Brainstem Gliomas and Gamma Knife


Abstract

Object. Focal tumors, a distinct subgroup of which is composed of brainstem gliomas, may have an indolent clinical course. In the past, their management involved monitoring of open-ended imaging studies and shunt placement if cerebrospinal fluid diversion was required. Nonetheless, their treatment remains a significant challenge for neurosurgeons. Gamma Knife surgery (GKS) has recently been tried as an alternative to surgical extirpation. In the present study the authors assess clinical and imaging results in 20 patients who harbored focal brainstem gliomas treated with GKS between 1990 and 2001.

Methods. There were 10 male and 10 female patients with a mean age of 19.1 years. Sixteen tumors were located in the midbrain, three in the pons, and one in the medulla oblongata. The mean tumor volume at the time of GKS was 2.5 cm³. In 10 cases a tumor specimen was obtained either by open surgery or stereotactic biopsy, securing the diagnosis of pilocytic astrocytoma in five patients and nonpilocytic astrocytoma in five others. In the remaining 10 cases, the diagnosis was based on clinical and neuroimaging findings. The prescription Gamma Knife dose varied between 10 and 18 Gy, except in three patients who were receiving a boost to a site in which external-beam radiation was previously delivered. An average of four isocenters were utilized per GKS.

Patients were followed up for a mean of 78.0 months. The tumors disappeared in four patients and shrank in 12 patients. Of these patients, one experienced transitory extrapyramidal symptoms and fluctuating impairment of consciousness (from somnolence to coma) for 6 months. Another patient whose tumor disappeared 3 years following GKS died of stroke 8 years postoperatively. The rest of the patients either remained stable or improved clinically. Tumor progression occurred in four patients; of these four, one patient developed hydrocephalus requiring a ventriculoperitoneal shunt, two showed neurological deterioration, and one 4-year-old boy died of tumor progression.

Conclusions. Gamma Knife surgery may be an effective primary treatment or adjunct to open surgery for focal brainstem gliomas.

Understanding of brainstem gliomas has increased in the last two decades, and nowadays they are regarded as a heterogeneous group of tumors with a tendency to appear in children, in whom they constitute 10 to 20% of brain neoplasms. Profound clinical deficits in patients with these lesions may be associated with insults to the brainstem, making treatment very complex. The diagnosis of brainstem glioma was long considered to define a single entity. However, since the advent of magnetic resonance imaging in the late 1980s, neoplasms within this anatomical region are now recognized to include several types of tumor with varied behaviors and natural histories. More recent reports of brainstem tumors include diverse sites such as the cervicomедullary junction, pons, midbrain, and tectum. In the study by Yen et al., the investigators assessed clinical outcomes and imaging findings in 20 patients who were treated by GKS for focal brainstem gliomas between 1990 and 2001. Sixteen tumors (80%) were located in the midbrain, three in the pons, and one in the medulla oblongata. This breakdown indicates that selected cases were included in the study. In the literature, brainstem gliomas are mainly located in the pons. Some relevant studies include the following: 1) Mantravadi and colleagues analyzed the extent of tumor at autopsy in 25 patients harboring a brainstem glioma. In the majority of cases, the primary tumor was located in the pons; this location was followed by the medulla oblongata and midbrain. 2) Kansal and associates analyzed 111 cases of brainstem glioma. The authors found that the most common site of tumor in both adults and children was the pons. 3) In a study spanning a 35-year period, Tokuriki et al. analyzed 85 cases of brainstem glioma; 69 of these cases included patients younger than 16 years of age. In these children, the tumors were located mainly in the pons.

In the study by Yen et al., tumor progression occurred in four (20%) of 20 patients. If these patients had not been treated with the Gamma Knife, what would the progression rate have been? Without an answer to this question, who can say that the Gamma Knife is safe for focal brainstem gliomas with 20% progression rates? Comparative studies should be made between patients treated by GKS and patients not treated by this means.

If the authors included selected cases, the finding of this study should be that “GKS may be an effective primary treatment or an adjunct to open surgery in cases of selected focal brainstem gliomas.”

Ayhan Kanat, M.D.
Government Hospital
Rize, Turkey

References


RESPONSE: In his letter, Dr. Kanat states: 1) the patients included in our report represent selected patient material; and 2) 16 satisfactory results among 20 patients do not warrant the contention that GKS provides effective management of focal brainstem gliomas.

The first comment is based on the fact that in most of our cases the brainstem gliomas were located in the midbrain, whereas in the literature quoted by Dr. Kanat the preponderant tumor locations are the pons and medulla oblongata. We emphasize that the only selection criteria in our study were a relatively well-defined margin of the tumor, progressive tumor growth, and/or neurological deficits.

Concerning the second objection to our paper, we agree with the unrealistic truism that randomized studies would presumably provide some answers to Dr. Kanat’s question: “If these patients had not been treated with the Gamma Knife, what would the progression rate have been? Without
an answer to this question, who can say that the Gamma Knife is safe for focal brainstem gliomas with 20% progression rates?" However, at least for our small series, a clear answer is provided by the fact that all treated cases presented with imaging and/or clinical progress.

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CHUN PO YEN, M.D.
JASON SHEEHAN, M.D., PH.D.
MELITA STEINER, M.D.
GREG PATTERSON, R.N., B.S.N.
LADISLAU STEINER, M.D., PH.D.
University of Virginia Health System
Charlottesville, Virginia

Thalamic Cysts


Abstract

Thalamic neuroepithelial cysts are rare lesions of the central nervous system. Surgical management of these lesions has varied and yielded mixed results. The authors identified 10 reported cases in the literature, five of which involved symptomatic lesions. The authors present three unique cases of symptomatic thalamic neuroepithelial cysts associated with hydrocephalus, which were all successfully treated using endoscopic third ventriculostomy and fenestration of the cyst into the third ventricle.

We certainly agree that endoscopic third ventriculostomy accompanied by fenestration of the cyst into the ventricle is the most elegant and probably the safest way of treating these cysts whenever they need to be treated. However, we were surprised by the interpretation proposed by the authors that the cysts they observed were neuroepithelial cysts. Biopsy of the cyst wall was deemed unnecessary and not obtained on purpose to avoid the risk of intracystic or intraventricular bleeding. Lacking histological analyses, the diagnoses of the nature of the cysts was based on the interpretation of magnetic resonance (MR) images and on analogies with a series of cases previously reported in the neurosurgical and neuroimaging literature.

Among the first papers that called attention to benign cysts in the thalami and midbrain, two were published in the Journal of Neurosurgery, one written by Nakasu et al.9 in 1986 and the other by Wilkins and Burger18 in 1988. The lesions were observed to be benign without an epithelial lining. Such cysts may have been discovered accidentally on neuroimaging examinations performed for unrelated reasons, or they may have been found because there were focal, mild neurological signs or because of the presence of hydrocephalus caused by compression of the aqueduct or the third ventricle by the cysts. Interpretation of the cysts as dilated perivascular spaces came later, when a series of MR imaging–based observations demonstrated that these cysts often present a distribution oriented along the course of the penetrating vessels.4,6–8,11,13–16

In the thalamomesencephalic region, the perforating vessels are posterior thalamic and paramedian mesencephalic arteries originating from the apex of the basilar artery or the proximal, precommunicating (P1) segment of the posterior cerebral artery. The vessels that enter the midbrain and reach the upper pontine tegmentum follow an arched course with an upward convexity, which was typically recognizable in a number of cases reported.4,7,8,14 In the paper by Schmidt and Coimbra, only the thalamic location is emphasized, but the authors state that the cysts in Cases 1 and 2 are multicocular and extend into the “right aspect of the brainstem” (Case 1) or “right midbrain” (Case 2). In Case 3, the cyst did not extend into the brainstem, but presented an oblique orientation on coronal MR images shown in Fig. 2 of that paper; the orientation of the lesion was particularly evident when it partially collapsed after fenestration. The caudocranial, mediolateral orientation of this cyst corresponded to the distribution of the penetrating posterior thalamic arteries. Therefore, we believe that the cysts reported by Schmidt and Coimbra are very likely dilated perivascular spaces rather than neuroepithelial cysts. Even if neither diagnosis can be definitely proved, the possibility of dilated perivascular spaces should have at least been mentioned in the differential diagnosis.

Pathological proof that dilated perivascular spaces may indeed manifest as cysts was mainly recognized by French authors,13,12 even before MR imaging made them more commonly observed during the patient’s lifetime.

A problem that remains unsolved is the pathogenesis of the dilation of the perivascular spaces. Sometimes the cysts are very close to the surface of the brain and, therefore, to the subarachnoid space; in other cases the cysts are deep in the brain substance. We could not find a clear description of how deep subarachnoid spaces accompanying penetrating arterioles may extend in different areas of the brain, particularly at its base where the anterior and posterior perforating substances are located. However, there is no question that the simplistic idea that Virchow–Robin spaces or perivascular spaces are extensions of the subarachnoid space along the penetrating arterioles, which are filled with cerebrospinal fluid (CSF), is not true.

Weller,17 who studied the microscopic morphological and histological characteristics of human meninges, showed that the subarachnoid space filled with CSF, which accompanies the arterioles penetrating the cortex, ends early, within the cortex itself. Thus the pia mater separates the subarachnoid space from the brain and from the perivascular space, which acts as a draining channel of interstitial fluid from the brain to the subarachnoid space. The perivascular space lies between the vessel wall and the basement membrane of the glia limitans. What can obstruct drainage into the subarachnoid space and cause the dilation of the perivascular space is unknown. Abnormal arterial wall permeability in possible segmental arteritis12 or difficult drainage due to increased intraventricular pressure1 has been considered. Analogies with deposits of β-amyloid in an experimental model of Alzheimer disease have also been proposed.15,17 The separation between the CSF in the subarachnoid space and the interstitial fluid of a perivascular space is impermeable to red blood cells from subarachnoid hemorrhage but not to inflammatory cells, which, in infections, can penetrate the perivascular space particularly along the veins.5,7 To our knowledge, no physicochemical comparisons of fluid obtained from the cystic perivascular spaces and CSF have been performed.

One difference between vessels that enter the brain over the convexity and those that penetrate the brain at its base (where the cystic dilation of the perivascular spaces is more common) is that the surrounding histological anatomy is different: instead of one layer of leptomeninges accompa-