

GLIOBLASTOMA: A CLINICAL CASE STUDY

Sautina Irina Igorevna¹, Golofaeva Tatyana Olegovna², Kuziev Ibrokhimdzhon Dzhakhonbekovich³, Gorelkina Alina Alexandrovna⁴, Sahakyan Alik Arturovich⁵, Kudin Egor Andreevich⁶, Mamedova Rosa Saidovna⁷, Pavlov Bogdan Vladimirovich⁸

¹Student of the Institute of Medicine and Health Care named after G. R. Derzhavin, Russian Federation, Tambov, ORCID: 0009-0003-4719-1529

²Student of the Institute of Medicine and Health Care named after G. R. Derzhavin, Russian Federation, Tambov, ORCID: 0009-0008-0363-7492

³Student of the Institute of Medicine and Health Care named after G. R. Derzhavin, Russian Federation, Tambov, ORCID: 0000-0002-3461-8285

⁴Student of the Institute of Medicine and Health Care named after G. R. Derzhavin, Russian Federation, Tambov, ORCID: 0009-0001-7890-9420

⁵Student of the Institute of Medicine and Health Care named after G. R. Derzhavin, Russian Federation, Tambov, ORCID: 0009-0004-4948-2474

⁶Student of the Institute of Medicine and Health Care named after G. R. Derzhavin, Russian Federation, Tambov, ORCID: 0009-0004-0548-9180

⁷General practitioner of AMAL Company LLC (YUMID Family Clinic), Russian Federation, Tambov, ORCID: 0009-0006-8468-5810

⁸Endocrinologist, assistant of the Department of Propaedeutics of Internal Diseases and Faculty Therapy of the Institute of Medicine and Health Care named after G. R. Derzhavin, Russian Federation, Tambov, ORCID: 0000-0002-1231-8695

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Abstract

Glioblastoma is a rapidly progressing tumor with a poor prognosis, marked by a 5-year survival rate of around 5%. Variability in survival outcomes is largely related to the tumor's molecular-genetic and histological characteristics. Despite ongoing efforts to develop new, effective treatments for glioblastoma, clinical practice still primarily involves surgery, radiotherapy, and chemotherapy, along with symptomatic treatment (anticonvulsants, anti-edema medications). Nevertheless, within the current clinical paradigm, optimal outcomes can be achieved by analyzing diagnostic and therapeutic errors.

The objective of this publication is to investigate ways to improve glioblastoma treatment outcomes through a clinical case study of a female patient with glioblastoma, tonic-clonic seizures, traumatic brain injury, residual encephalopathy, and left eye strabismus.

Materials and Methods

We present a clinical case involving a female patient born in 1988 who was diagnosed with glioblastoma in December 2019.

Results

The diagnosis of “glioblastoma” was made a year and three months after the onset of tonic-clonic seizures. Despite intensive treatment, the patient passed away in December 2019 due to the progression of recurrent tumor.

Conclusion

In patients with sudden onset of epileptic seizures, a history of traumatic brain injury, and uncorrectable vision impairment, oncological screening should be conducted. Early diagnosis can increase survival rates for patients with glioblastoma.

Introduction

Glioblastomas are classified as glial tumors and constitute approximately 57% of their total number. Among all brain tumors, glioblastomas account for 48-49% of cases [1, 2]. The age-adjusted incidence rate of glioblastoma in the United States is 3.22 cases per 100,000 people and is correlated with age and male gender. In Canada and the U.S., glioblastoma incidence has remained relatively stable over the years, while in the United Kingdom, it has been increasing in recent years [3]. Over a 20-year period (1995-2015), the incidence of glioblastoma (per 100,000 population) in the U.S., Canada, and England increased by 10.2%, 26.4%, and 110%, respectively [4]. A study on incidence rates among the elderly in the U.S. (2000-2017) showed that rates in men were 1.62 times higher than in women. Furthermore, age was found to influence incidence trends significantly ($p < 0.001$) [5]. The only well-documented factors affecting brain tumor development are ionizing radiation (which increases risk in both adults and children) and a history of allergies (which decreases risk) [6]. Monitoring the incidence of neuroglial brain tumors in the Arkhangelsk region's cancer registry from 2000 to 2020 revealed more than a twofold increase. During this period, a total of 1,699 malignant brain tumors were recorded, 27% ($n=476$) of which were glioblastomas. Glioblastoma's share increased from 23.4% in 2000 to 55.3% in 2020. The adjusted incidence rate of glioblastoma rose from 1.0 to 2.1 cases per 100,000 people (an annual increase of 6.2%). No differences in incidence were observed between men and women, but rural residents had a 50-70% higher incidence than urban residents. The study authors suggest that this increase in incidence is mainly due to improved diagnosis and case registration of glioblastoma [7].

The majority of glioblastomas have no family history, with only 5% considered familial, associated with Mendelian hereditary syndromes [3]. Mutations in specific genome regions predispose individuals to glioblastoma development. Recently, five single nucleotide polymorphisms (SNPs) were identified on chromosomes 1p31.3 (rs12752552, odds ratio (OR) = 1.22), 11q14.1 (rs11233250, OR = 1.24), 16p13.3 (rs2562152, OR = 1.21), 16q12.1 (rs10852606, OR = 1.18), and 22q13.1 (rs2235573, OR = 1.15), which increase the risk of glioblastoma [8]. Since gliomas are heterogeneous, a study of 1,659 tumors profiled for IDH mutation, TERT promoter mutation, and 1p/19q codeletion was conducted to examine associations between risk SNPs and glioma subtype, resulting in the identification of five molecular subgroups of glioma. These findings contribute to an improved understanding of glioma susceptibility [9].

Clinical Presentation and Diagnosis of Glioblastoma

The peak incidence of glioblastomas occurs between the ages of 65 and 75, with an average life expectancy ranging from 8 to 14 months. Depending on the tumor's location, the clinical presentation can range from asymptomatic progression to severe neurological symptoms. These may include neuropsychological changes, new-onset seizures, motor and/or sensory deficits, cerebellar symptoms, and parkinsonism. According to the 2021 CNS classification, molecular characteristics of primary brain tumors are essential for accurate diagnosis [10]. Typically, glioblastomas are wild-type IDH tumors, with additional molecular features that often include a TERT promoter mutation, EGFR gene amplification, chromosome 7 gain, and chromosome 10 loss. Molecular alterations play a crucial role in therapy planning. Temozolomide (TMZ) is more effective in the presence of certain molecular mutations. Unmethylated O6-methylguanine-DNA methyltransferase (MGMT) and TERT gene mutation are associated with a poorer patient prognosis [11, 12].

For diagnosing glioblastoma, magnetic resonance imaging (MRI) is essential and reveals typical tumor characteristics, including: 1) hypointense and isointense lesions on T1-weighted sequences; 2) heterogeneous contrast enhancement with a ring-like pattern (indicative of necrosis); 3) hyperintense lesions on T2-weighted and fluid-attenuated inversion recovery (FLAIR) sequences, associated with surrounding vasogenic edema. Perfusion-weighted imaging (PWI) indicates a relative increase in cerebral blood volume, while magnetic resonance spectroscopy (MRS) shows elevated

choline and lactate peaks with reduced N-acetyl aspartate. Occasionally, the imaging may be atypical, resembling autoimmune encephalitis [10].

Glioblastoma Treatment

Despite modern treatments, most glioblastoma patients experience aggressive disease progression. In 75-90% of cases, glioblastomas recur within 2-3 cm of the initial tumor site, and multiple lesions are observed in 5% of patients after treatment. Historically, treatment consisted of maximal surgical resection followed by adjuvant radiotherapy, or primary radiotherapy for inoperable tumors. In recent years, temozolomide (TMZ) and non-invasive tumor treatment with low-intensity alternating electric fields (antimitotic effect) have shown clinical efficacy and improved survival outcomes. Additional treatments that have demonstrated effectiveness include bevacizumab, lomustine, carmustine, PCV (a combination of procarbazine, lomustine, and vincristine), and regorafenib (a multikinase inhibitor), which has shown superior results compared to lomustine [13, 14].

According to the National Comprehensive Cancer Network (NCCN) 2020 Clinical Practice Guidelines in Oncology, glioblastoma treatment options depend on patient age, performance status, and O⁶-methylguanine-DNA methyltransferase (MGMT) promoter methylation status (methylated/unmethylated). Patients aged ≤ 70 years with good performance status, regardless of tumor MGMT methylation, should receive standard brain radiotherapy combined with adjuvant TMZ therapy and tumor treatment with alternating electric fields. Patients >70 years with good performance status should receive either hypofractionated or standard brain radiotherapy with concurrent and adjuvant TMZ therapy and alternating electric field treatment [13].

In recent years, the development of new immunotherapy methods, including immune checkpoint blockade, chimeric antigen receptor (CAR) therapy, oncolytic virotherapy, and vaccine therapy, has brought hope for improving glioblastoma treatment outcomes. Current efforts focus on overcoming the blood-brain barrier for targeted drug delivery [15]. Additionally, genetically modified immune cells—CAR-T cells (derived from T lymphocytes) and CAR-NK cells (derived from natural killer cells)—are being tested to target and destroy glioblastoma cells; however, experiments so far have been conducted only on animal models and cell cultures [16].

The aim of this article is to present a typical clinical case of a patient with glioblastoma, along with a discussion of potential advancements in diagnostic and therapeutic care.

Materials and Methods

This article presents a clinical case of a female patient with glioblastoma, documented chronologically from July 2018 to December 2021. Each stage of diagnosis, treatment, and patient management in both inpatient and outpatient settings is described in detail.

Results

Clinical Case

2018

A woman born on February 28, 1988, living in adequate social and domestic conditions, was hospitalized in the neurology department from July 18, 2018, to July 26, 2018, with the diagnosis: Status post first tonic-clonic seizure (July 18, 2018).

Complications: Partial pneumothorax on the right.

Comorbidities: Residual encephalopathy. Strabismus in the left eye. Consequences of a traumatic brain injury (TBI) from the year 2000 (cephalalgia).

The patient was brought to the hospital by emergency medical services (EMS) from a store, where she had experienced tonic-clonic seizures with cheek and tongue biting and involuntary urination. Upon EMS arrival, her blood pressure was 140/80 mmHg, and her heart rate was 88 bpm. She was administered sibazone and magnesium sulfate.

Complaints upon Admission: Weakness, headache.

Medical History: Traumatic brain injury (TBI) in 2000, followed by frequent headaches. Strabismus of the left eye since childhood. Non-smoker, does not consume alcohol. Denies epileptic seizures and sleep disturbances.

Upon admission, the patient's condition was moderately severe, sedated by the EMS team. She was emotionally labile but oriented to self, place, and time. The tongue was bitten, with blood on her clothing. The pupils were equal, 3 mm, with horizontal nystagmus to the left, and left eye strabismus. The face was symmetrical, and meningeal signs were absent. Muscle tone and strength in the neck were rated 5/5, reflexes were intact, with no pathological responses. Blood pressure was 140/80 mmHg, heart rate was 88 bpm, SpO₂ was 99%, respiratory rate was 16 breaths/min, and the breath sounds were vesicular with no wheezing. Percussion revealed normal lung sounds, heart tones were rhythmic and loud, the abdomen was soft and non-tender, and neither the liver nor spleen was enlarged.

Results of Special Studies

Clinical Blood Test (July 18, 2018)

Leukocytes – $7.4 \times 10^9/L$, Erythrocytes – $4.14 \times 10^{12}/L$, Platelets – $273 \times 10^9/L$, Hemoglobin – 124 g/L, Hematocrit – 38.1%, ESR – 11 mm/h, Formula (%): Lymphocytes – 13.42; Monocytes – 2.8; Granulocytes – 80.5.

Clinical Blood Test (July 26, 2018):

Leukocytes – $5.4 \times 10^9/L$, Erythrocytes – $4.49 \times 10^{12}/L$, Platelets – $255 \times 10^9/L$, Hemoglobin – 141 g/L, Hematocrit – 41.3%, ESR – 14 mm/h, Formula (%): Lymphocytes – 20.4; Monocytes – 6.4; Granulocytes – 67.7.

Biochemical Blood Test (July 18, 2018):

Total Protein – 78 g/L, Albumin – 47.4 g/L, Glucose – 7.9 mmol/L, Creatinine – 100 μ mol/L, Cholesterol – 4.82 mmol/L, Triglycerides – 0.92 mmol/L, LDL – 3.1 mmol/L, HDL – 1.27 mmol/L, ALT – 14.9 U/L, AST – 20.1 U/L, Potassium – 3.7 mmol/L, Sodium – 145.3 mmol/L, INR – 1.2, APTT – 33.5 s.

Biochemical Blood Test (July 26, 2018):

Total Protein – 77.4 g/L, Albumin – 45.4 g/L, Glucose – 4.4 mmol/L, Creatinine – 102 μ mol/L, ALT – 27.3 U/L, AST – 26.5 U/L.

Urine Analysis (July 19, 2018):

Transparency – clear, specific gravity – 1025, pH – 5.5, Leukocytes – 3-4 per field of view, Erythrocytes – 5-10 per field of view, all other components – below the sensitivity threshold.

Urine Analysis (July 26, 2018):

Transparency – clear, specific gravity – 1015, pH – 5.5, all other components – below the sensitivity threshold.

ECG (July 18, 2018):

Sinus rhythm, heart rate 74/min, normal variant.

Ophthalmologist (July 20, 2018):

Optic nerve disc (OND) pale-pink, well-defined, vessel course and caliber unchanged.

Spiral CT of the Head (July 19, 2018), Dose 3 mSv:

No focal pathology detected.

Chest X-ray (July 23, 2018):

Partial pneumothorax on the right side, no focal or infiltrative shadows.

Psychiatrist (July 24, 2018):

Unspecified organic disorder, seizure syndrome.

EEG (July 26, 2018):

Background shows irregular low-amplitude alpha rhythm, mild generalized cerebral changes, moderately expressed dysfunction of midbrain structures, no interhemispheric asymmetry or epileptic activity observed.

Treatment

Mode No. 1-2, OVD diet (basic diet variant), infusions of magnesium sulfate, mannitol, Lasix, phenobarbital, carbamazepine, Neurox.

The patient was discharged with improvement: seizures did not recur, she was conscious, no meningeal signs, reflexes were intact, positive Jacobson-Lask reflex bilaterally, no paresis, statocognitive tests were normal, sleep was undisturbed, mood was stable, horizontal nystagmus to the left, vesicular breathing in all fields, percussion revealed lung sounds. Heart rate: 70/min, blood pressure: 110/65 mmHg, respiratory rate: 16/min, temperature: normal.

Expert medical history – a sick leave certificate was not needed.

Recommendations: Diet with restriction of hard fat, sugar, salt; optimal work-rest regimen; course treatment with carbamazepine 200 mg 3 times/day for up to 2 months with gradual discontinuation (no driving); Mexazol 125 mg twice/day for up to 3 weeks. Scheduled follow-up: MRI angiography of the brain, chest X-ray control in one week. Discharged under the supervision of a neurologist and therapist at the place of residence.

2019 year

The patient (born on 28.02.1988) was treated in the neurology department from 25.11.2019 to 04.12.2019 with the diagnosis: Unspecified tumor of the left temporal lobe. Syndromes: seizure, post-seizure state following a series of tonic-clonic seizures (25.11.2019), cephalgia, left anisocoria, left eye strabismus.

The patient was admitted on referral from a neurologist after a series of seizures starting at 02:00 on 25.11.2019, which recurred during the hospital stay. In addition to the aforementioned medical history (traumatic brain injury, strabismus, single seizures in 2018, etc.), new seizures were observed, accompanied by episodes of "video clips" (the patient could not recall the content), unrelated to stress.

Upon admission to the neurology department, the patient was in a moderately severe state, with a bitten tongue on the left side, sluggish, and oriented. Left anisocoria was noted (larger on the left side), left eye strabismus was present, but no nystagmus was observed. The face was symmetrical, and there were no meningeal signs. Muscle tone and strength were rated 5/5. Reflexes were intact, with no pathological reflexes. Blood pressure: 115/70 mm Hg, heart rate: 76 bpm, respiratory rate: 16 bpm. Breath sounds were vesicular, no wheezing, percussion indicated normal lung sounds, heart tones were rhythmic and loud. The abdomen was soft and painless, with no enlargement of the liver or spleen. The function of the pelvic organs was under control.

Results of Special Investigations

Complete Blood Count (26.11.2019):

Leukocytes: $6.5 \times 10^9/L$, Erythrocytes: $3.7 \times 10^{12}/L$, Platelets: $212 \times 10^9/L$, Hemoglobin: 115 g/L, Hematocrit: 33%, ESR: 8 mm/h, Formula (%):

Lymphocytes: 6.2, Monocytes: 8, Granulocytes: 81.4.

Biochemical Blood Analysis (26.11.2019):

Total Protein: 69.3 g/L, Albumin: 38.8 g/L, Glucose: 4.8 mmol/L, Creatinine: 80 $\mu\text{mol/L}$, Cholesterol: 4.46 mmol/L, TG: 4.44 mmol/L, LDL: 2.71 mmol/L, HDL: 4.44 mmol/L, ALT: 10.4 U/L, AST: 23.7 U/L, Potassium: 3.96 mmol/L, Sodium: 139.6 mmol/L.

Urinalysis (26.11.2019):

Transparency: clear, Specific Gravity: 1025, pH: 5.0, Oxalates: positive, other parameters: below detection threshold.

Infections (28.11.2019):

HBsAg: negative, HIV Antibodies: negative.

ECG (25.11.2019):

Sinus rhythm, Heart Rate: 69/min, no pathology detected.

Ophthalmology Examination (27.11.2019):

Left: Optic disc pale-pink, well-defined contour, with pericapillary hemorrhage at the temporal edge of the disc; Right: Optic disc pale-pink, well-defined contour. Relative scotomas of the 1st and 2nd order on the left, and 2nd order on the right.

Spiral CT of the Head (27.11.2019, dose: 1.3 mSv):

Lesion in the left temporal lobe (likely meningioma).

X-ray Examination (29.11.2019, dose: 2.6 mSv):

No pathology detected.

Ultrasound of Abdominal Organs, Pelvic Organs, Kidneys, and Mammary Glands (28.11.2019):

No focal changes detected.

Treatment

Regimen No. 1-2, OVD diet, Relanium, Carbamazepine, Mannitol, Magnesium sulfate, Diacarb.

Expert Opinion:

Sick leave from 25.11.2019 to 05.12.2019, continues to experience pain.

In dynamics:

The patient is conscious, oriented, ambulatory, self-caring, with left-sided ataxia during complex tests, speech is clear, mild central left-sided facial paresis.

Blood pressure: 110/70 mmHg, Heart rate: 64/min, Respiratory rate: 16/min.

Breathing: vesicular, no wheezing. Heart tones: arrhythmic. Abdomen: soft, non-tender, liver and spleen not palpable. Pelvic organ functions under control.

Consulted with the head of the neurosurgery department (KKB No. 2). Further examination and treatment in the neurosurgery department recommended (the patient was subsequently admitted to the neurosurgery department on a planned basis).

Recommendations:

Ongoing medication: Carbamazepine 200 mg, 3 times a day.

From 04.12.2019 to 23.12.2019, the patient was in the neurosurgery department No. 1 (KKB No. 2), where she spent 19 days in the hospital.

Final Diagnosis (as of 23.12.2019):

Primary diagnosis: Unspecified tumor of the left temporal lobe. Symptomatic focal (temporal) epilepsy with rare secondary generalized tonic-clonic seizures of a serial nature and rare focal seizures of a hallucinatory type against the background of a space-occupying brain lesion (meningioma).

Syndromes: Seizure syndrome, post-ictal state following series of tonic-clonic seizures (25.11.2019), cephalalgia, left-sided strabismus (D43.0).

Surgical Procedures:

Craniotomy. Microscopic removal of brain neoplasms (16.12.2019).

Disease History:

Corresponds to the description above.

Life History:

Chronic diseases: left-sided strabismus (following a traumatic brain injury in childhood). Denies having Hepatitis (Botkin's disease), tuberculosis, and skin-venereal diseases. Family history is not burdened. No blood transfusions performed.

Allergic History: Denies allergies.

Physical Examination upon Admission:

No abnormalities detected.

Neurological Examination:

Conscious, Glasgow Coma Scale score: 15.

Cranial nerves: Pupils equal and reactive to light, both eyes (OD=OS). Left-sided strabismus, no nystagmus. Facial sensation intact. Nasolabial folds are symmetric. Corneal reflexes preserved. Hearing intact. Swallowing and phonation are unaffected. No tongue deviation.

Motor sphere: Tendon reflexes: D=S, weak in arms, normal in legs, symmetric. No paresis. Muscle tone normal. Pathological reflexes: Babinski signs negative bilaterally. Stable in Romberg's position. Coordination tests performed confidently.

Results of Instrumental Studies:

ECG (05.12.2019):

Sinus rhythm, heart rate 67 bpm, normal EOS, conduction features according to PNSP.

MRI Diffusion of the Brain + Brain MRI + Brain MRI with Contrast (10.12.2019):

A round solid mass is identified at the pole of the left temporal lobe with a clear, irregular contour, heterogeneous structure, moderately expressed perilesional edema, and intense, heterogeneous contrast enhancement, measuring 22*17*25 mm. No significant mass effect.

Midline brain structures are not displaced. Brain ventricles are not dilated, their shape is unchanged. The lateral ventricles are symmetric. Evans index is 27.1 (normal up to 60 years: 24-26.3), width of the 3rd ventricle is 6 mm (normal up to 60 years: up to 7 mm). Subarachnoid spaces are unchanged. Basal cisterns are differentiated satisfactorily. The cerebellar tonsils are located above the Chamberlain level.

Conclusion: MRI image of a mass in the left temporal lobe, likely corresponding to a glioma, Grade 2-3.

EEG Videomonitoring (11.12.2019) with daytime sleep:

Moderately expressed diffuse changes in the brain's bioelectric activity. During sleep, periodic low-index (subclinical "G"? presented) regional bursts of single complexes of brain tissue (BT) in the left temporal region with a phenomenon of the opposite phase at F7.

CT of the Brain (17.12.2019):

Removal of a mass in the left temporal lobe.

Histochemical Study Results (20.12.2019):

Glioblastoma was detected.

2020 year

Between February 19, 2020, and March 26, 2020, the patient was hospitalized in Radiotherapy Department No. 1. She reported symptoms of general weakness, weather sensitivity, and memory impairment.

Medical History: The patient (see detailed history above) is on carbamazepine at 400 mg twice daily. She discontinued finlepsin independently due to poor tolerance. The patient was referred to the Comprehensive Clinical Center for Oncology (CCCO) after examination by a neurosurgeon.

MRI Report from February 18, 2020 (T1- and T2-weighted imaging before and after gadovist contrast enhancement): The midline structures of the brain are not displaced. Normal cortical sulci are observed in the cerebral hemispheres and cerebellum. The subarachnoid spaces are not dilated. Basal ganglia, internal capsule, corpus callosum, thalamus, and cerebellum show an unaltered MR signal. No additional formations are detected in the sella turcica or pituitary. The parasellar structures appear normal in configuration. The optic chiasm is unaltered, and no abnormalities are visualized in the cerebellopontine angle regions.

In the pole of the left temporal lobe, a postoperative cyst measures up to 4 x 1.8 cm. Following contrast enhancement, an area with irregular enhancement up to 1.3 x 0.6 cm is observed along the cyst's lower contour (residual tumor? vascular network?).

The histochemical analysis of a previously obtained biopsy was reviewed, and the tumor was identified as a Grade 4 glioblastoma (see Figures 1-5). Macroscopic Description of Histological Specimen (February 19, 2020): The tumor tissue reveals multiple areas of coagulative necrosis, solid fields, and pseudopalisading structures composed of cells with moderate nuclear polymorphism and numerous mitotic figures. Vessels of varying calibers are present, displaying significant endothelial proliferation and glomeruloid structures.

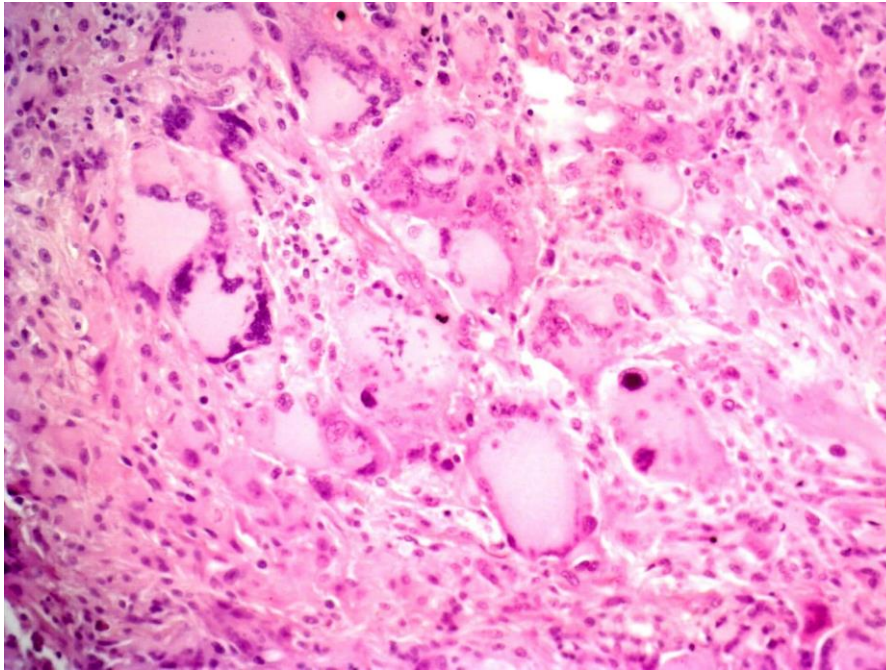


Fig. 1. Polymorphocellular malignant tumor with pronounced cellular and nuclear polymorphism, presence of pathological mitoses, areas of necrosis, and formation of pseudopalisades of tumor cells around these areas. Proliferating vessel groups and hemorrhages are observed.

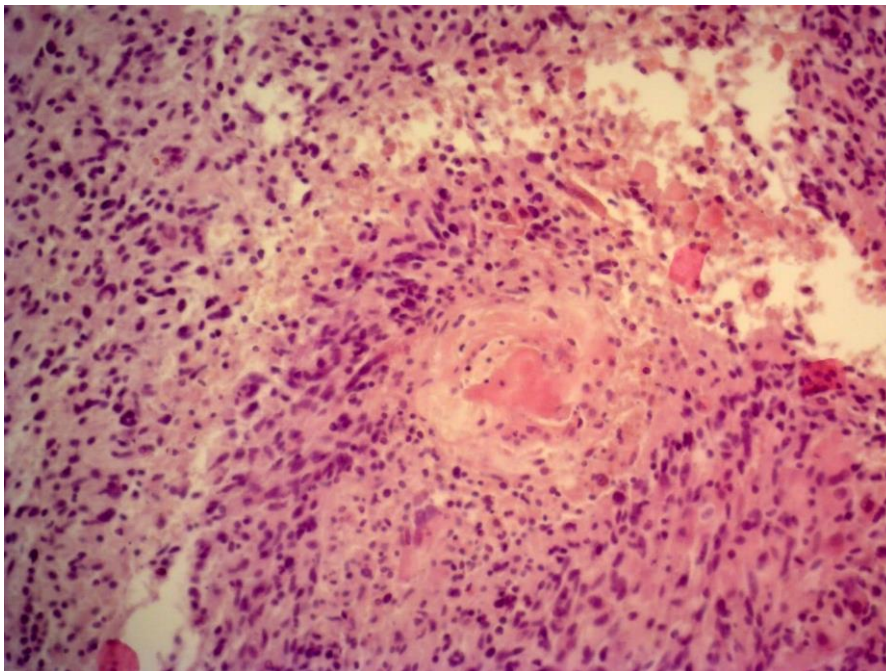


Fig. 2. Granular morphology of cells with abundant granular cytoplasm resembling histiocytes (H&E, 400x).

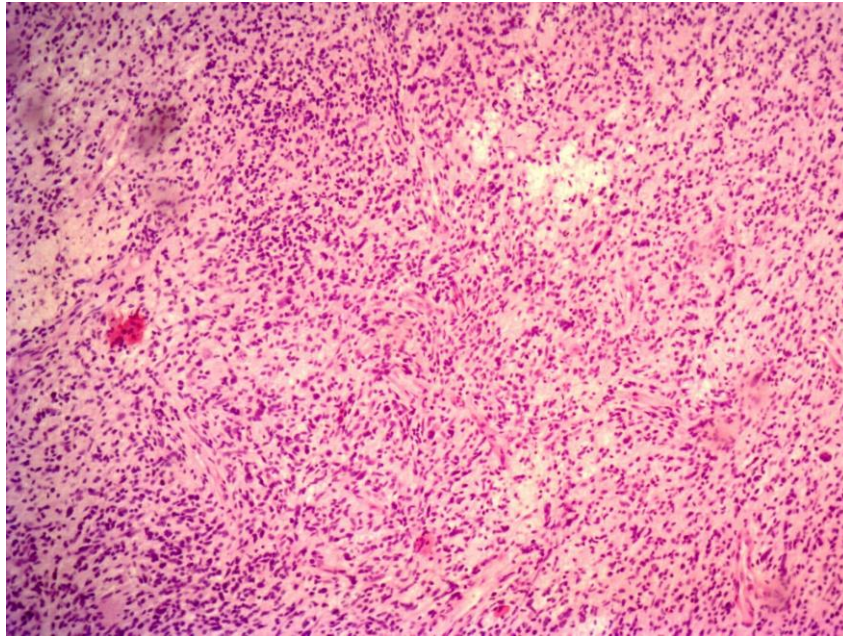


Fig. 3. Astrocytic cells with nuclear polymorphism and thin glial processes.

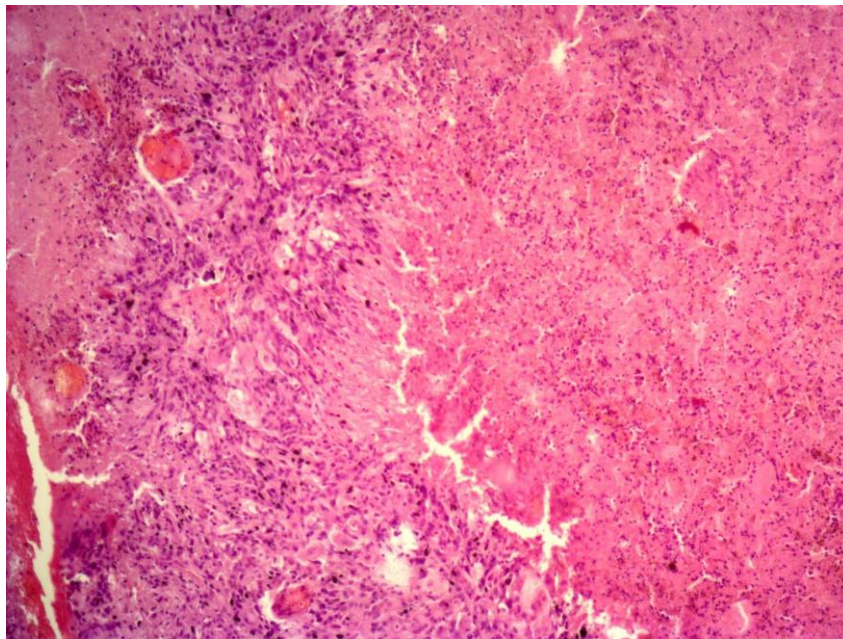


Fig. 4. Small cell glioblastoma with small monomorphic nuclei (H&E, 100x).

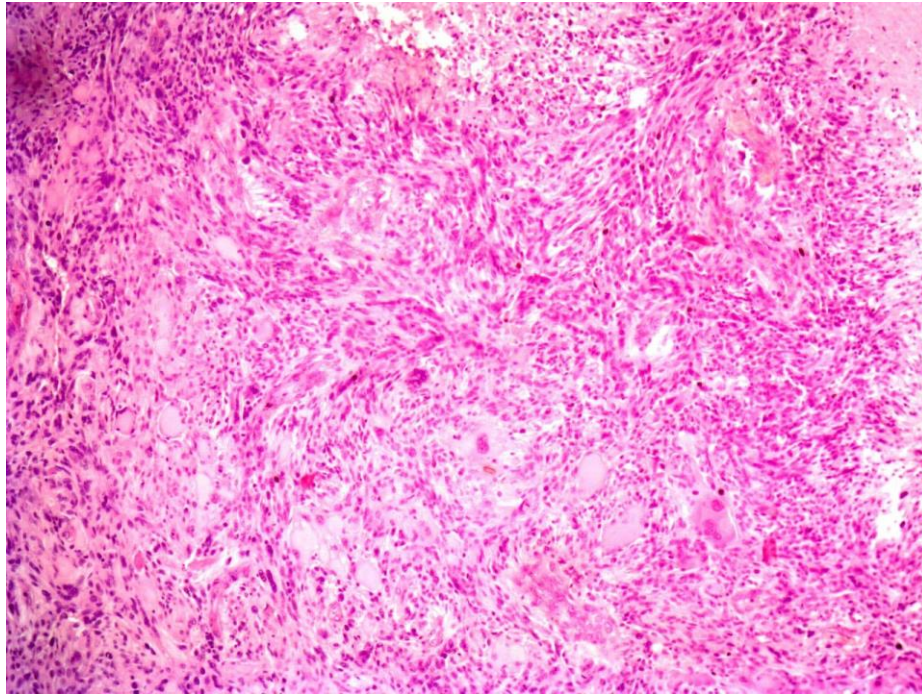


Fig. 5. Hypercellular neoplasm with infiltration into the surrounding brain parenchyma (cellularity gradient) (H&E, 40x).

Based on laboratory tests and examinations by a general physician and specialists prior to hospitalization in Radiotherapy Department No. 1, no pathologies were identified.

Ophthalmologist Examination (February 11, 2020): Mild myopia in both eyes. Retinal angioapathy in both eyes.

Abdominal Ultrasound (February 11, 2020): Moderate changes in the parenchyma of the liver and pancreas.

Consultation on February 19, 2020: A course of radiotherapy was recommended.

Primary Diagnosis: Glioblastoma of the left temporal lobe, subtotal tumor resection as of December 16, 2019, postoperative course of radiotherapy.

Secondary Diagnoses: Mild myopia in both eyes. Retinal angioapathy in both eyes. Symptomatic epilepsy with rare secondary generalized tonic-clonic seizures in clusters and occasional focal seizures, hallucinatory type, associated with a mass lesion.

Special Treatment: Postoperative radiotherapy was administered with moderate fractionation to the tumor bed and residual brain tumor, total dose (TD) of 55 Gy (60 Gy for Gross Tumor Volume) in 22 fractions on an Elekta Axesse device. (Discharged with improvement. Neurological condition stable.)

Symptomatic Therapy: Anti-edema, anti-ulcer, and anticonvulsant treatments were administered.

Blood Tests (clinical, biochemical), urinalysis, stool for helminth eggs, HIV tests, hepatitis, and RW: No pathologies detected.

Neurosurgeon-Oncologist Recommendations (March 25, 2020):

1. Dynamic monitoring by a neurologist (general physician) at the patient's place of residence.
2. Referral for medical examination to determine disability status.

3. Consultation with a chemotherapist to evaluate chemotherapy after 4 weeks post-radiotherapy (monitoring CBC, platelets, and blood biochemistry 2-3 days before each chemotherapy cycle).
4. Positron Emission Tomography (PET) of the brain with C11 methionine, follow-up 6 months after the end of chemotherapy.
5. MRI of the brain with contrast enhancement 6 months post-chemotherapy.
6. EEG every 6 months.
7. Dexamethasone 4 mg (1.0 ml), intramuscular, in the morning for 3 days, then 4 mg (8 tablets) in the morning for 2 days, gradually taper by reducing by 2 tablets every 2 days until full cessation.
8. Medication regimen:
 - Vitamin E 800 mg in the morning, 10 days monthly, continuously.
 - Diacarb 250 mg, ½ tablet in the morning, every other day, continuously + Asparkam 1 tablet 2 times daily on Diacarb days.
 - Carbamazepine (finlepsin) 400 mg twice daily for 3 years post-surgery (adjustment by an epileptologist).
 - Immunofan, 1 spray in each nostril for 10 days monthly, starting with the first chemotherapy course.
 - Dexamethasone 4 mg (1.0 ml), intramuscular, in the morning for 3 days following each chemotherapy cycle.
9. For headaches, Spazgan (Baralgin) 1 tablet 2-3 times daily.
10. Low-carbohydrate diet (diet table No. 9), including beets, parsley.
11. Work and rest regimen: avoid physical strain, overexertion, hypothermia, excessive sun exposure, coffee, baths, saunas, and flights.
12. Follow-up with a CCCO neurosurgeon with PET and MRI results.

2021 year

In 2021 (March 15), the patient underwent routine follow-up at the State Healthcare Institution "TOOKD."

Complaints: Headaches, weakness in arms and legs, visual disturbances (hallucinations).

Laboratory Test Results: No abnormalities detected.

Brain MRI: Tumor stability without signs of progression. Postoperative cyst in the pole of the left temporal lobe measuring up to 4 x 1.8 cm. Following contrast enhancement, an area of uneven enhancement along the lower contour of the cyst measuring 1.3 x 0.6 cm showed progression.

Ophthalmologist: No negative dynamics observed.

Conclusion:

- The patient's condition remains stable, with no signs of tumor progression.
- Epileptic symptoms are medically controlled.
- Eye condition remains stable, with no vision deterioration.

- A postoperative cyst in the left temporal pole measuring up to 4 x 1.8 cm, with an area of uneven enhancement that has shown progression.
- Histological examination confirmed the diagnosis of glioblastoma of the left temporal lobe, high histological grade (G4).

In December 2021, the patient passed away. Cause of death: Tumor progression with invasion into adjacent brain structures, likely resulting in disruption of vital centers' functions and subsequent death.

Discussion

This clinical case of a patient with glioblastoma highlights potential improvements in the quality of medical care for this patient group. The primary concern is the delayed diagnosis of the disease. In 2018, when the patient first experienced tonic-clonic seizures, only a spiral CT scan was performed, which did not detect focal lesions. However, MRI is the standard for diagnosing (and post-operative monitoring of) glioblastoma [17-21]. The definitive diagnosis is based on histopathological examination of the intraoperatively removed tumor or its fragments, using traditional histological, cytological, and histochemical methods. When neurosurgical resection of the lesion is not feasible, a fine-needle aspiration biopsy is performed [22-25]. Among CT-based methods, PET/CT is preferred, although it diagnoses glioblastoma less frequently than MRI and is used in specific cases for differential diagnosis of ambiguous neoplasms [26].

Another factor warranting attention is the patient's history of traumatic brain injury (TBI) at age 12, after which left-sided strabismus developed. Clinical cases and numerous studies have linked TBI with subsequent glioblastoma development [27-32]. In their publication, N. Ohana et al. suggest that brain trauma and glioblastoma are associated through three transcription factors: p53, c-MYC, and hypoxia-inducible factor-1 α (HIF-1 α) [31]. One probable mechanism described by the authors involves changes in brain energy metabolism due to TBI, resulting in the depletion of VDAC1, a voltage-dependent ion channel controlling cellular energy in mitochondria. This, in turn, alters the expression profile of p53, c-MYC, and HIF-1 α , which regulate metabolism, growth, proliferation, and cell differentiation. These factors also control the expression of certain molecules that support glycolytic metabolism, gradually fostering a tumor phenotype.

The "incubation period" between TBI and glioblastoma can be very prolonged. One reported case describes glioblastoma in a man 17 years after a TBI [28]. Additionally, a case was documented of a Pakistani girl who developed right-eye strabismus and partial, painless vision loss several years before glioblastoma diagnosis; ophthalmic surgery did not improve her vision. No history of TBI was indicated [33]. At the same time, strabismus can result from either TBI or a brain tumor [34]. Strabismus may be considered a precursor or marker of a brain tumor (or a consequence thereof).

The emergence of epilepsy symptoms for the first time in a patient with a history of TBI should have prompted a diagnostic focus on oncological screening. Several studies have demonstrated a link between glioblastoma (and brain tumors in general) and epilepsy [35-40]. Glioblastoma and tumor-associated epilepsy interact through several pathophysiological mechanisms, in which the neurotransmitter glutamate plays a central role. Glutamate engages with its ionotropic and metabotropic receptors, promoting tumor progression and excitotoxicity. On one hand, elevated glutamate levels stimulate glioma cell proliferation and invasion; on the other hand, they lead to epileptic discharges and excitotoxicity, which contribute to tumor growth [37]. Seizures occur in approximately 60% of glioblastoma cases [41]. Therefore, glioblastoma should be considered when seizures appear suddenly and as a primary symptom.

The obtained histological findings align with cases described in the literature. The biopsy of this patient revealed a malignant form of grade 4 glioblastoma, which, according to published data, originates from precursor or stem cells in the astrocytic lineage [42].

Approximately 3 years and 5 months passed from the first manifestation of the disease, in the form of a tonic-clonic seizure (July 18, 2018), until the patient's death (December 2021), and 2 years from the confirmed diagnosis of "glioblastoma" based on histochemical biopsy findings (December 20, 2019) to the fatal outcome. This is roughly consistent with published survival statistics. Despite considerable efforts and the search for optimal diagnostic and treatment protocols, the prognosis for glioblastoma remains poor: the 5-year survival rate is 5%, and the median survival for patients undergoing maximal safe resection and adjuvant chemotherapy is 14 months [43].

Conclusion

The data from the literature sources show that glioblastoma is a rapidly progressing tumor with severe neurological and psychiatric manifestations and a poor prognosis. Although different research groups are exploring new treatment methods, classical triad therapy remains standard in clinical practice: surgical tumor resection, chemotherapy, and radiotherapy. Additionally, symptomatic therapy is prescribed. In the clinical case discussed above, there was a delayed diagnosis of glioblastoma, despite strong indications for oncological screening. Early diagnosis and, accordingly, the initiation of treatment at an earlier stage would likely have prolonged the patient's life. The history of TBI and left eye strabismus, combined with the first manifestation of clonic-tonic seizures, should have raised the suspicion of the attending physicians and prompted them to refer the patient for MRI diagnosis. During the first year after the manifestation of the disease, antiepileptic treatment was administered, and the optimal time for oncological therapy was missed. After hospitalization in the neurosurgery department in 2019 and a prompt diagnosis, the tumor was surgically removed with simultaneous histopathological examination. Additionally, the patient underwent courses of radiotherapy and chemotherapy. However, in March 2021, MRI revealed a "postoperative cyst with an area of uneven contrast enhancement, which had progressed." The recurrence of the tumor, with rapid progression and invasion into neighboring brain areas, led to the patient's death. Nevertheless, the prognosis for grade 4 glioblastoma is very poor, and the efforts of medical personnel should be focused on prolonging the patient's life rather than preventing the fatal outcome. The development of new treatment methods and early diagnosis of glioblastoma will undoubtedly improve patient survival in the future. For this reason, scientific research in this field should be encouraged.

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