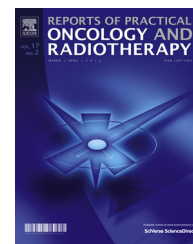


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Case report

Case presentation – A five-year survival of the patient with glioblastoma brain tumor



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ARTICLE INFO

Article history:

Received 31 January 2013

Received in revised form

27 February 2014

Accepted 5 April 2014

Keywords:

Glioblastoma

Survival

Brain tumors

Treatment

Radiotherapy

ABSTRACT

This paper presents an atypical case of a patient with brain tumor of the glioblastoma multiforme (GBM) type who achieved a 5-year survival. Some general information is provided including epidemiology, diagnostic and treatment procedures (surgery and radio-chemotherapy), and prognosis of survival related to GBM. The course of the disease, including its main symptoms, individual reasons for the delay of adjuvant treatment, after the primary surgical treatment, 37-month period of the disease free survival, as well as comprehensive management after the tumor recurrence are also presented. Histopathology confirming the clinical diagnosis is discussed in a separate chapter.

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1. Background

Primary brain tumors account for about 2% of all malignant neoplasms in adults. Approximately a half of them represent gliomas, derived from neuroepithelial cells, among which glioblastoma (GBM) is the most common type.

GBM cases represent about 20% of all primary brain tumors in the adult population, and about 75% of all the anaplastic gliomas.¹ The prevalence of GBM is about 2–4 cases per 100,000. It is more common in men than in women, and its incidence increases with age.² Only sporadically, GBM can be

found in individuals younger than 20 years of age, and its frequency rapidly increases, starting from the 5-th decade of life.

The treatment results of patients diagnosed with GBM are often unsatisfactory, and the outcome is usually poor. Currently, the main standard therapeutic methods include a radical surgical procedure, combined with radio-chemotherapy. Some innovative methods of radiotherapy based on the application of novel radiosensitizers of corpuscular irradiation or radio-immune-therapy are now being investigated. A median survival time of patients diagnosed with GBM, treated only with the use of neurosurgical procedures are 3–5 months.

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<http://dx.doi.org/10.1016/j.rpor.2014.04.002>

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The application of conventional adjuvant radiotherapy prolongs this average time about 3-fold, with a three-year survival for only about 6% of patients.

The post-treatment survival time depends on many clinical factors, such as general patient condition, age, and histopathological type of the tumor. Simson et al. demonstrated statistically significant longer survival periods among patients in whom the primary tumor location was in the frontal lobe, in comparison to the ones in whom it was located in the parietal or temporal cerebral region (11.4 months vs. 9.6 months vs. 9.1 months, respectively; $p=0.01$).³ Severity of neurological symptoms, limits of the performed surgical procedures, and response to the applied therapy, based on imaging tests, also represent prognostic factors.

Etiology of malignant neoplasms of the central nervous system (CNS) is still unknown. The most common of many probable carcinogens include: nitrosamines, pesticides, herbicides, petrochemical substances, polyvinyl chloride, and electromagnetic irradiation. However, the role of these pro-carcinogenic factors has not been unequivocally proven.^{4,5} In contrast, it has been documented that patients exposed to ionizing irradiation have an increased risk of the CNS malignant gliomas. According to the current state of knowledge in the field of molecular biology and genetics of these malignancies, two main hypotheses related to their development have been proposed. The first one includes *de novo* creation which is related to the loss of heterozygotic properties in chromosomes 9p, 10, 17p, and with the amplification of genes for the EGFR and CDK4 (this type of malignant growth occurs more often in older patients). The second one involves the creation of anaplastic gliomas, through the progression of gliomas with a lower malignancy grade (encountered more often in younger patients).^{6,7}

Currently, a required standard of therapy for patients with GBM is a combined treatment, including tumor resection, with following concomitant radio-chemo-therapy, and adjuvant chemo-therapy, based on Temozolomide. In patients who undergo non-radical surgery, or who are not treated surgically, the palliative whole brain radiotherapy (WBRT), stereotactic radiation surgery (SRS), or combination of both of these therapeutic methods are used. Also, the application of palliative chemotherapy and symptomatic treatment remain important. In addition, alternatively fractionated radiotherapy, brachytherapy, targeted molecular therapy, radio-immune-therapy, hadrone therapy, or radio-sensitizers can be considered in individual cases.

In 2005, Stupp et al. presented results of a randomized study conducted by EORTC (*European Organization for Research and Treatment of Cancer*) and NCIC (*National Cancer Institute of Canada*), comparing the application of combined radio-chemo-therapy based on Temozolomide and radical radiotherapy alone. The combined management in a statistically significant manner prolonged the total survival time from 12.1 to 14.6 months, and the rate of 2-year survival was 26.5%, compared to 10.4% for radiotherapy alone.⁸ The follow-up results, after a longer period of observation, confirmed the previous reports. The 2-, 3-, and 4-year survival rates were 27.3%, 16.7%, and 12.9%, respectively ($p < 0.0001$) in the patients' group treated with a combined therapy, and 11.2%, 4.3%, and 3.8%, in the patients' group treated with radiotherapy only.⁹

Unfortunately, despite the use of Temozolomide, the results are unsatisfactory. The reason for this therapeutic failure is the GBM resistance to most chemotherapeutic agents or rapid development of the GBM as a result of genetic transformations within the tumor cells. The main mechanism of the GBM resistance to alkylating agents, such as temozolomide, procarbazine, or nitrogen mustard derivatives, is the repair of damages caused by these drugs with involvement of protein coded by MGMT (*O⁶-methyl-guanine-DNA methyl-transferase*) gene.

A degree of methylation of the promoter's region of MGMT gene appears to be closely correlated with a therapeutic response of the glioma cells. Hypermethylation of this part of the gene significantly increases treatment efficacy among patients treated with Temozolomide,¹⁰ influencing their survival period, as well.⁹

2. Case presentation

The patient is a 38 year old Caucasian male, smoker (about 10–15 cigarettes per day for 20 years), without other relevant family or personal risk factors for neoplastic disease who had suffered from severe headaches and nausea (his first disease symptoms) since August of 2005. He did not seek any medical help until November of 2005, when he presented to his doctor, due to exacerbation of those symptoms. No abnormalities on both physical and neurological examinations were detected at that time.

On December 30th of 2005, the CT scan of his brain was remarkable for the following findings: "An expansive lesion of approximately 5 cm × 3 cm in size, located in the right temporal lobe, with nonhomogenic, post-contrast signal amplification. A large edema surrounding the lesion. A compression of the occipital corner of the right lateral ventricle. A slight enlargement of the supratentorial ventricular system, shifting to the left."

On January 25th of 2006, the patient underwent surgical therapy, including right temporal craniotomy, with total resection of the tumor. On February 7th of 2006, a histopathology examination (identification number 475,958; Info-Pat, Poznań, Poland), confirmed a diagnosis of the GBM IV stage (according to WHO classification). Microscopic images of the tumor are presented (Figs. 1–5).

After the surgery, the patient was referred to the Institute of Radiation Oncology in Gliwice, Poland, for the post-operative radiotherapy. Although the patient was qualified for this treatment, he did not arrive to the Institute of Radiation Oncology on the day of the scheduled preparatory procedures. The reason for his absence was a simultaneous diagnostic finding of the left lung's tumor, for which the patient underwent a thoracotomy with the wedge tumor resection (for diagnostic purposes). On June 12th of 2006, based on the histopathological examination results, which showed post-tuberculosis lesions, the patient's pulmonary treatment was completed.

In February 2007, approximately 13 months after his brain tumor surgery, the patient again presented to the Institute of Oncology, and according to the follow-up diagnostic work-up, no brain tumor recurrence was found. Due to the absence of tumor, no radiotherapy was considered, and "watchful

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