

Neoplasm

Anaplastic intraventricular oligodendroglioma: case report and review of the literature

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Abstract

Background: Intraventricular oligodendroglioma remains a rare diagnosis, with high-grade/anaplastic IVO being an even rarer subtype. These lesions vary in regard to tumor grading and clinical presentation, as compared with their intraparenchymal counterparts. A case report and review of the previous literature regarding IVO and tumor grading were conducted.

Case Description: A case report of a patient with an anaplastic oligodendroglioma confined entirely within the ventricular system is presented. The patient underwent gross total surgical resection with perioperative shunt placement, yet developed aggressive recurrence of disease. The literature regarding the clinical presentation, methodology of diagnosis, and treatment of IVO was reviewed. Thirty-three studies reporting 70 patients with IVO were identified in the literature. Only 2 previous case reports of high-grade/anaplastic IVO were identified. Accurate diagnosis of these lesions, including immunohistochemistry, electron microscopy, and molecular/chromosomal subtyping, is imperative. Surgical resection with frequent perioperative shunting, as well as chemotherapy, remains the mainstay of therapy. Adjuvant therapies may differ significantly according to the tumor grade and molecular subtype.

Conclusions: Intraventricular oligodendroglioma remains an infrequently encountered lesion, yet is usually found to be low grade at the time of surgery. Anaplastic IVO is an exceedingly rare lesion, with only 3 case reports in the literature. Future therapy for these aggressive lesions may be based on susceptibility to various chemotherapeutic agents according to molecular subtyping.

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Keywords:

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1. Introduction

Oligodendrogliomas are most commonly encountered in the frontal and temporal lobes, yet may infrequently be localized within the ventricular system. Intraventricular

Abbreviations: AMS, altered mental status; CSF, cerebrospinal fluid; CT, computerized tomography; EM, electron microscopy; EMA, epithelial membrane antigen; FISH, fluorescence in situ hybridization; GFAP, glial fibrillary acidic protein; HA, headache; H&E, hematoxylin and eosin; ICP, intracranial pressure; INO, internuclear ophthalmoplegia; IVO, intraventricular oligodendroglioma; LOC, loss of consciousness; MRI, magnetic resonance imaging; RUT, right upper extremity; SAH, subarachnoid hemorrhage; USC, University of Southern California; VP, ventriculoperitoneal; WHO, World Health Organization.

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oligodendrogliomas tend to be low-grade lesions and usually present because of signs and symptoms of CSF pathway obstruction and raised ICP. We present a case report of a patient with an IVO confined to the ventricular system that was a high-grade, anaplastic lesion on final histologic analysis. The aim of this study was to review the literature for previously reported cases of anaplastic IVO and to describe the defining features and diagnostic criteria for this tumor. The differentiating features between oligodendrogliomas and other intraventricular lesions, such as other types of gliomas, central neurocytomas, and ependymomas, are discussed.

2. Case study

A 22-year-old woman presented to the Los Angeles County–USC Medical Center with altered mental status and

lethargy for 2 days. Before this, she had complained of several weeks of headaches, nausea, vomiting, and blurry vision. On initial neurologic examination, she was somnolent and was oriented only to name when aroused. Cranial nerve examination revealed a right partial third nerve palsy. Papilledema was evident on fundoscopic examination. Motor examination demonstrated diminished tone and diffuse weakness in all extremities. A CT scan of the head revealed an isodense mass in the right lateral ventricle near the foramen of Monro, which enhanced uniformly with intravenous contrast (Fig. 1). Significant noncommunicating hydrocephalus was evident as well. A ventriculostomy catheter was placed, confirming elevated ICP. Over the next several hours, the patient's level of consciousness and mental status improved; yet a severe deficit of short-term memory was noted on follow-up examination. Subsequent MRI of the brain revealed a mass originating in the right lateral ventricle near the foramen of Monro and extending into the third ventricle (Fig. 2A, B). The mass was hypointense on T1 imaging and demonstrated avid enhancement with contrast administration. Magnetic resonance spectroscopy was nondiagnostic.

The patient was taken to the operating room for resection of the mass via an interhemispheric transcalsal approach. She was positioned in the right lateral decubitus position, allowing for gravitational retraction of the mesial right hemisphere. The tumor was identified and totally resected. Frozen pathologic specimens revealed a high-grade glial neoplasm. A ventricular catheter was left in the right lateral ventricle.

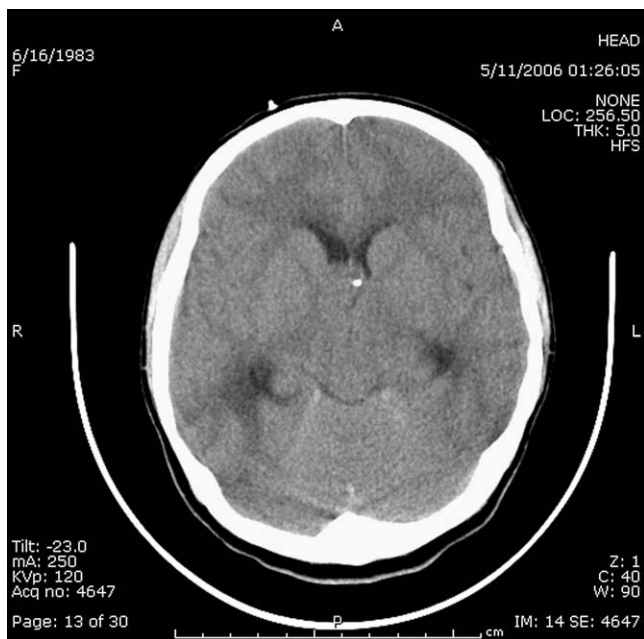


Fig. 1. Noncontrast CT image demonstrates a mass near the foramen of Monro in the right lateral ventricle. A ventriculostomy catheter is situated adjacent to the mass.

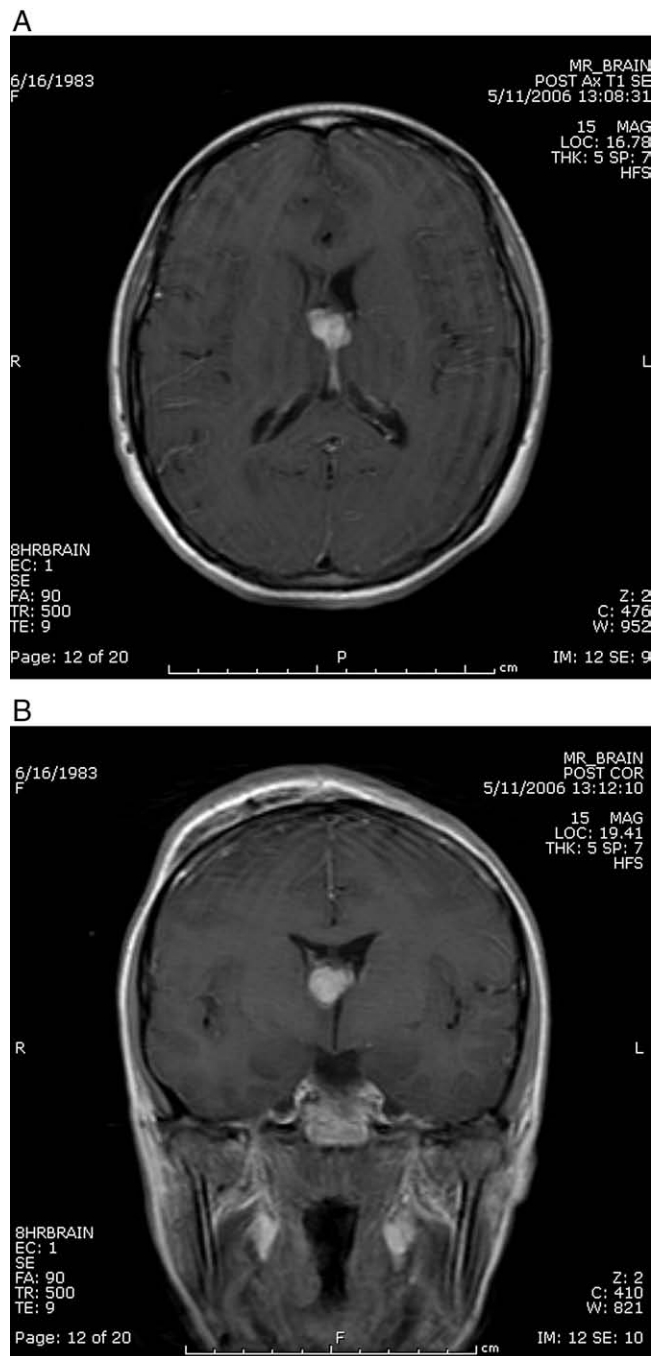


Fig. 2. A (axial) and B (coronal): T1 MRI after gadolinium administration demonstrates an avidly enhancing mass near the right foramen of Monro.

The patient did very well in the days after the procedure, with mild improvement in her short-term memory. She required placement of a VP shunt on postoperative day 7. Postoperative MRI demonstrated a gross total resection of the lesion with postoperative changes (Fig. 3). She underwent inpatient rehabilitation and was discharged home with plans for adjunct radiation and chemotherapy.

Histologic specimens revealed a glial-based tumor with malignant cytology and high mitotic index (Fig. 4A, B). The



Fig. 3. Axial MR T1 image after contrast administration confirming gross total resection of the intraventricular mass via interhemispheric craniotomy.

final pathologic diagnosis was interpreted as anaplastic (WHO III) oligodendroglioma. The diagnosis was supported by immunohistochemical staining as well as electron microscopy (Discussion).

The patient was readmitted approximately 3 weeks later with severe nausea, vomiting, and obtundation. The CT and MR imaging demonstrated dramatic tumor recurrence throughout the lateral and third ventricles (Fig. 5A, B). The VP shunt catheter tip was surrounded by tumor. After extensive consultation with the family regarding treatment options including emergent reoperation for tumor resection or VP shunt revision, the decision was made to provide comfort measures only. She died 1 day later.

3. Review of the literature

3.1. Patient characteristics and clinical presentation

A review of the literature demonstrated 33 studies reporting a total of 70 patients with IVO between 1926 and 2007 (Table 1). The mean patient age was 30 years. There were 58% female and 42% male patients. Twenty-five of 33 patients (76%) with available data presented with clinical symptoms reflecting elevated ICP. Less frequent clinical presentations included hemiparesis, spasticity, cranial nerve palsies, and hemifacial spasm [5,8,13,23]. Short-term memory loss was noted in our patient as well as in one additional patient with a tumor originating in the septum pellucidum [2]. Seizures were infrequently encountered with IVOs, and were reported in 1 patient (1.4%) [14].

3.2. Location of IVO

Twenty-seven (68%) of the 40 cases of IVO with available data were reported to occur within the lateral ventricles. Of these cases, IVOs were more than twice as likely to arise in the right lateral ventricle than the left (9 vs 4, respectively). Eight of these cases (20%) reported masses originating from the septum pellucidum. Six cases each (15%) were reported in the third and fourth ventricles. Finally, one case (3%) reported an IVO arising within the cerebral aqueduct [12].

3.3. Treatment and outcomes

Of 13 patients with available data, 3 were noted to have high-grade or anaplastic lesions, whereas 10 were noted to have low-grade lesions. Of 26 patients with available data regarding the degree of surgical resection, 15 were noted to have undergone a subtotal resection, whereas 9 were noted to have undergone a gross total resection. Most surgical

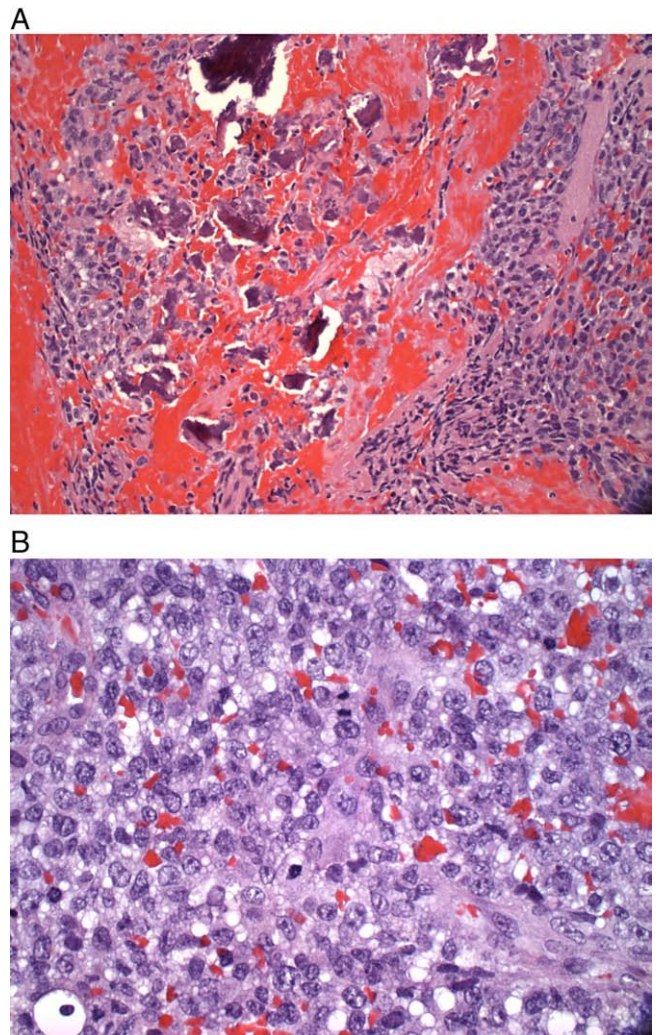


Fig. 4. A and B: Routine H&E images demonstrate high cellularity; cells with clear, abundant cytoplasm; and the presence of calcifications.

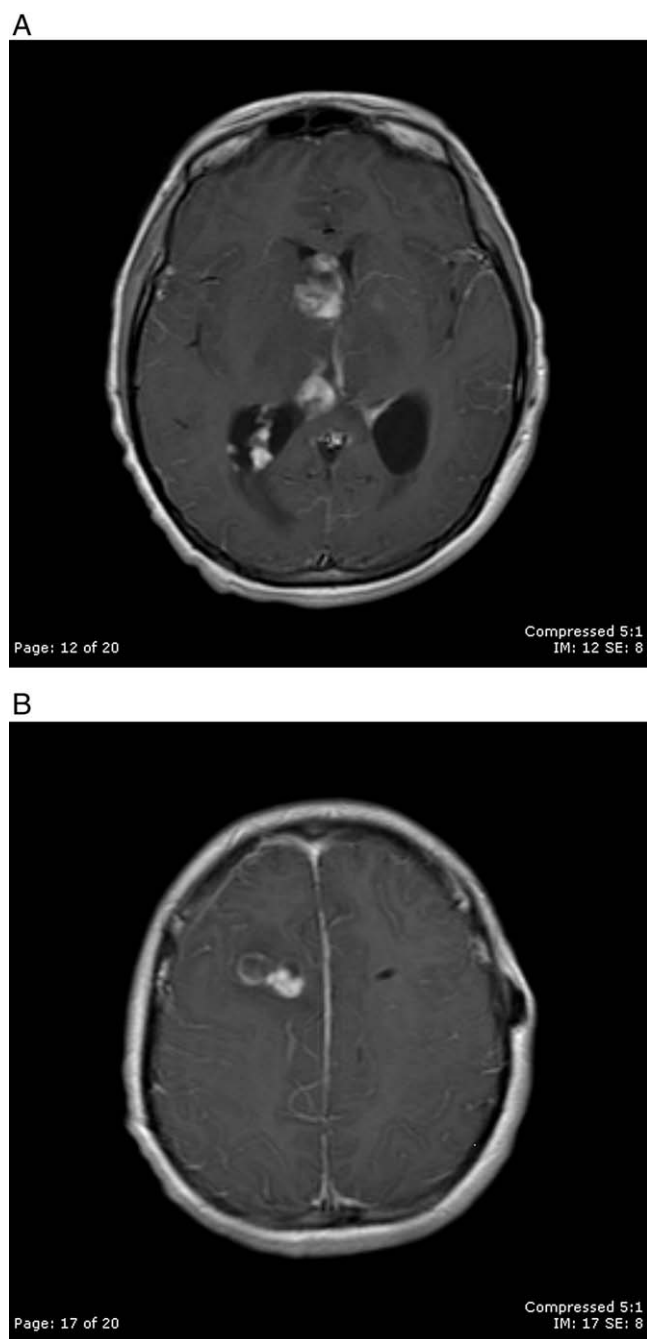


Fig. 5. A and B: Follow-up postcontrast T1-weighted axial MR imaging upon readmission several weeks after resection demonstrates rapid recurrence of the mass throughout the lateral ventricles (A) with invasion along the right frontal VP shunt tract (B).

procedures for resection of oligodendrogliomas originating in the lateral ventricles have been via transcortical transventricular approaches [13–16,7,11,18,23,24]. Some surgeons have used interhemispheric transcallosal approaches, especially when the third ventricle is involved [19,21]. Most fourth ventricular lesions have been resected via standard suboccipital approaches [9,20]. One author described the use of a stereotactic approach for resection of

2 cases of oligodendrogliomas confined to the lateral ventricles [17]. Of the 24 patients in the literature with available information, 11 (46%) required perioperative shunt placement. Outcome data were limited: of 23 patients with outcome data available, 8 patients were noted to have improved or good outcomes after resection, 8 patients were reported to have major morbidity after surgery, and 7 patients died after surgical resection or tumor recurrence. All patients with anaplastic lesions experienced recurrence.

4. Discussion

4.1. Incidence of IVO

Oligodendrogliomas account for approximately 5% to 7% of all primary brain tumors and frequently arise in the frontal and temporal lobes [14]. The mean patient age at presentation is during the fourth and fifth decade, with the classic presentation being new onset seizures. Oligodendrogliomas originating primarily within the ventricular system have been reported to account for approximately 8% to 10% of all oligodendrogliomas [6]. The first description of oligodendroglioma occurring primarily within the ventricular system was by Dickson in 1926 [3]. The seeding of oligodendrogliomas throughout the ventricular and leptomeningeal space, or *oligodendrogliomatosis*, was initially described by Beck and Russell in 1942 [1]. This process, however, has usually been associated with primary intraparenchymal oligodendrogliomas as opposed to intraventricular ones. According to the literature, 70 cases of primary IVO have been reported. Among these cases, most have been reported as low-grade neoplasms. Many authors have thus tended to regard IVOs as being lower-grade lesions because of the rarity of malignancy in these neoplasms as well as a tendency to present earlier in their course because of signs of CSF pathway obstruction [11,14,15].

Anaplastic (WHO grade III) IVO is an extremely rare entity, with only 2 previous cases reported in the literature. In 1984, Packer and colleagues described a case of an 18-year-old man with high-grade oligodendroglioma located in the fourth ventricle [20]. The patient underwent subtotal resection via a suboccipital craniotomy. This patient developed a new frontal lesion 21 months after surgery. No confirmatory immunohistochemical studies were provided for the tumor in this patient. In 1995, Natale et al described a woman with a fourth ventricular mass with metastases to the cauda equina that were determined to be anaplastic oligodendroglioma [18]. This case was verified by immunohistochemical staining and was noted to be immunoreactive for GFAP and negative for synaptophysin staining.

In our case, an anaplastic IVO rapidly recurred in a 22-year-old woman after a gross total surgical resection. The final diagnosis of this lesion was confirmed with immunohistochemical techniques as well as electron microscopy. This is the third report in the literature to describe a case of anaplastic IVO.

4.2. Accurate diagnosis of IVO and differentiation from other intraventricular masses

The current case involves a patient with a high-grade cellular tumor localized to the ventricular system. Routine H&E histology depicted a mass with high cellularity; cells with clear, abundant cytoplasm; and the presence of calcifications. There was no evidence of vascular or endothelial proliferation, or pseudopallisading necrosis, making a high-grade glial neoplasm less likely. Furthermore, GFAP staining was only focally and weakly positive. The neoplasm stained negatively for synaptophysin, thereby ruling out the possibility of central neurocytoma. Immunostaining for pancytokeratin, chromogranin A, CD45, PLAP, EMA, S-100, CD117, and CD34 were all negative, thereby ruling out additional possibilities such as clear cell ependymoma, germ cell tumor, or lymphoma. Results of FISH studies for 1p and 19q deletions were negative. Although the presence of either of these deletions would have strongly supported the diagnosis of oligodendroglioma, not all oligodendrogliomas, particularly anaplastic lesions, harbor these deletions. Electron microscopy demonstrated the presence of tumor cells with clear cytoplasm and few organelles. There was no evidence of junctional structures, neurosecretory granules, cytoplasmic filaments, neural tube formations, or luminal formations. The combination of histology, immunohistochemistry, and electron microscopy thus confirmed the diagnosis of anaplastic oligodendroglioma.

Of the 70 cases of IVO reported in the literature, most were diagnosed in the era preceding modern immunohistochemical and electron microscopy standards. Therefore, many previous reports were based on routine histologic specimens. The possibility that some of these intraventricular tumors were other entities cannot be completely excluded. Practitioners must be certain that a diagnosis of IVO is differentiated from lesions with potentially similar histologic characteristics and clinical presentations, as different treatment implications may exist for each diagnosis. Other intraventricular entities such as central neurocytoma, clear cell meningioma, metastatic lesions, subependymoma, astrocytoma, ependymoma, germ cell tumors, and ganglioglioma need to be considered.

Many authors have agreed that simple histologic staining is insufficient in confirming the diagnosis of IVO. For example, oligodendroglioma and central neurocytoma appear quite similar on routine light, smear, and cryostat microscopic examination [24]. Specific immunohistochemical staining methods and electron microscopy should be performed to confirm the diagnosis. Staining for GFAP and synaptophysin are crucial in differentiating IVOs from other types of gliomas and central neurocytomas. In central neurocytoma, staining for markers such as neurofilament protein, chromogranin, and synaptophysin is positive, whereas it remains negative in oligodendroglioma. GFAP is positive in oligodendroglioma, yet negative in neurocytoma [24]. Hasuo et al also noted that IVOs can be also be

differentiated from neurocytomas based on electron microscopy because the latter have mature neuronal cells with well-formed synapses [10].

4.3. Origin and development of IVO

The precise origin of IVOs remains unclear. Maiuri et al postulated that these tumors originate in the subependymal region and are actually of neuronal origin [14]. Sakai et al reported that these lesions originate from a precursor that is common to both oligodendroglial cells and ependymal cells [22]. Electron microscopic studies have demonstrated that these lesions have microtubules measuring 20 to 25 nm in diameter, dense-cored vesicles measuring 100 to 200 nm in diameter, and simple maculae adherens, yet no well-formed synapses [10]. Hasuo and Nishio have thus referred to these lesions as *intraventricular neurocytoma* to more accurately reflect the neuronal origin of these neoplasms. On the other hand, Yuen et al reported that IVOs do not have neurotubules or neurosecretory granules [24]. The cellular precursors and origin of these lesions thus remain a subject for further investigation.

4.4. Clinical manifestations of IVO

It is well known that lesions originating within the ventricular system clinically present in a manner that is much different than their intraparenchymal counterparts. According to the current review, 76% of patients presented with clinical symptoms reflecting symptoms and signs of ventricular outflow obstruction and elevated ICP. Short-term memory loss was noted in our patient as well as in one additional patient with a tumor originating in the septum pellucidum [2] and was felt to be secondary to fornix compression and/or invasion. The mean age of patients presenting with IVOs is generally younger than that described for patients harboring intraparenchymal oligodendrogliomas. According to the current review, the mean age of 70 patients with reported IVOs was 30 years.

4.5. Treatment of IVO

The principles of treatment of primary IVO are similar to those for other intraventricular lesions. Attempted gross total surgical resection remains the mainstay of treatment, followed by adjuvant radiotherapy and/or chemotherapy. There have been no reports regarding endoscopic resection of IVO, although this is likely to be a promising approach for this entity as surgeons become more familiar with the benefits and limitations of neurosurgical endoscopy. In recent years, significant advances have been made in the treatment of oligodendrogliomas, based primarily on molecular subtyping of lesions. Deletions resulting in loss of heterozygosity of the 1p and 19q segments of intratumoral chromosomes have correlated closely with a favorable response to chemotherapy. Standard chemotherapeutic regimens for such lesions now include procarbazine, lomustine, and vincristine. More recent trials are being

Kikuchi	1985	2	17	F	Right lateral ventricle	ICP	Transcortical transventricular	Gross total	Low grade	Yes	Hemiparesis
			21	F	Left lateral ventricle	ICP	Transcortical transventricular	Gross total	Low grade	No	Hemiparesis
Packer	1985	1	18	M	Fourth ventricle	Diplopia, INO, AMS, ICP	Suboccipital	Subtotal	High grade	–	Recurrence (frontal) at 21 mo
Ng	1986	2	–	–	–	–	–	–	–	–	–
Martinez-Lage	1986	1	43	M	Right lateral ventricle	HA, SAH	Transcortical transventricular	Low grade	No	–	Left hand weakness
Hasuo	1987	4	22	M	Septum pellucidum	ICPs in 3, 1 incidental	–	–	–	–	–
			24	M	Septum pellucidum	–	–	–	–	–	–
			30	F	Septum pellucidum	–	–	–	–	–	–
			39	F	Lateral ventricle	–	–	–	–	–	–
Garza-Mercado	1987	1	22	M	Septum pellucidum	ICP, speech disturbance, ataxia, RUE weakness	Transcortical transventricular	Low grade	No	Improved	
Dolinskas	1987	9	–	–	–	Unknown	Unknown	All 8 subtotal	–	6 of 8	–
Nioka	1987	2	29	F	Lateral ventricle	ICP	Interhemispheric transcallosal	–	–	–	–
			19	F	Lateral ventricle	ICP	Interhemispheric transcallosal	–	–	–	–
Lee	1990	1	25	F	Lateral ventricle	ICP, hemiparesis	Transcortical transventricular	Subtotal	–	Yes	Asymptomatic at 6 mo
Tekkok	1992	1	39	F	Left lateral ventricle	Hemifacial spasm	Transcortical transventricular	Subtotal	Low grade	No	–
Yuen	1992	1	33	M	Lateral ventricle	Ataxia, ICP	Transcortical transventricular	Gross total	Low grade	No	Death at postoperative day 3
Morita	1993	2	–	–	–	–	Stereotactic	Gross total	–	–	–
Romero	1996	2	18	F	Right lateral ventricle	ICP, ataxia	Unknown	Gross total	Cellular pleomorphism	No	–
			38	M	Third ventricle	Hemiparesis, ICP, visual loss	Interhemispheric transcallosal	Subtotal	Cellular monomorphism	No	–
Natale	2005	1	67	F	Left lateral ventricle, cauda equina	Paraparesis, ICP	Transcortical transventricular	Gross total	Anaplastic (WHO grade III)	No	Death at 8 mo postoperation
Zada	2007	1	22	F	Right lateral ventricle	ICPs, memory loss	Interhemispheric transcallosal	Gross total	Anaplastic (WHO grade III)	Yes	Recurrence, death

conducted to test the efficacy of temozolamide for anaplastic oligodendroglioma.

A significant proportion of patients undergoing treatment of IVOs will develop CSF outflow obstruction and will require perioperative ventricular shunting. According to our review, 46% of patients required perioperative shunt placement. A previous report by Dolinskas and Simeone reported that 6 of 8 patients (75%) required VP shunt placement [4].

The outcomes for patients with intraventricular anaplastic oligodendroglioma remain poor. Treatment based on targeted chemotherapy, perhaps via an intrathecal route, remains a possibility for patients diagnosed with these lesions. Further research is required in identifying subtypes of oligodendroglioma that may be amenable to various chemotherapeutic regimens.

5. Conclusions

Intraventricular oligodendrogliomas are infrequently encountered entities and tend to be low-grade lesions. Anaplastic IVO is an exceedingly rare diagnosis, with only 3 cases reported in the literature. Immunohistochemistry and EM remain standard techniques in establishing an accurate diagnosis of oligodendroglioma. Chromosomal analysis can be of great utility in establishing a diagnosis and predicting response to chemotherapy. Although outcomes remain poor, current multimodal treatment options include surgical resection, radiation, and possible targeted chemotherapy based on molecular subtyping.

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