation was done by integrating anatomical studies, motor functional MR (fMR) imaging, and diffusion tensor (DT) imaging). Intraoperative neuroradiography included direct cortical and subcortical stimulation and localization of the central sulcus by using cortical multipolar electrodes and storing the obtained data in navigator).

In our study, 2 patients had subtotal resection (17%) compared to; 50% in Lubrano et al. [8] study (awake craniotomy and direct brain mapping) and 17.6% in González-Darder et al. [7] study.

In our study, 8 patients had gross total resection (67%) compared to; 64% in Feigl et al. [6] study (pre-operative functional MRI combined with 5-aminolevulinic acid and intra-operative real time monitoring), 62.50% in Lubrano et al. [8] study and 47.1% in González-Darder et al. [7] study.

Regarding postoperative complications, regarding motor power; one patients (8%) had new onset transient motor weakness.

Regarding speech, one patient (8%) had new onset transient dysphasia. Compared to; 47% in González-Darder et al. [7] study and 25% in Lubrano et al. [8] study.

Out of the 12 patients included in our study, 6 patients (50%) presented with focal neurological deficit compared to 72% in Feigl et al. [6] study, 58.8% in González-Darder et al. [7] study, and 37.5% in Lubrano et al. [8] study.

Out of the 6 patients who presented with pre-operative neurological deficits in our study, 2 patients (17%) had permanent deterioration of their existing deficits(one patient that developed global aphasia one patient that had deterioration of motor weakness) compared to; 55% in Feigl et al. [6] study, 80% in González-Darder et al. [7] study and 16.66% in Lubrano et al. [8] study.

Conclusion:
Management of gliomas in eloquent cortical areas still represents a challenge that requires proper solving and adjustment of a complex multifactorialequation in order to achieve an accepted surgical outcome while maintaining properfunctional neurological integrity Individualized preoperative neuroimaging, including FMRI and DTI followed by an awake craniotomy, may be able to maximize the extent of resection and preserve long-term neurological function.

References
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