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A rare variant of glioblastoma is gliosarcoma: 11-case clinical trial

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Abstract

Gliosarcoma is a rare subtype of glioblastoma, IDH wild type. Its characteristic features are a biphasic configuration with mixed glial and mesenchymal components. Here in, we present a rare case of Gliosarcoma that has been operated in our clinic in the last 10 years. Patients with gliosarcoma pathology results were collected from the ones operated in our faculty within 10 years. Patients from all age groups were included in the study. 1 of 11 gliosarcoma cases was described in detail. Seven of the cases were male, while 4 were female. Regarding tumor location, six 6 were located in the right, while 5 were in the left hemisphere. The average survival time of all 11 patients was 11 months. In 6 cases, the initial pathologic diagnosis was gliosarcoma, while in 5 cases, it was glioblastoma, and in the 2nd case, the pathology result was gliosarcoma. Gliosarcomas have a worse prognosis in terms of survival. Clinically, it is not possible to distinguish between glioblastomas and gliosarcomas. Treatment proceeds in the same way.

Keywords: glioblastoma, gliosarcoma, isocitrate dehydrogenase,brain tumor

1. Introduction

Gliosarcomas (GS) are primary brain tumors with mixed glial and mesenchymal components and were first described in 1895 by Heinrich Stroebe (1). Gliosarcomas are uncommon high-grade tumors, representing up to 2%–8% of all glioblastoma (GBM) cases (2). A separate histopathological evaluation was needed because of its more aggressive course, higher probability of developing extra-cranial metastases, and lower survival compared to glioblastoma (3). It is seen mostly between 40 and 60 years of age, with a mean age above 50 years, is more common in males and occurs mainly in the cerebral hemispheres, with the temporal and frontal lobes being the most typical locations (4). The pathogenesis of GS remains unknown, but findings of common genetic alterations in both the gliomatous and sarcomatous components support the hypothesis that GS tumors are of monoclonal origin (5). It has a biphasic morphological pattern with both glial and malignant mesenchymal components. Therapeutic modalities include maximal surgical resection, external beam radiotherapy and chemotherapy, but the prognosis is poor in terms of survival (6).

2. Materials and Methods

2.1. Research Group

The charts of consecutive patients who were operated in our neurosurgery clinic from January 2013 to May 2023 and had histopathologically confirmed gliosarcoma were reviewed retrospectively. Pathological diagnosis of glioblastoma was made according to the most recent revision of the original World Health Organization (WHO) classification of central nervous system tumors. Demographic and clinical features were recorded, and neuroimaging findings and survival times were noted. Patients older than 18 years were included in the study. Primary, as well as secondary gliosarcoma cases were included in the study (Table 1).

Table 1. Demographical and clinical features of patients

Age (Years) (Mean)	58.27
Sex (Male/Female)	7/4
Survey (Mean)	11 Month
Tumor Localization	Right hemisphere, n=6 Left hemisphere, n=5

3. Results

We retrospectively evaluated the 11 gliosarcoma cases we found. Seven of the cases were male, while four were female. Regarding tumor location, 6 cases were located in the right, while 5 were in the left hemisphere. All patients received standard gross-total resection followed by radiochemotherapy. In 6 cases, the initial pathologic diagnosis was gliosarcoma, whereas the remaining 5 cases were recurrent, and their initial diagnosis was glioblastoma. The average survival time of all 11 patients was 11 months.

Among the 11 cases, we wanted to describe the most interesting one in more detail.

A 58-year-old male patient was diagnosed with Parkinson's disease 2 years ago due to a resting tremor in the right hand. Since the patient had complaints of headache, apathy and

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forgetfulness for the last 2-3 months, the clinic considered it to be due to Parkinson's disease. The patient's medical treatment was arranged, but there was no change in his clinic.

In the preoperative examination of the patient, their consciousness was confused, and the Glasgow Coma Scale (GCS) was 13 with limited orientation and cooperation. Pupils were isochoric, direct-indirect light reflex was positive, and there was no facial asymmetry. Motor examination was evaluated as intact.

Magnetic resonance imaging (MRI) showed that the right frontal lobe occupied a lesion with multiple linear projections measuring approximately 5x4 cm. The mass was heterogeneous, with a prominent peripheral rim and vasogenic edema, a cystic component. A midline shift of 0.5 cm was noted without any evidence of hydrocephalus. The impression of MRI was likely glioblastoma multiforme (Fig. 1).

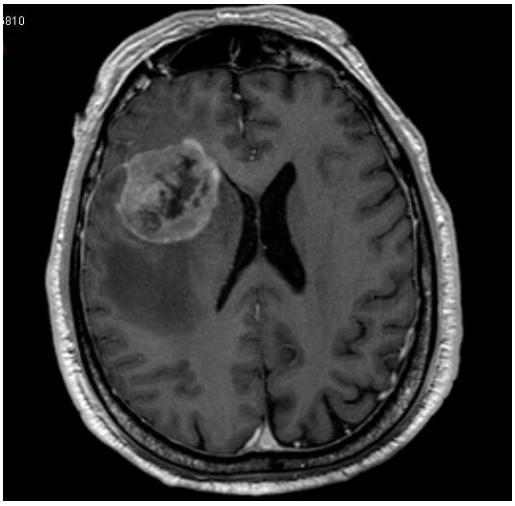

Fig. 1. Magnetic Resonance Imaging (MRI) finding

The surgical intervention consisted of a right frontal craniotomy with gross total tumor resection. No complications were encountered in the post-operative period.

In the histopathological examination of the patient, GFAP (Glial Fibrillary Acidic Protein) was positive in the glial component, and reticulin and vimentin were widely positive in the sarcomatous component. When the pathology result was *non-IDH (Isocitrate dehydrogenase) mutant, GFAP + gliosarcomatous glioblastoma*, the patient was evaluated in the multidisciplinary oncology council and cranial radiotherapy was planned. After radiotherapy, temozolamide chemotherapy was started. Intermittent clinical and radiological follow-up continues.

4. Discussion

Gliosarcoma usually occurs in the 5th and 6th decades. It is about 2 times more common in men than women (7). Equivalent to the literature, 7 of our series of 11 cases consisted of male patients. Unlike the literature, Yi et al (8) analyzed 48 cases of gliosarcoma and the median age was 52.5 years, Rath et al (9) The median age was reported as 45 in the series of 27 cases (10,17). The mean age of our series of 11 cases was 58 years.

The location of gliosarcoma is usually the supratentorial region and the most common involvement is the temporal lobe. This is followed by the frontal lobe, parietal lobe, and occipital lobe, respectively (10). Kumar et al (11) in a series of 24 cases, reported that the most common location of GS was the temporal lobe with 37.5%. When we look at the localization of our cases, we see 4 temporal lobe, 4 frontal lobe, 2 occipital lobe and 1 parietal lobe localization.

Despite the differences in molecular profile, histopathological appearance, and tendency to develop metastatic disease in gliosarcoma, the treatment approach is similar to glioblastoma. After surgical resection, radiotherapy and chemotherapy are the main treatment modalities for gliosarcoma (12). Treatment with concomitant chemoradiotherapy with temozolomide is suggested to improve overall survival (13). Although the dose of adjuvant radiotherapy varies according to the performance status of the patient, it is usually 60 Gy (Gray) in 30 fractions for 6 weeks . In patients with poor general condition, a hypofractionated dose may be preferred (14).

Although distant metastases were not observed in our cases, lung, lymph nodes and bone metastases have been reported in the literature (15). Clear evidence about the pathogenesis of gliosarcoma has not yet been found. The most widely accepted view is the abnormal mesenchymal differentiation of malignant glioma based on monoclonal origin (16). GFAP and reticulin help to differentiate between glial and mesenchymal elements. In ourcases , GFAP + in the glial component and reticulin and vimentin positive in the sarcomatous component were shown in the histopathological examination.

Since gliosarcoma cases are extremely rare, no specific treatment modality for Gliosarcoma has been defined in the literature. Studies suggest that survival and prognosis are worse than glioblastoma. Domadoran et al (17) found that while the median survival rate was 5.2 months in patients with gliosarcoma, it was 12.2 months in patients with glioblastoma. The median survival time of our cases was 11 months. In the same study, the patients' Magnetic Resonance (MR) images were examined and classified as peripheral and centrally located gliosarcoma. While dural thickening was detected in all peripherally located tumors, transependymal infiltration into the ventricles was observed in centrally located cases (17). Our case was also centrally located, and there was transependymal infiltration

Gliosarcoma, a histological biphasic tumor showing separate glial and sarcomatous components, is a very rare clinicopathological entity that was diagnosed only once in the last 10 years in our center. It is associated with a very aggressive clinical course with patient's rapid deterioration and poor outcome. The patients' mean survival rate averages less than a year, even with a combination therapy comprising radio

and chemotherapy

Conflict of interest

The authors declared no conflict of interest.

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None to declare.

Authors' contributions

Concept: R.E., F.T., Design: R.E., Data Collection or Processing: R.E., Analysis or Interpretation: R.E., F.T., G.G., M.A., C.C., Literature Search: R.E., F.T., G.G, M.A, C.C., Writing: R.E.

Ethical Statement

Approval was obtained from Ondokuz Mayıs University Clinical Research Ethics Committee, the study started. The ethics committee decision date is 24/1/2023 and the number of ethical committee decisions is 2023/373.

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