MULTIFOCAL INTRACRANIAL GANGLIOGLIOMA IN A SEXAGENARIAN: CASE REPORT AND REVIEW OF THE CURRENT LITERATURE

POSTER ID 2578

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We have no financial or organizational relationships with commercial interests or other entities. There are no disclosures relating to this study.
Gangliogliomas are rare, well differentiated, low grade neoplasms composed of both neuronal and glial cellular components, accounting for less than 2% of all CNS tumors.

Primarily diagnosed in children or young adults < 25 years of age, gangliogliomas are significantly less common above the age of 40, however those that do occur in these patients tend to be higher grade tumors with concordantly worse prognoses. Gangliogliomas tend to occur as unifocal lesions, most often identified in the temporal lobe.

There have been very few reports of multifocal gangliogliomas, with only 6 documented cases, one of which was in the spine. Furthermore, all previously reported cases have been in either children or young adults. Therefore, we present the first case ever reported of a multifocal intracranial ganglioglioma in a sexagenarian as well as a review of the available literature on these rare tumors.
CASE DESCRIPTION

- A 60-year-old female presented to her ophthalmologist with blurry vision in the right eye and unremarkable neurological exam. She was referred for brain imaging, which showed multiple lesions in both cerebral hemispheres (Figure 1). Cerebrospinal fluid studies showed normal profiles. Biopsy of the right temporal lesion was elected, as it enhanced most on MRI.

Figure 1. Brain magnetic resonance imaging at initial presentation. (A) Fluid-attenuated inversion recovery (FLAIR) signal abnormalities in bilateral frontal lobes. (B) FLAIR signal abnormalities in bilateral occipital lobes. (C) Focal areas of enhancement in the left frontal lobe. (D) Focal area of enhancement in the right occipital lobe.
Histopathological analysis revealed a tumor composed of mildly atypical glial and dysplastic ganglion cells without perivascular inflammation, mitoses, necrosis, or vascular proliferation (Figure 2). Scattered Rosenthal fibers and rare granular eosinophilic bodies were also appreciated.

Immunohistochemistry staining of glial cells was positive for vimentin and p16 (focally), and 10% were positive for p53. The neuronal ganglion cell population stained positively for CD34, NF-1, Neu-N, and synaptophysin. All tumor cells were negative for IDH-1, H3K27M, and BRAF V600E mutations. The Ki-67 proliferation index was found to be <1%, and PHH3 stain did not reveal significant mitotic figures. The histopathological features observed in the specimens obtained were consistent with a WHO grade I ganglioglioma.

Figure 2. Histopathological analysis of ganglioglioma. (A) Original magnification 100x; hematoxylin and eosin (H&E) stain. Moderately cellular neoplasm with densely fibrillar background. (B) Original magnification 400x; H&E stain. Neoplastic ganglion cells, some with multiple nuclei. (C) Original magnification 200x; neurofilament Immunohistochemical study. Abnormal somatic labeling of neoplastic neurons and beaded thick neurites. (D) Original magnification 400x; CD34 stain. Abnormal labeling of the membrane and processes of neoplastic neurons. (E) Original magnification 100x; olig-2 immunohistochemical study. Sparse labeling of glial component. (F) Original magnification 100x; collagen type 4 immunohistochemical study. Abnormal collagen deposit in tumor stroma.
Given that the patient was relatively asymptomatic, the decision was made to proceed with repeat neurologic examination, neuro-oncology and neuro-ophthalmology referral, as well as repeat MRI after her initial diagnosis. MRI at the 8-month follow-up demonstrated stability of her lesions (Figure 3), with normal postsurgical changes and no evidence of increasing enhancement or size of preoperative lesions.

**Figure 3.** Brain magnetic resonance imaging at the 8-month follow-up. (A) Stable fluid-attenuated inversion recovery abnormalities in bilateral frontal lobes. (B) Stable focal areas of enhancement in the left frontal lobe.
Our patient’s presentation with multifocal ganglioma at age 60 is a rare occurrence, and the first of its kind. A list of the currently available studies on multifocal intracranial gangliogliomas is summarized in Table 1. The average age was 19.2 (n=5; range, 7-33 years), and 80% of the cases had at least 1 lesion in the temporal lobe, which is also the most common location in which primary unifocal gangliogliomas occur. There were no reported mortalities in any study at the time of publication.

<table>
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Table 1. Summary of current reports in the literature.
We present the first case of an intracranial multifocal ganglioglioma in a patient over 40 with lesions in the occipital lobe, corpus callosum and frontal lobe at presentation.

We aim to contribute to the growing body of information surrounding multifocal gangliogliomas and believe that further studies are warranted to elucidate prognosticators and management guidelines of these lesions.
REFERENCES