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The Therapeutic Strategy of the Pediatric Glioblastoma

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1. Abstract

1.1. Introduction: Although common in adults, glioblastoma remains a rare disease in children. Comprising approximately 6.5% of all intracranial neoplastic disorders in the pediatric population. His prognosis is better compared to the adult if the treatment is fast.

1.2. Materiel and Methods: We present to you our experience of pediatric glioblastoma through a 10-years study carried out in the neurosurgery department of Ait IDDIR Health Hospital Establishment between the period of January 2007 and December 2017. We had 16 cases of pediatric glioblastoma, in each case, diagnosis was made clinically and confirmed radiologically and histo-pathologically. All patients were operated and received the adjuvant treatment.

1.3. Results: Our study identified 16 patients from 01 to 15 years of age between January 2007 and December 2017. Comparisons were made among demographics, clinical characteristics, treatment, and survival variables.

We had 04 boys and 12 girls. The boy / girl sex ratio was 0,33. Median Age was 9 years, (Females = 75%). Median overall survival was 18 months, while the median progression-free survival was 11.5 months. Clinical manifestations depended mainly on the tumor size and location, they were characterized by rapid progression of symptoms. The most frequent clinical manifestations found were Intracranial hypertension (68.75%) followed by neurological deficit (25%), alternating brain stem syndrome (12.5%), altered level of consciousness (18.75%) and epilepsy (31.25%). Approximately 50% of patients underwent either partial or complete resection. Adjuvant therapy was used variably, and its use increased with patient age. The most common complications were as follows: Intra-parenchymal hematoma (12.5%), epilepsy (18.75%), hemiplegia (12.5%), mixed nerves palsy (6.25%) and shunt dysfunction (18.75%). For mortality, two cases dead immediately (16.6%), however two cases dead at 01 years, two cases at 02 years and three cases at 04 years after surgery.

1.4. Discussion: High-grade gliomas, including glioblastoma multiform and anaplastic astrocytoma are very difficult to treat in children. Despite aggressive treatment with multimodal therapy, most children with these diseases do not survive. Patients who have had aggressive resections tend to have a longer survival than those who have undergone only biopsies or partial resections. Other biologic therapies, including gene therapy, are also being investigated. Improved survival for these patients will likely require combined therapy that includes novel treatment.

1.5. Conclusion: Glioblastoma in children is an aggressive disease with no defined standard therapy. Pediatric glioblastoma is particularly challenging in terms of therapeutic treatment. Engaging early and adequate filler can improve the survival rate.

2. Introduction

Glioblastoma is the most aggressive primary brain tumor, accounts for 5 to 10% of intra-cranial tumors in children [1] and 2.8% of primary tumors of the central nervous system [2].

2.1. Goal of The Study

We present cases of pediatric glioblastoma. It is a rare pathology in

comparison to adult population and the survival rate is much better in case of gross total resection. A multi-disciplinary management is of a paramount importance.

3. Materials and Methods

We had 16 cases of pediatric glioblastoma over a period of ten years from January 2007 to December 2017. All patients were admitted to the Neurosurgery department in Ait IDDIR Health Hospital Establishment in Algiers between a period of January 2007 and December 2017.

Radiological examinations were based on CT scan and Cerebral MRI. The CT Scan was performed in all patients and the Cerebral MRI in (87.5%) cases.

The treatment is based on Surgery, radiotherapy and chemotherapy.

3.1. Postoperative follow-up/

Early CT scan was performed to rule out early complications. Patients were followed clinically in our hospital then in outpatient neurosurgery clinic and also radiological through a period of 10 to 48 months. CT ± MRI with contrast was done at 1st to 6th month of postoperative period then 1-2-3-4 years later. All intraoperative and postoperative complications were collected and reviewed, to detect any recurrence of the excised tumour.

(Figures 1, 2 and 3)

4. Results

A total of 16 cases of pediatric glioblastoma were identified and operated. In this study 16 children were between 01 and 15 years old. The boy / girl sex ratio was 0,33. We had 04 boys and 12 girls. The age distribution was heterogeneous between the two sexes; there was a clear female predominance.

Clinical manifestations depended mainly on the tumor size and location, they were characterized by rapid progression of symptoms. The most frequent clinical manifestations found were Intracranial hypertension (68.75%) followed by neurological deficit (25%), alternating brain stem syndrome (12.5%), altered level of consciousness (18.75%) and epilepsy (31.25%).

According to tumour location, we had: Fronto-temporal tumor in 05 cases (31.25%), Temporo-parieto-insular tumor in 04 cases (25%) and occipital tumor 03 cases (18.75%) (Table 1).

For the Surgical outcome of this study: The Ventriculo-peritoneal shunts were placed in 05 cases (31.25%), the total tumor excision was done to 04 Cases (25%), the subtotal tumor excision was done to 3 cases (18.75%) and the partial tumor excision was done to 05 cases (31, 25%). We had doing the Stereotactic biopsy for 04 cases (25%).

In our study, the most common complications were as follows: Intra-parenchymal hematoma (12.5%), epilepsy (18.75%), hemiplegia (12.5%), mixed nerves palsy (6.25%) and shunt dysfunction (18.75%) (Table 2).

For mortality, two cases dead immediately (16.6%), however two cases dead at 01 years, two cases at 02 years and three cases at 04 years after surgery. The average age of survival was 18 months while the median progression-free survival was 11.5 months.

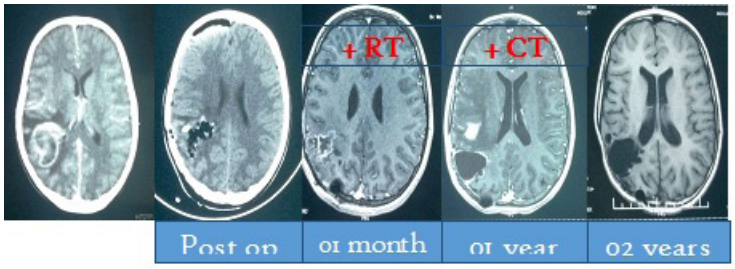

Figure 1: Axial Brain CT Scan images of a 10-year-old patient operated in 2012 for parieto-occipital glioblastoma Parietal glioblastoma with spontaneously heterogeneous density and signal contrast uptake with significant perilesional edem

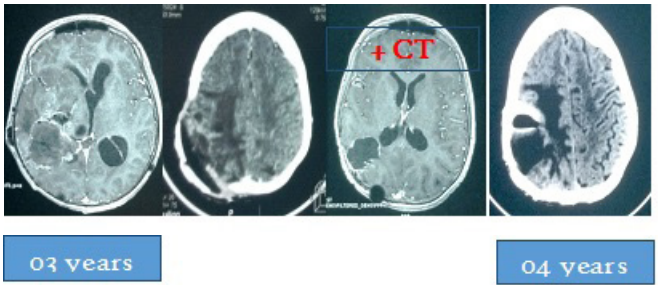

Figure 2: Post-surgical cerebral CT scan and MRI of a 10-year-old patient operated in 2014 for a Parieto-occipital glioblastoma, these images allow the assessment of the nature of the surgical excision, after radiotherapy and chemotherapy.

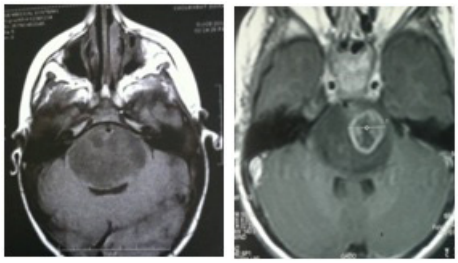

Figure 3: Cerebral MRI of a glioblastoma of the brainstem of a 4-year-old patient operated in 2014 for a glioblastoma of the brainstem, these images show a T1 hyper signal on MRI and a very intense contrast enhancement in peripheral and irregular, she takes a characteristic ring-like appearance around necrotic areas

Table 1: Tumor location of Pediatric glioblastoma of our patients

Tumor location	cases	Percentage
Fronto-temporal	5	31.25%
Temporo-parieto-insular	4	25%
Occipital	3	18.75%
Stereotaxic biopsy in brain stem Tumor	4	25%

Table 2: Post-Operatives complications of Pediatric glioblastoma surgery of our patients

Complications	cases	Percentage
Intra-parenchymal hematoma	2	12.50%
epilepsy (18.75%)	3	18,75%
hemiplegia	2	12.50%
mixed nerves palsy	1	6,25%
shunt dysfunction	3	18.75%.

5. Discussion

The percentage of pediatric glioblastoma does not exceed 10% of all glioblastoma [3].

The main characteristic is the rapid progression of the clinical manifestations, With a time frame between the first clinical sign and the histological diagnosis of less than three months [4]. Intracranial hypertension is in the foreground sometimes decompensating quickly [5].

The role of adjuvant chemotherapy in the treatment of pediatric high-grade glioma (HGGs) was established in 1980, which is based on the results of a randomized Cancer Group study using lomustine and vincristine in children [5, 6]. Recently, studies have shown a slight increase in survival rates using temozolomide and lomustine to treat pediatric glioblastoma.

In this new era, molecular markers have been extensively explored to overcome the limitation in the histopathological diagnosis of glioma, the expression of gene profiling has given rise to a new molecular classification [5].

Methylation of the methyltransferase promoter Methyguanine (MGMT) has been found to predict longer survival and the response to some chemotherapy agents in the treatment of glioblastoma [7].

6. Conclusion

Glioblastoma in children, when compared with adults, is relatively rare. Despite this rarity, it is apparent from the limited number of publications that pediatric glioblastoma is quite distinct from

their adult counterparts. The differences pertain to the molecular genetics, effectiveness of the adjuvant therapies, and possibly the prognosis after treatment. The prognosis remains extremely poor and as Jean Froncois guyot 1987 wrote “Our problem is to make illusion some time and to help as much as possible the patient and his family for the few months of reprieve”.

The current progress of neuroimaging as well as the progress in the protocols in the molecular research which augur’s changes of the prognostic and therapeutic approach of these tumors.

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