

## Posterior Fossa Glioblastoma, Case Report, and Reviewed Literature

### Abstract

Glioblastomas multiformes (GBMs), are the most common primary malignant tumors of the Central Nervous System. Frequently located in supratentorial topography, infratentorial location is rare, around 0-3.4% of primary GBMs. The diagnosis of these tumors is uncommon in adults, few cases have been reported, being even more infrequent in elderly patients. The most typical clinical presentation is a rapidly growing posterior fossa lesion, increased intracranial pressure, and cerebellar signs associated with the mass and perilesional edema. Clinical presentation, computed tomography (CT), and magnetic resonance imaging (MRI) provide useful information about the possible diagnosis but are not definitive. We describe a clinical case, 76 years old female with a clinical history of hypertension, depressive syndrome, and dyslipidemia. Started progressively with ataxy, imbalance, and vertigo. Brain CT shows an intra-axial, infiltrative lesion in the superior and middle vermis. MRI presents a heterogeneous lesion in the superior and median vermician region of the cerebellum with ring enhancement and central necrotic area. Was performed a middle suboccipital approach, corticectomy in the superior vermis. The intraoperative histological study reveal a high-grade malignancy astrocytoma, which was released through a subtotal resection. The histological result was a high-grade astrocytoma, grade IV in WHO classification. Four weeks after the surgery the patient started treatment with chemotherapy and radiotherapy. The main point of this case is the atypical location of the tumor. These lesions are rare in this location but they will do considering the differential diagnosis of posterior fossa tumors. However, the most frequent lesions with high percentages of incidence are metastatic lesions.

**Keywords:** Glioblastoma, Cerebellar tumor, Sub-occipital approach, Subtotal resection, Radiotherapy, Chemotherapy

### Introduction

With a frequency that ranges between 15 and 50%, glioblastoma multiforme (GBM) is the most common intracranial primary tumor in adults. GBM typically affects patients in their fifth or sixth decade of life and primarily develops within the cerebral hemispheres. Only 1% of cases of GBM in the posterior fossa, and more specifically in the cerebellar parenchyma, are reported.<sup>[1, 2]</sup>

Cerebellar glioblastoma in the elderly is uncommon; as far as we know, only 33 cases have been documented in the literature, which lends relevance to our work.<sup>[3]</sup>

A rapidly expanding posterior fossa tumor with increased intracranial pressure and cerebellar symptoms is the most common clinical presentation.<sup>[4]</sup>

Developing a viable treatment plan for cerebellar glioblastoma requires an accurate

diagnosis. As always, it's important to combine the clinical manifestations with in-depth neurological testing and imaging studies. However, it can occasionally be challenging to diagnose these cancers. However, they might not result in a conclusive diagnosis. Clinical presentation, computed tomography (CT), and magnetic resonance imaging (MRI) might all offer significant information. Positron emission tomography/computed tomography (PET/CT) with fluorine-18-fluorodeoxyglucose (FDG) is sometimes advised and may provide additional alternatives for differential diagnoses when accessible.<sup>[5]</sup>

Similar to PET/CT, Thallium-201 (TI) single photon emission computed tomography (SPECT) imaging can be used to diagnose brain cancer if it is accessible. SPECT and PET both have the ability to identify biological processes at the cellular and molecular levels. They offer biochemical or molecular details on the tissues of brain tumors in this way. In most

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malignant tumors located in the posterior fossa, it is observed with contrast enhancement, the differential diagnosis with CT or MRI does not have 100% specificity or sensitivity. Even in cases where spectroscopy is used. As a complement to the possible options for differential diagnosis, radioisotope imaging, which reflects the functions and characteristics of the tumor, is also a useful method, when available.<sup>[6]</sup>

Independent of the technique the radiological features are non-specific and the diagnosis was made only with histological examination, obtain with histological samples obtained during the surgery/biopsy.

It is useful to make the differential diagnosis between metastases, anaplastic astrocytomas, GBM, vascular lesions such as cerebellar infarction, and infectious lesions among other possible pathologies because their treatment modalities, prognosis, and evolution are different. Even the surgical approach could certainly be different.

The recommended treatment is radical resection if possible and without new neurological deficits after surgery, radiotherapy, and chemotherapy with temozolomide.<sup>[7]</sup>

With just 33 occurrences reported in the literature, we offer a clinical case of a primary cerebellar glioblastoma in an elderly woman. Describe clinical presentation, radiological diagnosis and pathological features, our management of the case, and review the literature.

### Case report

A woman in her 76s who had a two-month history of intracranial pressure along with nausea, vomiting, and headaches was hospitalized to our hospital. She also had a history of hypertension, depressive syndrome, and dyslipidemia.

Cerebellar symptoms, including cerebellar ataxia, dysmetria, and dysdiadochokinesia, were seen during the neurologic examination. Bilateral papillary edema was visible in the fundus oculi.

In order to look for any intracranial lesions, a cerebral computed tomography (CT) and nuclear magnetic resonance (MRI) were carried out, focusing on the posterior fossa and taking into account the patient's symptoms. The CT revealed a lesion located in the upper part of the cerebellar vermis. The lesions were spontaneously hypodense with a mass effect on the roof of the fourth ventricle. The MRI showed a lesion in the upper vermis in the medial part, with irregular contours. After gadolinium administration, the lesion 3-4cm in size had ring enhancement and a central necrotic area (**Figure 1**).



**Figure 1.** Brain MRI (a) axial, (b) sagittal, (c) coronal slices with midline superior vermis intraxial lesion, heterogeneous, ring enhancement and a central necrotic area.

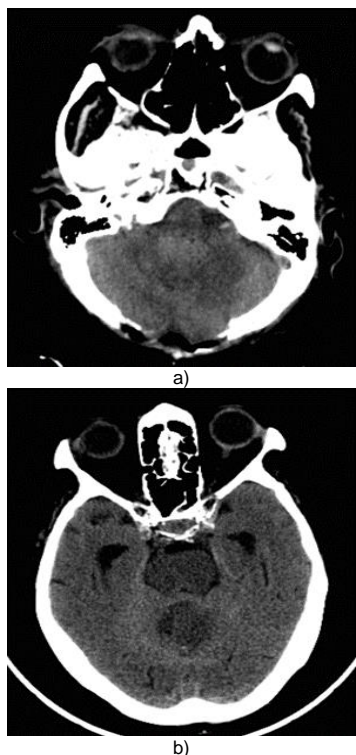
Before surgery, the diagnosis of cerebellar glioblastoma is infrequently made, despite the fact that the picture may show other types of lesions. Adults most frequently develop metastatic lesions in the posterior fossa. The systemic neoplastic search was unsuccessful in our situation.

It is important to think about the differential diagnosis before the surgery, being true that in many cases the form of surgical approach does not change.

Under general anesthesia, in the prone position. We used a midline incision and after displacing the occipital muscles we released a sub-occipital craniotomy. After opening the dura mater and performing the corticectomy, a white, infiltrating, friable, slightly hemorrhagic lesion was identified that did not present cleavage planes with the surrounding cerebellar parenchyma. The intraoperative histological study reveals a

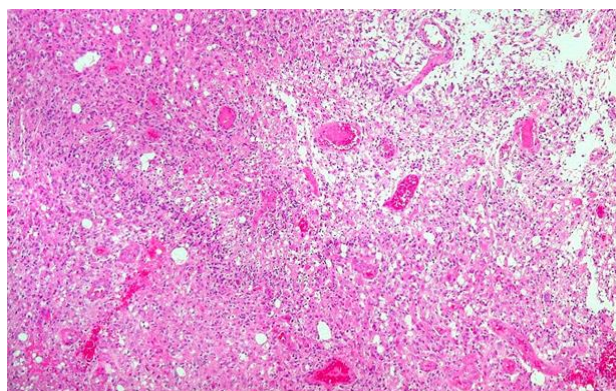
high-grade malignancy astrocytoma. A subtotal tumor resection was performed.

The patient presents a good evolution in the postoperative period, don't present worst symptoms, and release a CT scan to control and exclude complication (**Figure 2**).



**Figure 2.** CT, axial slices, status post middle sub-occipital craniectomy, without complications.

The histological analysis revealed elongated spindle cells with irregular, somewhat pleomorphic, and large nuclei, proliferative blood vessels, and necrosis (**Figure 3**). These characteristics are compatible with glioblastoma (World Health Organization grade IV).



**Figure 3.** coloring displays a strong cellular density. An obvious anisokaryosis clearly defines the cells. The nuclei are fairly big. The cells have a large amount of eosinophilic cytoplasm. There were numerous mitoses found. Magnification: A-200; stain: hematoxylin and eosin.

In resume, in our case, the surgery allowed the diagnosis of glioblastoma to be confirmed histologically. The postoperative

course was uneventful. The patient received postoperative radiotherapy to the posterior cranial fossa. The outcome was favorable during one year of follow-up, the neurologic signs gradually improved nonetheless maintain ataxy and dyskinesic movements.

## Results and Discussion

Malignant brain tumors are uncommon tumors when their frequency is compared to that of other neoplasms seen in other parts of the human body. The mortality rate is disproportionately high for them nonetheless. The glial cells that cover and support neurons give rise to gliomas. According to the WHO classification, grade IV tumors include glioblastoma multiforme (GBM). tumor that is extremely malignant. With a frequency that ranges between 15 and 50%, this tumor with infiltrating growth is the most common intracranial primary tumor in adults. GBM often affects individuals in their fifth or sixth decade of life and primarily develops inside the cerebral hemispheres, although it can also arise infratentorially, in the brainstem, or in the cerebellum. The appearance of glioblastoma in the posterior fossa and particularly in the cerebellar parenchyma is a rare occurrence, representing only 1% of all GBM cases.<sup>[1, 2]</sup>

As far as we know, only 33 cases of cerebellar glioblastoma in the elderly have been recorded in the literature.<sup>[3]</sup> This point gives relevance to our report.

The clinical presentation is correlated with the location of the tumor and the involvement of surrounding anatomical structures. Headaches, seizures (which are uncommon in posterior fossa injuries), motor weakness, and focal neurological deficits like hemiparesis, aphasia, ataxia, sensory loss, hemianopsia, and cranial nerve dysfunction are frequently reported symptoms in these cases. These neurological changes take days or weeks to manifest. The most typical clinical presentation is a rapidly growing posterior fossa mass with increased intracranial pressure and cerebellar signs.<sup>[4]</sup>

Establishing a proper treatment plan requires a precise diagnosis of cerebellar glioblastoma. As always, it is essential to combine the clinical manifestations with thorough neurological testing and imaging studies.

The differential diagnosis requires analyzing the imaging features and taking into account the clinical presentation. In cases in which the presence of multiple cortical/subcortical nodular lesions that capture ring contrast is observed, the main diagnostic suspicion should be secondary lesions.

The presence in the imaging tests of large volume masses located deep in the white matter should make us think of the presence of diffuse glioma. If a heterogeneous enhancement is also observed, it is probably a glioblastoma.<sup>[8]</sup>

When interpreting the cases, parameters such as clinical progression (acute, subacute, chronic), the location of the



lesion (intra-axial/extra-axial), or secondary effects caused by its presence such as volume, edema, or herniation must be taken into account. The characteristics of the contrast coating must also be considered (solid, annular).<sup>[8]</sup>

In Neuro-Oncology the more rapid onset symptoms occur especially with metastatic diseases and GBM. Intracranial neoplasms occupy space, causing a mass effect and causing displacement of adjacent structures. In this context, secondary damage and the occurrence of herniation arise.

Both primary and secondary lesions cause volume and cerebral edema due to an abnormal increase in permeability due to the rupture of the blood-brain barrier (BBB), and vasogenic edema.<sup>[8]</sup>

Intracranial lesions can present as a single lesion or multiple lesions. In cases of single lesions, we must consider the diagnostic possibility of primary neoplasia, hematoma, abscess, or infarction. For other parts in cases with multiple lesions, we must consider that these lesions are associated with a systemic disease. In this context, we must think of inflammatory, toxic, metabolic, genetic, or hematogenous dissemination.<sup>[8]</sup>

The majority of primary intra-axial neoplasms arise from the glial cells or precursors. In the case of gliomas, the classification generally divides them into circumscribed or diffuse. Glioblastoma multiforme (GBM), the most prevalent glioma in adults and the one with the poorest prognosis.<sup>[8]</sup>

White matter tracts are a means of spreading diffuse gliomas. Through the association and corticospinal pathways, both vertically and horizontally, through the corpus callosum. The cortical surface and the gray matter can both be invaded by diffuse gliomas.<sup>[8]</sup>

For diffuse gliomas, there are numerous gliomagenesis pathways. A complicated cascade of mutations leads to glioblastoma. Wild IDH is the diagnosis in 90% of instances. Since it is not a progression from a low-grade lesion, it is typically a primary GBM. Older patients are more likely to experience these situations. The remaining 10% result from a low-grade glial lesion that is progressing.

The patients, in this case, are usually much younger than in the other group, often under 40 years of age.<sup>[8]</sup>

The preferred imaging technique for detecting and tracking glioblastomas is magnetic resonance imaging (MRI). For people who cannot have an MRI, computed tomography (CT) is an option. The MRI results of tumor necrosis and bleeding are very indicative of glioblastoma; however, they are frequently non-specific. On MRI, GBMs typically show up as heterogenous masses because necrosis and/or cysts have formed. usually appears as a single peripherally enhanced lesion on imaging. There can be several enhancing lesions, which are either multicentric or multifocal depending on whether there is communication between them.<sup>[1, 6]</sup>

Cystic lesions are hypointense while solid lesions are isointense, according to certain investigations on T1-weighted imaging. They appear as heterogeneously hyperintense lesions on T2-weighted imaging. The presence and quantification of perilesional edema are best seen on FLAIR and T2-weighted images. Advanced MR techniques such as spectroscopy, when available, are useful methods for differential diagnosis. Depending on the metabolites examined, this approach allows for the separation of tumors from other disorders. The usual peak of NAA (N-acetyl-aspartate) is lower in GBM, and the ratio of choline to creatine is more than 3:1. Due to the loss and degeneration of neurons brought on by the presence of tumor cells, NAA levels have decreased. On the other hand, an increase in cell and membrane production results in a decrease in creatine due to metabolic changes and an increase in choline.<sup>[8, 9]</sup>

Diffusion-weighted MRI is another method utilized in the differential diagnosis of rim-enhancing cerebellar mass lesions (DWI). Low signals in DWI and high apparent diffusion coefficient (ADC) values are characteristics of cystic or solid tumor components. Low ADC values on ADC maps and low signals on high b-value DWIs are indicative of the cystic or necrotic components of these tumors.<sup>[11]</sup>

Positron emission tomography/computed tomography (PET/CT) with fluorine-18-fluoro-deoxyglucose (FDG) is sometimes advised and may offer additional alternatives for differential diagnoses when accessible.<sup>[5]</sup>

As in the case of PET/CT, if it is available, the Thallium-201 (Tl) single photon emission computed tomography (SPECT) imaging can be also used in the diagnosis of brain tumors. Both techniques, SPECT and PET, characterize and measure biological processes. They provide different biochemical or molecular information about tumor tissues, reflecting the functions and characteristics of the tumor. They can be considered an additional option for the diagnosis of these lesions.<sup>[6]</sup>

At first glance, the combined ability of fluorine-18-fluoro-deoxyglucose (FDG)-PET and thallium-201 (Tl)-SPECT for the diagnosis of posterior fossa brain tumors presents an accuracy of about 70%. The overall diagnostic accuracy was not very high when using this method.<sup>[6]</sup>

This study described 18 patients with poorly differentiated gliomas of the cerebellum, and 5 were glioblastoma multiforme. Each patient underwent surgical resection, and 16 of the 18 patients also got radiation therapy and chemotherapy. The median survival time was 31.5 months overall. With a median survival of 32 months, recurrent illness claimed the lives of patients in 55% of cases.<sup>[10]</sup>

If we compare the overall median survival presented in this study and recent studies unfortunately don't find many differences or better results including with the use of new surgical devices and new protocols of adjuvant treatments.

In this retrospective cohort that included 86 cerebellar glioblastoma, the authors reviewed histologically and did a methylation analysis and an algorithm with methylation classes (MCs). The MCs GBM IDH wildtype subclass mesenchymal and subclass RTK II were underrepresented in the cerebellum when comparing the methylation profiles of supratentorial versus infratentorial lesions. The cerebellar GBM represent different entities with diverse prognosis and therapeutic options when taking into account the molecular aspects.<sup>[11]</sup>

As final remarks on diagnosis, we currently have multiple tools to define a differential diagnosis. It is important to use "pattern analysis". Key features include lesion location, size and relative 'bulk effect', vasogenic edema, lesion characteristics such as homogeneity/heterogeneity, and contrast enhancement/non-enhancement patterns.

A definite diagnosis is made with a histopathological examination of the samples obtained during resection or biopsy. These tumors present high vascularization and central necrotic foci. Actually as described above the genetic compound of the tumor is associated with the response to the treatment and with overall survival.<sup>[12, 13]</sup>

Currently, there are different treatment modalities. For this reason, it is very important to carry out an adequate differential diagnosis, including metastasis, the most frequent pathology, astrocytomas, hemangioblastoma, infratentorial GBM, as well as cerebellar infarction. It would always be rational to try a full macroscopic resection of the tumor, especially in malignant glial tumors like the one described in our case. However, because GBM is an infiltrative lesion, it is frequently challenging to attain that goal, and neurological impairments following resection would be taken into consideration. Because of these points, in our case, we decide to perform a partial resection.

Current recommendations are aimed at carrying out a multimodal treatment, with total surgical resection when possible. As previously mentioned, GBMs have high proliferative activity, causing rapid infiltration of surrounding tissues. In this context, complete resection is not always possible, having to resort to complementary treatments such as radiotherapy and chemotherapy. Therefore, after the most radical surgical resection, supplementary therapy with radiotherapy and chemotherapy is a well-established treatment option. Chemotherapy is especially recommended for children due to the harmful and debilitating effects of radiotherapy at such young ages.

It has been described that cerebellar GBM may have a better evolution in young patients, even so, the median survival of this pathology is around 19 months.

All current forms of treatment have the goal of prolonging survival while maintaining the quality of life.<sup>[1, 12-14]</sup>

It is established, for the moment, that surgical resection is the first step toward treatment. However, as previously described, surgery with the objective of total resection is not always feasible. This restriction is brought on by where the tumor is located and how close it is to important neurovascular structures. In these situations, subtotal resection or biopsy are advised to make the conclusive diagnosis that is necessary to determine the course of treatment.

Standard treatment recommendations for the elderly are limited by the lack of inclusion in clinical trials of patients older than 65 years.<sup>[15]</sup>

Currently, after resection or biopsy, concomitant chemotherapy with radiation therapy is continued, followed by monthly adjuvant chemotherapy, when no tumor progression is observed.<sup>[15]</sup>

Temozolomide is an alkylating agent that is administered orally or by intravenous infusion. This drug is a treatment option when well tolerated, in elderly patients with glioblastoma. The DNA repair enzyme MGMT (O[6]-methylguanine-DNA methyltransferase) protects tumor cells against damage brought on by alkylating agents, which prevents the tumor cells from responding to chemotherapy with alkylating agents. When the methylation of this enzyme is present, a greater median survival has been demonstrated with the administration of the aforementioned drug.<sup>[15]</sup>

It is recommended, whenever possible, to institute the combined treatment modality with surgery, radiation, and chemotherapy. Some studies consider temozolomide as a reasonable treatment option, especially in cases in which methylation of the MGMT promoter is observed.<sup>[12, 15, 16]</sup>

It has been demonstrated that both surgery and radiation therapy enhance overall and progression-free survival. Keep in mind the limited amount of information accessible for treating the older population, like in the scenario we present.

In addition, it should be noted, although taking into account the limitations of the published studies, that radiotherapy has not been shown to induce cognitive impairment in elderly patients.<sup>[16]</sup>

This paper outlines various tumor therapy options (TTFields). The tumor cells' mitotic processes are halted by these 200 kHz alternating electric fields.

Randomized clinical trials have shown that this method improves survival. But a lot of the information refers to instances with supratentorial GBM.

In this study, they have investigated alternative configurations for treatment with this technique in lesions located in the posterior fossa. The different configurations modified for the posterior fossa's pathologies result in an average 46.6% increase in the electric field. The top 5% of intensity TTField hotspots or areas of interest increased by 95.6% on average.

Future research is required to confirm or clearly rule out the efficacy of this approach for treating posterior fossa cancers.<sup>[17]</sup>

As described in the references selected to support this case report, despite combined treatment, tumor recurrence/recurrence is the most frequent evolution. In these cases, the treatment options are even more limited.<sup>[18]</sup>

More research and well-designed studies with statistical value are required to establish a treatment that can prolong survival, guaranteeing the quality of life of these patients. Taking into account, especially the elderly population that often has multiple comorbidities.

Future molecular studies may allow a better understanding of this pathology and may lead to new targeted immunotherapies.

## Conclusion

Glioblastoma is the most frequent, aggressive, and lethal primary tumor of the central nervous system in adults. These tumors in the cerebellum are quite uncommon. Nevertheless, it must be taken into account when making a differential diagnosis for aggressive lesions that are found in the posterior fossa, particularly if they have an impact on the cerebellar parenchyma. The main points in our clinical case are the age of the patient and the atypical location of the lesion.

Actually, MRIs are the gold standard and permit the characterization of the lesions, the surrounding edema, and the mass effect, but the findings and clinical symptoms are insufficient for an accurate diagnosis.

Surgery permit obtaining samples for a definitive diagnosis and decompressing the surrounding neurological structures.

The goal of achieving treatment that ensures prolonged survival while maintaining the quality of life remains a challenge. Despite aggressive surgical treatment, when possible, supplemented by radiation and chemotherapy remains the established management strategy to date. Treatment must be adapted to each patient, especially in older patients, in order to achieve the longest possible survival while maintaining the quality of life.

The fact that these tumors occur in the elderly, as in our case, who usually present a greater number of comorbidities makes management even more challenging.

Finally, the outcome for patients with this pathology is mainly worst and many of them don't have a large follow-up.

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## Conflict of interest

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## Ethics statement

None.

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