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Late Effects of Radiation in Children Treated for Cerebral Glioblastoma: A Case Report of Glioblastoma Patient who's Survival Exceeds 10 Years

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Abstract **Case Report**

Glioblastoma is one of the most aggressive cancers. The prognosis is generally poor despite surgery and adjuvant treatment. Improved management has resulted in a significant increase in overall survival. However, oncological treatments can lead to long-term complications. We report the case of a 13 year old girl with a case of glioblastoma in the brain surviving more than 10 years, during regular follow up we found a delay in school with concentration and memory problems which pushed us to make a neuropsychological evaluation that showed Intelligence below average with IQ between. The aim of this study is to share a case of glioblastoma brain surviving more than 10 years and to evaluate neurocognitive sequelae in children treated for brain tumor and management modalities through our case and literature reviews.

Keywords: Radiation, Glioblastoma, cancers, oncological treatments, brain tumor.

INTRODUCTION

Glioblastoma is one of the most aggressive cancers. The prognosis is generally poor despite surgery and adjuvant therapy. This condition usually affects adults. Its incidence in the pediatric population is low, about 0.6/100,000 in children [1].

Improved management has led to a significant increase in the 5-year overall survival rate [aa]. However, oncological treatments (surgery, chemotherapy and radiotherapy) can lead to long-term complications (second cancer, organ dysfunction, reduced fertility, cognitive impairment, growth impairment) [2].

Radiotherapy is a major therapeutic weapon in the management of childhood brain cancers allowing for improved survival, especially in high-grade glial tumors, medulloblastoma, ependymomas, germ cell tumors, and more rarely low-grade gliomas [3].

More and more children are recovering from cancer. This observation leads to questions about the neurocognitive future of these children and their quality of life. Neurocognitive sequelae may involve working memory, learning difficulties, executive function disorders, attention disorders, reasoning difficulties and reading difficulties [4].

The aim of this study is to share a case of glioblastoma brain surviving more than 10 years and to evaluate neurocognitive sequelae in children treated for brain tumor and management modalities through our case and literature reviews.

PATIENT AND OBSERVATION

This is a 3-year-old girl with no particular pathological history, followed for a cerebral glioblastoma revealed by a syndrome of HTIC and a left hemiparesis in March 2012, on brain CT: an infiltrating right parietal solidokystic tumor, the clinical examination on admission showed no neurological deficit.

Operated on 07/05/2012 a macroscopically complete tumor exeresis on anatomopathological examination: morphological and immunohistochemical aspect of a glioblastoma (anti GFAP +; anti ki-67 positive at20%; anti- vimentin positive ;anti -chromogranin negative) ,postoperative MRI showed the persistence of frontal tumor residue in the form of a mixed lesion with cortico -sub cortical cystic predominance measures 44*36*29 mm with moderate mass effect on the medial structures .

The patient underwent HTR 59.4 Gy in 33 sessions of 1.8Gy with good tolerance then the patient presented tonic-clonic left hemicorporeal convulsive seizures and was put under antiseizure treatment. The control brain MRI performed 3 months after HTR showed the persistence of a right frontal tumor process with a double fleshy and cystic component measuring 25*18mm vs 65*65mm, presence of small lesions of the semi -oval center and of the cortico- subcortical junction in the bifrontal and in the right parietal (fig. 1&2).

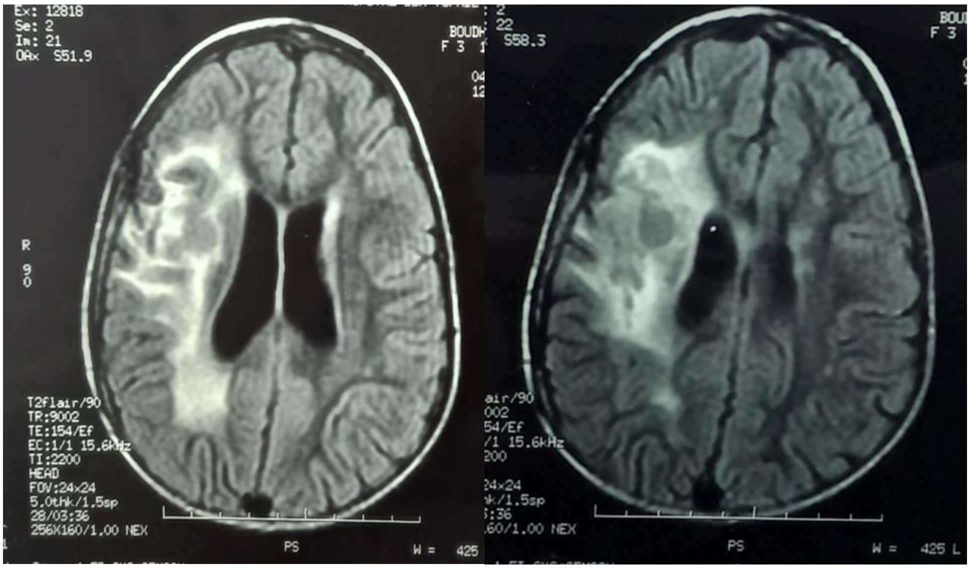

Figure 1 **Figure 2**

Figure 1 & 2 : MRI image in axial section T2 flair sequence showing partial regression of the right frontal tumor residue with perilesional area (post radiotherapy)

The regular follow-up by clinical examination and quarterly MRI was marked by the disappearance of seizures, the absence of neurological disorders and a stable aspect of the right frontal lesion on MRI. However, a delay in schooling with concentration and memory problems was noted, which led us to carry out a neuropsychological evaluation that showed below-average intelligence with IQ scores between (80-89). IQ scores provide a measure of global intellectual functioning as standard scores with a mean (M) of 100 and a standard deviation (SD) of 15.

DISCUSSION

In recent years, the vital prognosis of children treated for a brain tumor has improved, thanks to a multidisciplinary approach that adds the joint progress of surgery, radiotherapy and chemotherapy. The question of the quality of life of cured children is now more acute. Among the sequelae of a brain tumor, neuropsychological sequelae are often in the foreground, as their impact on quality of life is important. The repercussions of a brain tumor and its treatment in children will be greater than in adults because it occurs in an organ that is in full development.

These neurocognitive sequelae are linked to a certain number of factors:

➢ **Risk Factors for Neurocognitive Sequelae:**

- **Patient-Related Factors:**

❖ **Age at Diagnosis:**

The younger the child, the greater the sequelae. Duffner's study shows that the psychometric profile of children treated for a brain tumor will differ according to the age at which the child was treated (radiotherapy and/or chemotherapy) [5]. In some studies, no association was found between age at diagnosis and cognitive difficulties, suggesting the multifactorial nature of the occurrence of neurocognitive sequelae [6].

- **Tumor-Related Factors:**

❖ **Tumor Site:**

Tumors in the posterior brain fossa more frequently result in: slowness, mental flexibility, reasoning, motor skills, attention, dysarthria. In school subjects, these children have difficulties in reading and arithmetic. The sequelae of supratentorial tumors are more difficult to study because of the wide variety of locations. Hemispheric tumors mainly cause behavioral and motor disorders [6].

It is not a difference in IQ that will be explained by the site, but mainly the type of disability encountered [7].

For certain higher functions, it is not always easy to distinguish between the role of the treatment, and in particular of the irradiation, and that of the tumor location.

❖ **Type of Tumor:**

Patients treated for malignant tumors have significantly more sequelae than those treated for benign tumors, although it is not possible to differentiate between tumor and treatment effects [8].

❖ **Clinical Presentation:**

The clinical features associated with each pediatric brain tumor may affect neurocognitive outcomes differently. For example, tumors with seizure disorders and hydrocephalus at diagnosis are associated with poorer neurocognitive outcomes and lower IQ than tumors without these findings [9].

- **Treatment-Related Factors:**

❖ **Radiotherapy:**

Radiation is the most important risk factor for treatment induced cognitive decline [13].

In an effort to determine the role of radiation dose in the cognitive outcomes of children treated for brain tumors, Grill et al. compared children treated with posterior fossa radiation alone with those receiving either 2500 cGy or 3500 cGy craniospinal radiation (CSRT) [10]. There was a significant correlation between FSIQ and CSRT dose, with the children who had received the lower doses having IQ scores of 76.9 compared with 63.7 in those who had received 3500 cGy. In another study, patients who received 18 Gy whole brain radiations had IQ scores that were 12.3 points higher than those who had received 36 Gy while those who received 24 Gy scored on average 8.2 points higher than those receiving 36 Gy. Thus it was concluded that higher doses of radiation to the brain would be associated with more severe cognitive declines [11].

The volume of radiation has gained increasing attention as the ability to deliver conformal focused radiation to the tumor bed has become possible. The larger the volume of radiation, the worse is the cognitive outcome. Thus patients who have received craniospinal or whole brain radiation fare worse than those with local or no radiation [12].

❖ **Chemotherapy:**

Chemotherapy has also been implicated in the occurrence of neurocognitive impairment in children treated for brain tumor. However, it is currently difficult to estimate the specific impact of chemotherapy on cognition in patients treated for brain tumor, due to the association with surgery and radiation therapy [6].

➢ **Care and Management of Neurocognitive Sequelae:**

Due to the fact that neurocognitive injury is multifactorial and the lack of validated pediculators prevention remains best. To address this need, there are active studies of neuroprotective agents such as memantine (an NMDA receptor antagonist frequently used in Alzheimer's disease) for children on CRT. These efforts are supported by adult data showing that patients receiving memantine during CRT were less likely to have decreases in memory, executive function, processing speed, and global cognitive function [14].

Other interventions that have been or continue to be studied include exercise programs and fitness challenges as a means to improve cognitive function and facilitate neurological recovery from therapy-related impacts on neurocognition. The mechanism by which physical activity improves cognitive function and performance may be related to an increase in cortical thickness and overall brain volume and attenuation [15].

CONCLUSIONS

The complexity of the management of children with brain tumors increasingly requires the cooperation of a multidisciplinary team for which the concern for intellectual sequelae must be at the forefront in order to offer cured children the best chances of reintegration.

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