

## CASE REPORT

# Primary glioblastoma multiforme of medulla oblongata: Case report and review of literature

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## ABSTRACT

Glioblastoma multiforme (GBM) is the most common glial tumor of the adult brain. However, the primary GBM of medulla oblongata is a rarity. To the best of our knowledge, only four cases of GBM of medulla oblongata have been reported so far in the literature, and this is the second report of conventional GBM of the medulla oblongata in adults. We describe a case of 51-year-old female, who presented with a heterogeneous mass with exophytic feature located in the caudal brain stem that was approached and a near total tumor removal was achieved by median suboccipital route. A literature review with emphasis on anatomical location, radiological and histopathological findings, extent of tumor resectability, and outcome is included.

**Key words:** Brain stem, exophytic lesion, glioblastoma multiforme, medulla oblongata

## Introduction

Glioblastoma multiforme (GBM) is the most common and lethal adult primary brain tumor, representing about 50% of all gliomas.<sup>[1]</sup> It is characterized by a morphological diversity and a dismal prognosis, despite multimodality therapy.<sup>[2]</sup> The most frequent site of occurrence is the subcortical white matter of the cerebral hemisphere, the temporal (31%) being the most common, followed by parietal (24%), frontal (23%) and occipital (16%) lobes.<sup>[1]</sup> The presence of this tumor in medulla oblongata is considered exceptional. An extensive review of well described cases as well as the brain gliomas' series yielded only four cases of histologically documented GBM of medulla oblongata.<sup>[3-6]</sup>

## Case Report

We report a case of 51-year-female, who presented with a short history of right sided paresthesias accompanied by progressive headache and vomiting. Neurological examination

of the patient showed an ataxic gait, right paresthesia, and numbness. The past history was significant for benign neoplasm of ovary, which was surgically treated in 2003. The pathologic report documented mucinous cyst adenoma of the right ovary. Preoperative magnetic resonance imaging (MRI) depicted a large multi-lobulated, heterogeneous, rim enhanced mass on lower aspect of fourth ventricle and foramen of magendie with exophytic feature and measuring 25×27×40 mm [Figure 1].

The tumor was approached via a median suboccipital craniotomy with additional removal of the C-1 arch while the patient was in a prone position, after a Y-shaped opening of the duramater. Under the intraoperative motor evoked potential and somatosensory evoked potential monitoring, microsurgical excision was performed very cautiously. During this procedure, the exophytic character of the tumor was evident. The tumor was adherent tightly to the medulla oblongata, but it could be removed safely in a step-wise pattern. At the caudal portion, there was severe adhesive lesion with poor dissection margin. Furthermore, abnormal signal with the MEP monitoring was detected. Intraoperative histopathology suggested that the tumor was a high grade glioma. Near total removal was achieved except for the caudal lesion.

Histopathological examination of the serially sectioned paraffin embedded brain tissue confirmed the diagnosis of GBM [Figure 2]. The characteristic pseudopalisading appearance with geographical necrosis and pleomorphic nuclear atypia, and microvascular proliferation was observed. Immunohistochemical staining of the tumor cells demonstrated diffuse glial fibrillary acidic protein activity with a proliferation rate of 10-20% as determined by Ki-67 labeling index. Tp53

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upregulation was demonstrated in 20-30% of the neoplastic cell nuclei. Immunohistochemical staining for epidermal growth factor receptor in the tumor cell nuclei was negative.

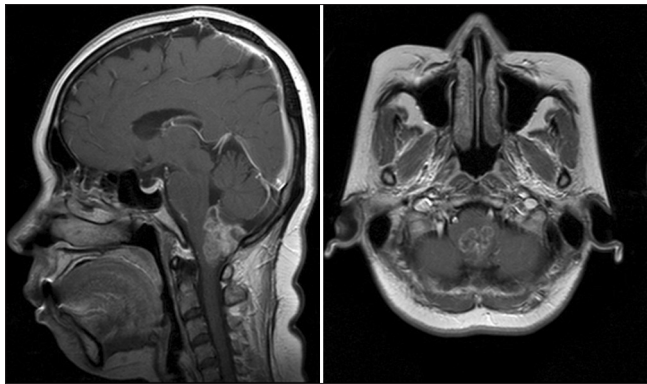
Postoperative MR imaging [Figure 3] showed a small remnant tissue with enhancement at the foramen of magendie. Immediate postoperative course was uneventful. No cranial nerve dysfunctions were noted. Radiation therapy with a

total dose of 54 Gy over a period of six weeks and concurrent chemotherapy with temozolomide for six months were administered. The patient developed difficulty swallowing, six months, postoperatively. CT scan revealed enhancement on the right medulla. The postoperative follow-up at 19 months revealed that the difficulty swallowing persists, and the patient is admitted to rehabilitation facility.

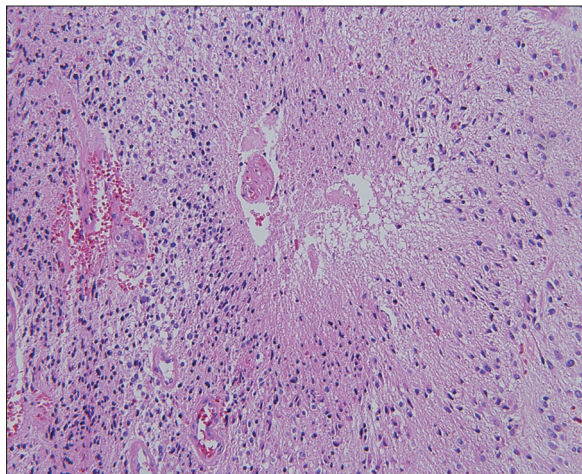
### Discussion

High grade gliomas' of the brainstem are extremely rare in adults (<2%).<sup>[1]</sup> The most common location is deemed to be pons followed by medulla and midbrain.<sup>[7,8]</sup> The grade IV glioma, GBM, is rarely encountered in medulla oblongata, and an extensive review of literature could garner only four cases, [Table 1],<sup>[3-6]</sup> all of which have been histologically documented to be GBM by the respective authors. Although in the early report by Queiroz Lde *et al.*, there is mention of few other cases of GBM of medulla oblongata, but none of those cases are histologically documented.<sup>[6]</sup>

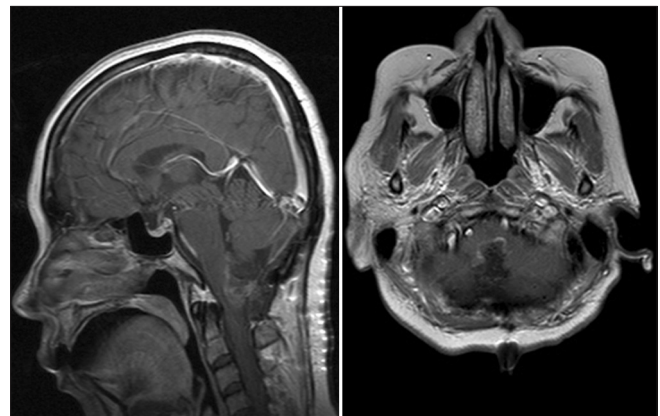
Histopathological characteristics of GBM has been marked by conspicuous cellular heterogeneity ranging from closely packed small cells with scant cytoplasm, round to oval variably hyperchromatic nuclei to bizarre, and multinucleated giant cells<sup>[9]</sup> Only three distinct morphological variants of GBM are recognized by the current World Health Organization



**Figure 1:** Preoperative MRI shows a large multi-lobulated, heterogeneous and rim enhanced mass on lower aspect of fourth ventricle and foramen of magendie, measuring 25x27x40 mm in volume with exophytic feature



**Figure 2:** Hematoxylin and eosin stain with x100 magnification: The characteristic pseudopalisading appearance with geographical necrosis, pleomorphic nuclear atypia, and microvascular proliferation are observed



**Figure 3:** Immediate postoperative MR imaging showed a small remnant tissue with enhancement at the caudal and ventral portion of previous tumor

**Table 1: Summary of documented GBM of medulla oblongata reported in the literature**

Authors and references	Year	Age	Pathological type	Treatment modality	Outcome
Queiroz, <i>et al.</i> <sup>[6]</sup>	1974	13	No comment	Supportive	Died
Abbott <i>et al.</i> <sup>[3]</sup>	1991	Pediatric	No comment	Tumor removal	Died 3 months postoperative
Kyoshima, <i>et al.</i> <sup>[4]</sup>	2004	55	Conventional GBM	Extensive tumor removal	2 year and 3 months
Luetjens, <i>et al.</i> <sup>[5]</sup>	2009	40	Giant cell GBM	Near total tumor removal+radiotherapy +temozolomide	2 year postoperative survival with no recurrence
Our case	2010	51	Conventional GBM	Near total tumor removal+radiotherapy +temozolomide	19 months postoperative survival

GBM - Glioblastoma multiforme

classification scheme, which includes the conventional GBM, giant cell GBM, and gliosarcoma.<sup>[9,10]</sup> Queiroz L de *et al.*<sup>[6]</sup> and Abbott *et al.*<sup>[3]</sup> has not commented on the histological type of GBM; however, the pathological findings described by Kyoshima *et al.*<sup>[4]</sup> were consistent with conventional GBM. Luetjens *et al.* describes the reported GBM to be of giant cell variety.<sup>[5]</sup> Histological finding in our case was confirmed to be conventional GBM [Figure 2]. An interesting difference between giant cell and conventional GBM is that the survival is superior in giant cell to that observed in conventional GBM. This finding might be attributed to the younger age, tumor histology, and better surgical resection, as giant cell variety being the better circumscribed tumor.<sup>[11]</sup> However, in conventional GBM after the gross total removal the progression free survival (PFS) of two year and three months is reported while PFS of two years have been reported in the giant cell variety after near total removal.<sup>[4,5]</sup>

Radiologic features of GBM of medulla oblongata are consistent with those of GBM at other sites. Of the four reported cases including our case, exophytic growth of the tumor was observed in three cases (60%). Based on the location of tumor, the differential diagnosis includes metastatic tumors, subependymal astrocytomas, and ependymomas.<sup>[7,8]</sup> In our case, an MR imaging findings of a heterogeneous mass with a ring like enhancement, and a poorly defined margin, exophytic nature of the tumor, tumoral hemorrhages, and the histopathological findings favors the diagnosis of GBM. It is needed to be emphasized that the exophytic lesion in the caudal brain stem could be a GBM, and although rare, it should be included in differential diagnosis of tumors of caudal brain stem.

The initial reports of GBM of the medulla oblongata documented no survival with or without treatment.<sup>[3,6]</sup> In their series, Abbott *et al.* reported six pediatric patients with intrinsic gliomas of the medulla oblongata, who underwent radical excision, one of them had a GBM, and died from tumor progression three months postoperatively.<sup>[3]</sup> However, two more recent publications reported a median survival of two years, after tumor removal, radiotherapy, and chemotherapy.<sup>[4,5]</sup> Kyoshima *et al.*<sup>[4]</sup> performed gross total removal of the tumor and reported a survival of two years, and emphasized that more favorable outcomes can be achieved with aggressive resection of the tumor. However, they encountered caudal cranial nerve dysfunctions after the extensive resection. Luetjens *et al.*<sup>[5]</sup> also reported a survival of two years in exophytic giant cell GBM, following near total tumor removal, radiotherapy, and chemotherapy. The patient did not develop any cranial nerve dysfunction. The overall survival in both of these cases was impressive, though cannot be compared due to different histological variants. No evidence of recurrence was recorded in both cases.<sup>[4,5]</sup> Surgical resectability depends

primarily on intraoperative cleavage planes. The giant cell variants permits more aggressive tumor resection due to the clear, non-infiltrative, and better circumscribed margin.<sup>[11]</sup> In view of infiltrative and adhesive nature of tumor, near total removal with a small remnant of the tumor left at the foramen of magendie was considered, in our case, over total gross tumor removal. Although overall survival may be prolonged with total surgical resection, quality of life is an important factor to consider while making treatment decisions<sup>[12]</sup> for malignant tumors of medulla oblongata. Total removal of such a tumor might lead to brainstem dysfunction.<sup>[4]</sup> Further, the residual tumor can be better dealt with postoperative radiotherapy and chemotherapy.<sup>[12]</sup> Indeed, in our case, no immediate postoperative complications or neurological deterioration were noted. Although, with near total removal, the initial postoperative phase was uneventful, the involvement of the lower cranial nerve attributable to the tumor recurrence was found to be inevitable.

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