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Original research

MULTIDISCIPLINARY IN TREATMENT OF BRAIN GLIOBLASTOMA: THE COMBINATION OF SURGERY, RADIOTHERAPY AND CHEMOTHERAPY

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ABSTRACT

Objectives: *To describe the clinical features and magnetic resonance imaging of cerebral glioblastoma. And to evaluate the results of surgery combined with radiotherapy and chemotherapy for the group of patients.*

Methods: *A case series study was conducted on 38 patients with brain glioblastoma who underwent microsurgery combined with radiochemotherapy and Temozolomide at a dose of 75mg/m^2 daily and maintenance chemotherapy with Temozolomide at a dose of 175mg/m^2 for 6 cycles at Hue Central Hospital during 9/2019 - 6/2023.*

Results: *The mean age was 54.5 ± 10.3 with the male/female ratio = 1.57. The location was mainly in frontal lobe (26.3%). The tumor size 3 - 5 cm accounted for 50% of the patients. Magnetic resonance imaging showed mixed structures (47.4%) and heterogeneous enhancement (94.7%). Most patients underwent partial resection (65.8%). The main radiation dose was 59.4gy - 60gy, the patients with IMRT radiotherapy technique accounting for 23.7% After treatment treatment, the percentage of patients with symptoms such as headache and nausea reduced by about 30%. Partial response accounted for 50% of cases. The mean progression-free survival was 10.2 ± 1.06 months. The mean overall survival was 19,9 ± 1,84 months.*

Conclusion: *Glioblastoma was a highly malignant and rapidly progressive. Combination of radiotherapy and chemotherapy after surgery improved symptoms and increased overal survival.*

Keywords: *Glioblastoma, multidisciplinary treatment.*

I. BACKGROUND

Glioblastoma is a primary tumor of the central nervous system, originating from neuroglial cells, which develop mainly from the astrocytes. According to the World Health Organization (WHO), it has the highest malignant degree (grade 4) [1].

The rate of glioblastoma is quite high, accounting for about 12 - 15% of intracranial tumors and 60 - 75% of astrocytomas. In the US, the incidence is about 2.96 new cases/100.000 people/year [2]. In the UK, glioblastoma occurs in 7.36/100,000 people and the most common age group is 50 - 59 (Baker 1976). In Vietnam, some authors investigated investigate glioblastoma include: Hoang Minh Do (2009), the rate of glioblastoma in the brain was 17.2%; Kieu Dinh Hung (2006) the rate is 62.7%; Hoang Van Manh (2013) rate 45.3% [3 - 5].

Glioblastoma treatment includes 3 main methods: tumorectomy, radiotherapy and chemotherapy [9]. Currently, many centers are applying new radiotherapy techniques and new treatment drugs, combining many methods to improve treatment effectiveness and improve the quality of life for patients. For many years, Hue Central Hospital has applied multidisciplinary treatment and high-tech radiotherapy in brain tumors, especially glioblastoma. Therefore, we conducted this research to evaluate the results during the recent treatment period.

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II. SUBJECTS AND METHODS

We retrospectively analyzed 38 glioblastoma patients receiving multimodality treatment at Hue Central Hospital from September 2019 to June 2023

Steps for data collection: Glioblastoma patients underwent microsurgical tumor removal surgery at the Department of Neurosurgery, then were transferred to the Department of Radiation Therapy - Oncology Center to undergo radiotherapy combined with oral doses of Temozolomide 75mg/m^2 daily, then maintained chemotherapy Temozolomide 175mg/m^2 for 6 cycles and follow up every 3 months. All patients had a MRI and clinical symptom monitoring at each follow-up visit. RECIST 1.1 criteria is used to assess response.

III. RESULTS

3.1. Clinical and subclinical characteristics

The average age was 54.5 ± 10.3, gender ratio male/female = 1.57. Reasons for hospitalization included headache (86.8%) and hemiplegia (52.6%). Interval time from first symptom onset to hospital admission mainly less than 1 month (50%). Patients had Karnofsky score mainly from 70% - 90%.

Table 1: Onset clinical signs

Sign	N	Rate (%)
Headache	33	86.8
Vomit	10	26.3
Dizzy	8	21.1
Blurred vision	9	23.7
Mental disorder	5	13.2
Speech disorder	4	10.5
Epileptic	9	23.7
Hemiplegia	20	52.6
Memory decline	17	44.7
Total	38	100

Headache accounted for 86.8%, the others signs were under 50%

3.2. Imaging

Table 2: MRI Imaging

Result		N	Rate (%)
Location	Frontal lobe	10	26.3
	Parietal lobe	3	7.9
	Occipital lobe	4	10.5
	Midline	4	10.5
	Posterior fossa	7	18.4
	Multiple lobe	7	18.4
Dimension	< 3cm	12	31.6
	3 - 5cm	17	44.7
	> 5cm	11	28.9
Component	Solid	6	15.8
	Cyst	14	36.8
	Mixture	18	47.4
Contrast enhancement	No	3	15.8
	Homogeneous	2	5.3
	Heterogeneous	36	94.7
	Marginal enhancement	25	65.8
Necrosis	Yes	21	55.3
	No	17	44.7
Midline shift	Yes	9	23.7
	No	29	76.3
Haemorrhage	Yes	20	52.6
	No	18	47.4
Edema	No	2	5.3
	Grade I	14	36.8
	Grade II	15	39.5
	Grade III	7	18.4

The most frequency tumor location was in frontal lobe (26.3%) and multiple lobe (18.4%). 44.7% patients had tumor's size 3 - 5cm. 40% tumor's component was cyst and mixture. 94.7% tumor present heterogeneous enhancement on MRI. Necrosis and haemorrhage accounted for more than 50%. Grade II edema rate was 39.5%.

3.3. Treatment characteristics

Table 3: Type of surgery

Type of surgery	N	Rate (%)
Total tumorectomy	9	23.7
Partial tumorectomy	25	65.8
Tumor biopsy	4	10.5
Total	38	100

Most of patient underwent partial tumorectomy (65,8%)

Table 4: Radiotherapy characteristics

Result		N	Rate (%)
Dose	35gy/10Fx 59.4gy/33fx 60gy/30fx	8 14 16	21.1 36.8 42.1
Technique	IMRT/ Vmart 3D	9 29	23.7 76.3
Number of 3D field	2 3 4	12 17 9	31.6 44.7 23.7

Two third patients received radiotherapy dose from 59.4 to 60 Gy. IMRT accounted for 23.7%. 2 radiotherapy field rank first with 44.7%.

Table 5: Radiotherapy adverse affects

Adverse affects	N	Rate (%)
Hair loss	25	65.8
Vomit, nause	17	44.7
Anorexia	21	55.3
Fatigue	31	81.6
Otitis	3	7.9
Total	38	100

On top of the list was fatigue with the rate of 81.6%. The next frequent adverses affected hair loss, anorexia and vomit, nause with the figures around 60%.

3.4. Response evaluation

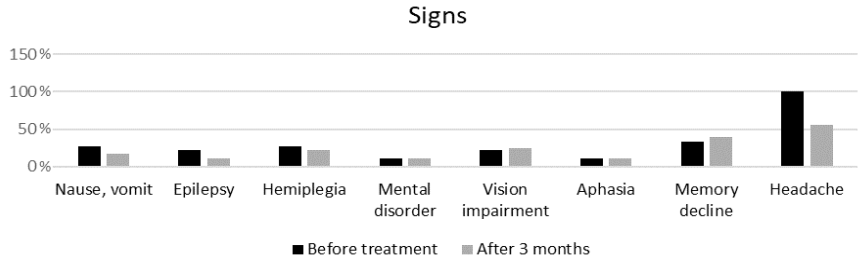

Figure 1: Clinical improvement after 3 months

After treatment, headache and nause eliviated by approximately 30%. Memory and vision impairment was more serere by nearly 10%.

Table 6: Response evaluation on MRI

Response rate	N	%
Complete response	3	7.9
Partial response	17	44.7
Stable disease	12	31.6
Progression	6	15.8
Total	38	100

Partial response rank first by 44.7%. The second belong to stable disease with 31.6%.

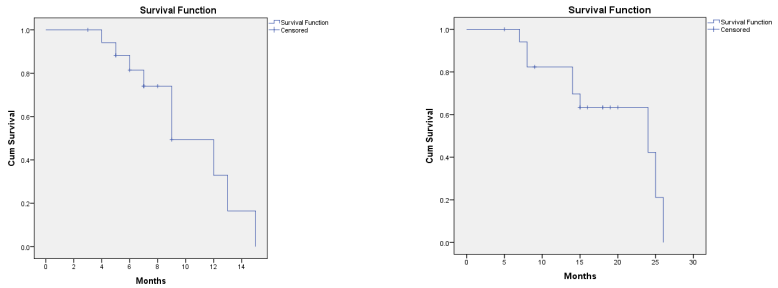

Figure 2: Progression free survival and overall survival

PFS was 10.2 ± 1.06 months and OS was 19.9 ± 1.84 months.

IV. DISCUSSION

4.1. Clinical features

In our study, the average age of patients was 54.5. Our research results were consistent with the one of Hoang Minh Do (2009) that the most common age group was ≥ 40 years old, accounting for 59.3%. Hoang Van Manh (2013) also state that the most common age group was over 50 years old, accounting for 25.3% [3, 4].

Regarding gender, in our study, the disease was more common in men than in women with the figures is 61,1% and 38,9% respectively. This result was similar to the results of Dong Van He (2013), Hoang Minh Do (2009) with 60% male and 40% female [3, 6].

According to Bajcsay and colleagues: High degree malignant gliomas had a rapid growth time, 70% - 80% was less than 3 months [7]. Headache symptoms: According to our results, headache was a common symptoms of glioblastoma, accounting for 86.8%. This is also a symptom of brain tumors in general. This result was consistent with the results of Hoang Van Manh that headache was encountered in 92% of patients [4]. Headache symptoms occurred in 96% of Muller's study [5]. Increased intracranial pressure: Symptoms include headache, vomiting, and papilledema. This is the specific clinical sign of intracranial mass. In our study, vomiting occurred in 26.3%, vision impairment occurred in 23.7%. According to Wiegrat, increased intracranial pressure syndrome is common in the tumor group.

4.2. Imaging features

Glioblastoma is the brain tumor with the highest malignancy, the diagnosis based on MRI usually has high accuracy. This type of tumor has many cysts in the tumor, producing irregular hyperintensity on T2 Flair, extensive cerebral edema around the tumor.

About the location: Frontal lobe and multiple lobes accounted for 26.3%, the others were in other areas. According to Hoang Minh Do, the most common tumor location was the temporal region (33.1%), followed by the frontal area (26.9%) [3]. Kieu Dinh Hung studied the group of malignant gliomas and found that the frontal area was found by 41.9% [5]. Hoang Van Manh stated that tumor in the temporal region was found in 30.7% and in the forehead was 29.3% [4].

In our study, tumors with a large size of 3-5cm accounted for the highest rate (44.7%), tumors with a size of > 5cm accounted for 16.7%. According to Ali Mehdi Ayoub, in France, 72% of patients with malignant glioma were diagnosed with tumor diameter less than 5cm [8], Yabroff KR showed that 81% of malignant glioblastoma and less differentiated astrocytoma tumor diameter from 2 - 5cm [9].

Tumor intensity in T1W, T2W

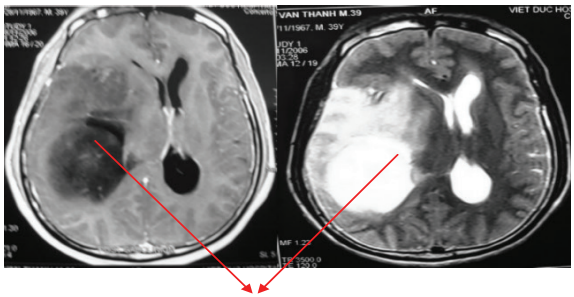

Figure 1: MRI show that the tumor hypointense in T1W, hyperintense in T2W, cerebral edema, grade II midline shift

4.3. Degree of invasion and pressure on surrounding tissues

The phenomenon of the tumor pressing on surrounding tissues is due to the size of the tumor itself and brain edema. The larger the tumor size, the more brain edema causes the more severe compression. This feature is common in high-grade malignancies. Images of compression appear on computed tomography and magnetic resonance imaging: collapsed, dilated ventricles, midline shift and deformation of the entire brain lobe. In our study, the tumor caused edema: grade II accounted for 36.8%, grade III accounted for 39.5%.

4.4. Surgical results (Based on the method of surgery)

In this study, the majority of cases had partial tumorectomy (66.7%), 16.7% of cases had the entire tumor removed. Patients underwent surgery to remove part of the tumor were cases which the tumor invades important functional areas, the tumors had unclear boundaries. If an attempt is made to remove the entire tumor, it will cause serious neurological deficits, even death.

4.5. Results of multidisciplinary treatment with surgery combined with radiation and chemotherapy

In our study, about 4 weeks after surgery, patients received chemoradiotherapy and then maintained for 6 more cycles of Temozolomide. About the characteristics of radiotherapy, 1/3 of patients received radiation therapy with IMRT/ Vmart technique, applied in tumors located next to critical organs such as brain stem, eye socket to avoid side effects. There were two radiotherapy dose options: 35gy/10Fx in patients in poor condition, low KPS, and 59.4gy/33Fx or 60gy/30Fx in better-fit patients allowing spread radiation. Regarding 3D radiotherapy, the majority of cases included 3 fields. The side effects after chemotherapy and radiotherapy were relatively mild. Fatigue, hair loss and loss of appetite accounted for 66.7%. There were no severe symptoms affecting chemotherapy or radiotherapy.

Evaluation of treatment results: Based on Recist criteria for evaluating solid tumors based on imaging, 7.9% patients had complete response, partial response accounted for 44.7%.

The average progression-free survival time in the patient group was 10.2 ± 1.06 months. Overall survival in the study group was 19.9 ± 1.8 months. According to Thakkar's research from epidemiological reports in the US from 2006-2010, the average overall survival time of patients was 15 months [10], the survival rate after 2 years was 13.7%. According to Patrick Y. Wen (2008), postoperative radiotherapy increased the survival in GBM patients from 3 - 4 months to 7 - 12 months [11]. According to Stupp Roger's study (2005), Temozolomide combine with radiotherapy resulted in improving overall survival to 14.6 months compared to 12.1 months with radiotherapy alone. Resulted from the study, this is a type of brain tumor with high malignancy degree and rapid progression [12]. The combination of multimodality treatment increased survival time and reduces symptoms for patients.

V. CONCLUSION

Glioblastoma was a highly malignant and rapidly progressive. Combination of radiotherapy and chemotherapy after surgery improved symptoms and increase overal survival.

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