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FOCUS SESSION

Cerebellar mutism syndrome: current approaches to minimize risk for CMS

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Abstract

Purpose Cerebellar mutism syndrome (CMS) is a serious source of morbidity following posterior fossa surgery in the pediatric population. However, methods for effectively decreasing its incidence and impact remain unclear. It is our aim to examine the impact of adjusting surgical factors, namely the use of a telovelar approach and avoidance of cavitronic ultrasonic aspirator, on the incidence of CMS in our population as well as outlining potential pre-, intra-, and postoperative factors that may contribute to its development.

Methods Retrospective review was performed to identify patients undergoing posterior fossa surgery for resection of a medulloblastoma. Demographic, surgical, and postoperative data were collected. These data were analyzed for possible correlations to the risk of developing CMS via univariate analysis. For factors found to be significant, a multivariate analysis was performed to assess their independence.

Results Seven of 65 patients (10.8%) developed CMS postoperatively. Factors found to be significantly associated with a higher risk of CMS were the degree of retraction utilized during the procedure ($p = 0.0000$) and incision of the vermis ($p = 0.0294$). Although they did not reach the threshold of statistical significance, tumor vascularity ($p = 0.19$), adoption of a transvermian approach ($p = 0.19$), and lack of intraoperative imaging ($p = 0.17$) exhibited strongly suggestive trends towards a correlation with CMS.

Discussion In an effort to reduce the incidence and severity of CMS in our population, our institution adopted surgical practices that minimize tissue trauma and mitigate postoperative edema. This included the use of a telovelar over a transvermian approach to obviate the need for vermian incision, avoidance of the CUSA, and minimization of heavy retraction during surgery. This was successful in reducing the incidence of CMS from 39% in our medulloblastoma patients to 10.8%. The development of CMS after posterior fossa surgery appears to be a "two-hit" phenomenon requiring a combination of existing predisposition, surgical injury, and postoperative exacerbation. Therefore, it is critical to identify the factors involved at each stage and investigate treatments to target them appropriately.

Keywords Cerebellar mutism · Transient cerebellar mutism · Posterior fossa syndrome

Introduction

Although the surgical treatment of posterior fossa tumors in children is fraught with innumerable challenges, the potential presentation of postoperative cerebellar mutism syndrome (CMS) is among, if not, the most formidable concerns. The first explicit use of the term "cerebellar mutism" dates to 1985 by Rekate et al. [1], but was likely described in earlier case reports under different labels [2, 3]. CMS is most often seen in the pediatric patient with a posterior fossa tumor [4] (especially medulloblastoma). However, similar symptoms have been seen in non-surgical patients [5–8] and adults [9–11].

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Historically, these conditions have been inconsistently labeled as *posterior fossa syndrome*, mutism with pseudobulbar palsy [3], and other names with no clear delineation, adding to ambiguity in clinical understanding of CMS. Since its initial description, over 500 reports on the subject have been published in the literature, with an incidence ranging from 20 to 38% in large tumor series [4, 12–15]. Recent work has increasingly focused on understanding the etiology of the condition, with an emphasis on the neuropathophysiological mechanisms that may be involved. This shift has come in conjunction with recommendations to establish preoperative risk assessments [16] and to standardize practices that minimize the clinical appearance of CMS. While many factors have been identified—and some discarded—as bearing etiological implications for CMS, it is likely that the true onset is multifactorial, involving (1) preoperative propensity for the condition and (2) exacerbation by some element(s) of intraoperative and/or postoperative insult.

Numerous mechanisms have been proposed for the delayed development of paucity of speech, irritability, emotional lability, ataxia, dysarthria, hypotonia, and occasionally cranial nerve deficits and dystonia [1–6]. In the most common progression of this phenomenon, symptoms peak within a few days of surgery and gradually improve over time. However, there is often an element of long-term deficit, particularly with respect to speech and cognitive deterioration, resembling the cerebellar cognitive affective disorder [17, 18].

CMS's delayed onset suggests that its clinical picture develops via a process of injury following an initial insult, rather than an immediate response to a particular action. The implication of this has been closer scrutiny of surgeons and their potential to set this process in motion. The location of the tumor and the extent of its resection—particularly when it involves the lateral margins of the 4th ventricle, in the vicinity of the dentate nuclei or the superior/middle cerebellar peduncles—appear most likely to disrupt the dento-rubro-thalamo-cortical (DRTC) pathways and cause deficits in speech and other cognitive functions. This trend is corroborated by multiple studies in which the intraoperative and postoperative DTI deficits seen when these areas were surgically affected (especially bilaterally) were found to correlate with the clinical development of CMS [14, 18–21]. The role of surgical exposure, the retraction of the actual tumor tissue, and the use of particular surgical tools have also been debated extensively. The size and location of the tumor and the presence of comorbidities such as hydrocephalus may contribute to the difficulty involved in accessing and resecting midline/4th ventricular tumors [22–24]. Ultimately, the choice of surgical route, extent of resection, rigor of necessary retraction, and choice of tools in tumor extirpation may all have the potential to affect the likelihood of CMS development.

Historically, surgical approaches to the fourth ventricle have utilized the most direct attack via an incision in the vermis. While often the shortest avenue to the tumor, it is usually necessary to resect a significant amount of vermis to achieve adequate visualization, particularly for large masses. While there are a number of studies implicating incision of the vermis in the development of CMS [22, 25–27], there are also a number of other reports that fail to find any association [28, 29]. Subsequently, there are many advocates who favor using a telovelar approach to access the midline for 4th ventricular tumors [26, 27]. This approach (Fig. 1) takes advantage of natural tissue planes between the vermis and cerebellar hemispheres for a less traumatic way to approach midline posterior fossa tumors. Not only does this approach potentially offer greater superior (cephalad) exposure but it can also provide additional lateral exposure when compared with the more *limited* midline vermal incision one might use in an effort to minimize vermal resection. Up until now, the value of a telovelar approach has been difficult to assess in the setting of posterior fossa tumors and prevention of CMS. Nevertheless, institutional experience at Children's National Medical Center appears to support the benefit of this surgical approach in reducing the incidence of CMS.

Owing to its improved exposure and visualization of 4th ventricle tumors, the telovelar approach most likely requires less retraction to access lesions that would otherwise be difficult to reach. This may, in turn, lead to less postoperative edema and fewer delayed manifestations of the injury process. Other adjunctive measures to minimize the impact of surgical injury on CMS may involve the avoidance of the Cavitron Ultrasonic Surgical Aspirator (CUSA®), judicious dissection at the lateral margins of the fourth ventricle, and limited or no cerebellar retraction [30, 31]. Ultimately, objective identification of the factors that contribute to the development of CMS will allow appropriate therapeutic modifications to reduce this catastrophic outcome and mitigate an important source of morbidity for these patients and their families.

Methods

Study population

The departmental database for all brain tumor surgeries performed at Children's National Medical Center (CNMC) between January 2000 and February 2016 was reviewed. Of the 521 resections, 285 (55%) were done for lesions located in the posterior fossa and 65 (23%) of those cases were confirmed as medulloblastoma. Two of those 65 cases were repeated resections on patients who had undergone their first resection during the specified time frame. The resulting cohort size was 63 unique patients.

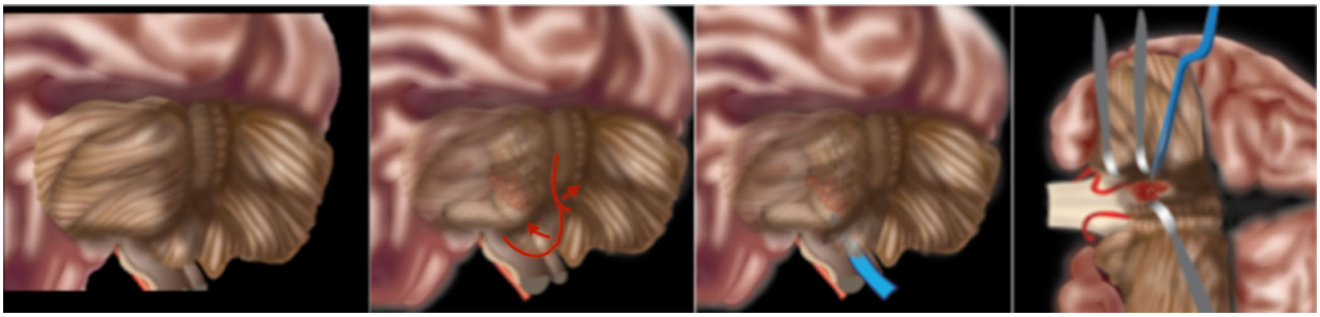


Fig. 1 Telovelar approach to the 4th ventricle. The telovelar approach takes advantage of existing anatomical planes to minimize disruption of tissue. Superolateral retraction of the tonsil and superomedial retraction of the vermis (**b**) opens up the cerebellomedullary fissure and the uvula tonsillar space to provide adequate exposure for access to the majority of 4th ventricle tumors (**c**). This approach achieves improved exposure over traditional transvermian routes and thereby obviates the need to make a vermian incision, while potentially decreasing the degree of retraction that is necessary to access the lesion (**d**)

Chart review

Following IRB approval (CNMC IRB Pro#08777) of our study, a retrospective chart review was conducted for the 63 patients meeting our inclusion criteria. Demographic and surgical data were collected. Tumor-specific information included whether the lesion was a recurrence, the degree of vascularity, lateral recess involvement, adherence to 4th ventricle, and brainstem invasion. Degree of tumor vascularity was determined from the operative note and was graded from non-vascular to highly vascular. The other variables were coded as binary (yes/no) findings.

Patients' medical records were also reviewed for the following surgical factors: estimated blood loss (EBL), length of surgery, transfusion, cerebrospinal fluid (CSF) diversion, mode of retraction, stealth neuronavigation, intraoperative imaging, vermian incision, surgical approach, neuromonitoring, mode of extirpation, and extent of resection. Transfusion, CSF diversion (either external ventricular drain (EVD) or shunt), frameless neuronavigation, vermian incision, and neuromonitoring were coded as binary (yes/no) outcomes, while EBL and length of surgery were continuous variables. The mode of retraction was determined by explicit descriptors in the operative notes and graded into categories of none, minimal, handheld, and self-retaining retractor system. Intraoperative imaging referred to the use of no imaging, intraoperative magnetic resonance imaging (iMRI), or ultrasound (US). The mode of extirpation was classified as direct (surgical dissection or suction/bipolar) or ultrasonically aspirated using CUSA® or Sonopet®. The extent of resection was categorized as sub-total resection (STR), near-total resection (NTR), or gross-total resection (GTR).

Chart review was blinded, in that data collection was performed using standardized keywords established prior to the commencement of the review process and without study staff knowledge of postoperative CMS outcome. This approach was implemented to minimize interpretation and judgment bias. Univariate and multivariate regression analyses were performed on our data using R statistical software to elucidate whether any of the aforementioned factors bore statistically significant associations with CMS outcome.

Results

Sixty-three patients underwent surgical resection of a posterior fossa or 4th ventricular medulloblastoma over 16 years at CNMC in Washington, DC (Table 1). The average age at surgery was 8.31 years. The cohort was 54% male and 46% female. Seven of the 65 cases we examined in this study were for secondary debulking or resection of recurrent tumor, though five of the initial resections were performed elsewhere. Seven of the 65 cases (10.8%) were complicated by postoperative CMS.

Our univariate analysis of potential operative factors associated with CMS yielded two statistically significant associations. The degree of retraction utilized during the procedure was graded on a scale from 0 to 3—denoting no retraction, minimal, handheld, or self-retaining. Retraction was found to be strongly related to the risk of developing CMS in our cohort, with average retraction scored at 2.00 in patients with CMS and 1.38 without ($p = 0.0000$). Incision of the vermis also bore a statistically significant relationship to CMS ($p = 0.0294$). Six out of 7 (85.71%) of the patients who went on to develop CMS underwent some degree of vermal incision, versus 26/58 (44.83%) of those who did not. Although not statistically significant, there were a number of other relationships that were strongly suggestive. Tumor vascularity was graded on a scale of 0–3, from "non-vascular" to "extremely vascular" based on operative notes. Average tumor vascularity was scored at 2.00 in the CMS cohort and 1.43 in the non-CMS group ($p = 0.1918$). Adoption of a transvermian approach ($p = 0.1878$) and lack of intraoperative imaging ($p = 0.1701$) also demonstrated a trend towards correlation with CMS. A multivariate analysis was then performed on this subset of variables, which confirmed their independence (Fig. 2).

Table 1 Characteristics of the 65 cases queried and results of a univariate analysis

Variable	CMS	Non-CMS	*p* value
Avg. age at surgery (years)	8.07	8.34	0.8104
Recurrent tumor	1/7 (14.29%)	6/58 (10.34%)	0.7983
EBL (mL)	160.71	172.59	0.7716
Transfusion rate	1/7 (14.29%)	7/58 (12.07%)	0.8860
CSF diversion	1/7 (14.29%)	15/58 (25.86%)	0.4740
Tumor vascularity	2.00	1.43	0.1918*
Retraction	2.00	1.3793	0.0000**
Stealth	2/7 (28.57%)	4/58 (6.90%)	0.2889
Intraoperative imaging	4/7 (57.14%)	40/58 (68.97%)	0.1701*
Vermis incision	6/7 (85.71%)	26/58 (44.83%)	0.0294**
Transvermian approach	5/7 (71.43%)	25/58 (43.10%)	0.1878*
Lateral recess involvement	1/7 (14.29%)	6/58 (10.34%)	0.7983
Extirpation	0.1429	0.1724	0.8503
Adherent to 4th ventricle floor	3/7 (42.86%)	14/58 (24.14%)	0.4021
Brainstem invasion	2/7 (28.57%)	16/58 (27.59%)	0.9608
Neuromonitoring	4/7 (57.14%)	35/58 (60.34%)	0.8841
OR time (h)	5.44	5.29	0.8423
Extent of resection	1.4286	1.7241	0.4671

Tumor vascularity was rated on a 0–3 scale from “non-vascular” through “extremely vascular.” Retraction was graded from 0, “no retraction,” through 3, “self-retaining retractors.” Extent of resection was rated 0 for “sub-total,” 1 for “near-total,” and 2 for “gross-total” resection. The amount of retraction and incision of the vermis was found to be significantly associated with CMS. Tumor vascularity, lack of intraoperative imaging, and a transvermian approach exhibited a trend towards association, but were not statistically significant.

**Statistical significance

*A trend

Discussion

Clinical considerations/incidence

As treatment options for patients with posterior fossa tumors expand and improve, clinicians have been able to shift their attention to quality of life considerations in addition to survival [32]. As such, the avoidance of devastating potential outcomes like CMS has been a subject of significant interest. Incidence of CMS has been broadly reported around 25% following posterior fossa surgery, and as high as 40% at our own institution when the tumor is a medulloblastoma [33]. Older reports place the incidence much lower (around 8%) [34]. This increase is potentially secondary to greater scrutiny, more specific clinical and radiographic definitions, or more aggressive surgical techniques, among other factors. The recent establishment of a consensus definition [35] will ideally mitigate some of the variability and confusion that have been associated with defining the clinical syndrome in the past.

Neuroanatomical boundaries

Before one can make meaningful modifications to surgical strategies in an effort to mitigate CMS, we must first gain a more robust understanding of its pathophysiology, mechanisms of injury, and the anatomical structures that are affected. The understanding of CMS as a largely anatomic phenomenon is rooted in Fraioli and Guidetti’s 1975 description of delayed-onset mutism, emotional lability, and cognitive dysfunction in 2 patients who had undergone direct lesioning of the dentate nucleus for dyskinesia [2]. The current leading hypothesis implicates injury to the dento-rubro-thalamo-cortical tract (DRTCt) as the primary culprit. This theory suggests that disruption of proximal cerebellar efferents leads to decreased input from the cerebellum to the cortex and this, in turn, may contribute to a reciprocal hypoperfusion and decreased metabolism in the corresponding cortical areas, ultimately leading to decreased function [21, 36, 37]. This is supported by a number of studies that have found reduced fractional anisotropy in the superior cerebellar peduncle (SCP) on immediate postoperative scans [18, 20, 21, 38]. The anatomic location of these fibers in the SCP—which is just lateral to the wall of the 4th ventricle and medial to the middle cerebellar peduncle—corroborates this theory, as it has been widely reported that the odds of developing CMS are significantly increased when the tumor is in the midline, invades (or compresses) the brainstem, or adheres to the wall of the 4th ventricle. This significant increase in the risk of CMS is also present in the context of bilateral invasion of the dentate nuclei or involvement of the superior and middle cerebellar peduncles [22–24, 31, 34].

Etiological and preoperative risk considerations

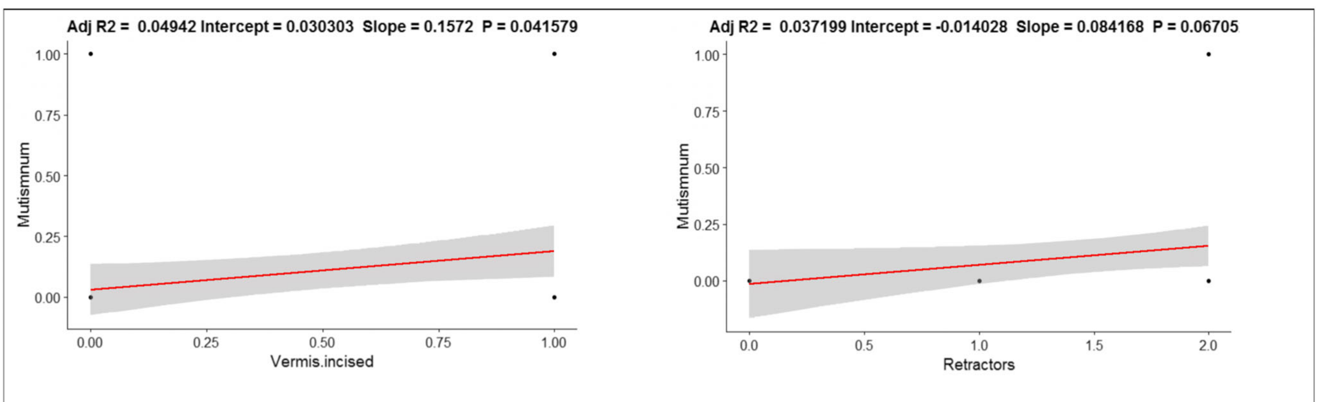
A comprehensive approach to the minimization of CMS during treatment of PF tumors must begin with consideration of etiological and preoperative factors. Some authors have suggested that the presence of preoperative deficits or subclinical injury from the tumor itself may be predisposing factors [18, 24, 39, 40]. Factors associated with the tumor—size, pathology, and location of the lesion—have also been considered, with significant evidence to support that the location of the mass and the extent of brainstem involvement are closely related to an individual's risk [22–24, 31, 34]. The significance of preoperative (and postoperative) hydrocephalus or the tumor size has been less clear.

The ability to understand which preoperative factors are relevant to CMS is important both for the purpose of risk stratification and for the potential to optimize a patient's condition to minimize their individual risk. In this vein, Walker and colleagues developed a preoperative scoring system to determine which patients are at highest risk [24]. Their proposed final model included six predictors—MRI primary location, bilateral middle cerebellar peduncle involvement (invasion and/or compression), dentate nucleus invasion, and age at surgery > 12.4 years—and had an accuracy of 88%. The ability to accurately make these predictions based on information that is available prior to surgery is critically important, not only because understanding and communicating the risk of this devastating outcome is central to informed consent but also because it could potentially alter surgical strategy, including the approach, extent of resection, choice of monitoring, and optimization of the patient's pre- and postoperative condition. Examples of measures that can be taken by the surgeon preoperatively include radiologic assessment of the DRTCt for careful surgical planning, risk stratification, and discussion of potential harms, benefits, and alternatives, and the use of adjunctive treatment with steroids, chemotherapy, or embolization as appropriate.

Surgical strategies

Given that CMS occurs almost exclusively as a postsurgical complication, surgical strategy is central to its prevention. Current hypotheses on how surgery contributes to the underlying pathophysiology of CMS include transient ischemic injury secondary to blood loss, hypoperfusion, injury to vasculature or vasospasm, direct surgical injury to the cerebellar nuclei or the involved white matter tracts, postsurgical edema caused by surgical injury and exacerbated by excessive retraction, axonal injury and disruption, and thermal injury from the use of the CUSA.

The impact of a telovelar versus a transvermian approach remains contentious. A number of studies have suggested that splitting of the vermis may increase the risk of CMS [25–27, 41], while others have found no significant decrease in the incidence of CMS when vermal splitting was avoided [28]. The use of a telovelar approach, which avails natural anatomic



R^2	P-value	Predictor	Unstandardized Beta Coefficient
0.08857	0.05643	Vermis Incision	0.2011
		Retraction	0.1644

Fig. 2 Multivariate Analysis. The variables found to bear significant associations with CMS in the univariate analysis were subjected to a multivariate analysis in order to assess their independence. This found that incision of the vermis and degree of retraction were not significantly associated with one another ($p = 0.056$, $R^2 = 0.089$)

planes for access to the 4th ventricle without vermal splitting, has been a popular alternative, though its actual benefit in reducing CMS remains in question.

At our institution, 6/7 (85.7%) of patients who developed CMS underwent incision of the vermis, versus 26/58 (44.8%) who did not ($p = 0.029$). We also found that the degree of retraction had significant impact, with self-retaining retraction systems strongly correlating with a higher risk of CMS when compared with gentle, handheld retraction ($p < 0.001$). This association of excessive retraction with CMS may be responsible for some of the benefit seen with a telovelar approach, as this method provides improved access to the 4th ventricle that may require less retraction [42]. A recent 2015 review by Avula et al. also points to the thermal injury inflicted by the use of CUSA®, which may potentially worsen the vasogenic edema found on postoperative imaging of CMS patients and exacerbate the pathologic process [30].

The rapid advancement of imaging technologies has lent itself to the common use of intraoperative imaging and neuronavigation. As such, these systems could be useful in the avoidance of particular tracts or structures. The evidence on this question is unclear as of yet. A number of studies show that iMRI improves the extent of resection, but at the cost of increased morbidity while other studies demonstrate equivocal results [38, 43]. The majority of our patients with CMS (4/7, 57.1%) had intraoperative imaging during their case, versus 40/58 (69%) who did not ($p = 0.17$), which was found to be suggestive although not statistically significant. Another significant question is whether there is any clear survival or quality of life benefit from attaining gross-total resection versus a near-total resection. In cases where the location, size, or invasiveness of the tumor makes a GTR challenging, the benefits of maximal resection must be weighed against potential injury to critical neurologic structures, bleeding, and heavy-handed retraction. This is clearly a difficult question that should be considered on a case-by-case basis depending upon the relative prognosis, risks of neurologic injury, and aggressiveness of the specific pathology. Although there have been multiple studies showing that outcomes are positively correlated with greater extent of PNET resection, the increased percentage of patients with GTR has been mirrored by a corresponding increase in highly morbid complications like CMS. In fact, Korah et al. found when examining the differences between PNET resections in 1990–2000 versus 2001–2007, the percentage of GTRs rose from 83 to 93%, while the incidence of CMS rose from 17 to 39% [31]. Judicious resection with respect to the location of important anatomy and the eloquence of the region should be practiced to avoid needless complications and elevated morbidity. Especially in cases where achieving a GTR would require extensive manipulation, retraction, or injury to eloquent areas, the benefits of this result must be weighed against the probability of causing CMS in pursuit of the "complete" resection. All these considerations should be part of a comprehensive approach when counseling patients and their families.

Prior experience at our institution found the incidence of CMS following medulloblastoma resection to be 39% [33]. In response to this significant complication, we have undertaken a systematic change in surgical techniques to favor vermis-sparing approaches that minimize direct injury as well as injury secondary to heat and retraction. Namely, this has involved utilizing a telovelar approach, avoiding the use of CUSA, and minimizing retraction. Even as the overall incidence of CMS across centers has increased, we have seen the incidence at our institution fall from 39 to 10.8% over the past decade.

Postoperative challenges

When managing these patients postoperatively, prevention of secondary injury is key to avoid worsening of existing damage. Given that the symptoms of CMS tend to peak within the first few postoperative days before making a gradual improvement, it is widely thought that postsurgical edema may be responsible for bridging much of the gap between microsurgical injury and clinical deficits. The role of postoperative fever has also recently come under scrutiny. Pols et al. found that a 0.5 °C increase in mean body temperature in the first four postoperative days profoundly affected the risk of CMS, increasing the odds ratio almost fivefold [23]. Some have also suggested a potential role for oxygen saturation and hypoperfusion of important anatomical structures that are related to the coordination of speech and emotional regulation [44]. Injury to particular vascular structures, vasospasm or hypoperfusion secondary to blood loss or low MAPs may be sufficient to cause transient ischemic injury. This ischemia could itself lead to symptoms of CMS, or may be the key instigating event that leads to further edema, delayed healing, and subsequent reperfusion injury.

Postoperative preventative measures that have been proposed include the use of steroids to reduce edema, aggressive treatment of postoperative fever, and avoidance of hydrocephalus [45]. There has also been a discussion of using dopamine, low-dose mannitol, and vasoactive medications such as nimodipine to enhance perfusion and avoid vasospasm. Bromocriptine [46] (and in one case, midazolam [47]) has also been used, presumably in an attempt to mitigate inhibition of cortical activity by altering neuro-modulation at the level of thalamic nuclei, thus circumventing the ultimate results of "diaschisis." Some authors have also reported success with fluoxetine [48] and zolpidem [49].

A postoperative scoring system is currently in development to further elucidate which of these mechanisms may be responsible for causing harm and which treatment strategies are most effective. Currently, treatment strategies target pathophysiologic mechanisms that are largely theoretical, with a focus on rehabilitation of patients when CMS does develop [50–52]. Additional systematic evidence-based approaches to the issue of postoperative management of these cases are clearly needed.

Conclusion and future directions

Despite prodigious advances in the treatment of pediatric brain tumors over that past few decades, we remain tethered to unacceptably high complication rates in the setting of surgical treatment of posterior fossa tumors. CMS continues to plague pediatric neuro-oncology specialists and remains *pervasive* globally with incidence rates in the vicinity of 25%.

Although it is very likely that CMS needs to be understood as a multifactorial "*two-hit*" phenomenon (whereby susceptibility and injury eventually coalesce) before we will be able to effectively combat this challenging complication, there are nevertheless a number of strategies that can be effectively employed today to reduce its presence.

From a *preoperative* perspective, a number of new approaches can assist the surgeon beforehand in elucidating preoperative risks and helping to formulate surgical strategies for safe and effective tumor removal. Earlier tumor diagnosis inevitably leads to fewer postoperative deficits and potentially less susceptibility to postop comorbidities. Accurate *preoperative risk stratification*, recently developed by David Walker et al. [24], also allows for more realistic resection goals with respect to the likelihood of a causative injury in addition to helping establish more realistic expectations for both the surgeon and the patient and family. Knowing ahead of time if and where tumor is invading the region of the dentate nuclei or the superior and middle cerebellar peduncles, and whether abnormalities can be noted on DTI tractography, all contribute to directing the surgeon to safer approaches to the tumor resection. This can also help in defining the likelihood of a gross total tumor resection relative to the risk-to-benefit ratio.

There are also numerous steps that can be employed *during surgery* that may have a meaningful effect to reduce the incidence of CMS. In view of the unacceptably high rate of CMS (39%), we observed at our institution in past decades a number of intraoperative modifications were undertaken to improve this situation. Utilization of a *telovelar approach* to midline/4th ventricular tumors, instead of vermian incisions, appeared to reduce the development of CMS significantly. A total of 85.7% of patients who developed CMS underwent incision of the vermis, while only 44.8% of patients who had telovelar exposure developed CMS ($p = 0.029$). Whether vermian incision truly causes or contributes to CMS is likely to remain contentious, but perhaps the greatest factor involves the degree of retraction necessary in the setting of the initial exposure. It is likely that a telovelar approach offers greater exposure, which in turn requires less retraction. As part of a surgical strategy to *minimize retraction* in this setting, we found that the degree of retraction had a significant impact on the presence of CMS, with self-retaining retraction systems correlating with higher risk of CMS when compared with gentle, handheld retraction ($p < 0.001$). It is our practice to avoid retraction (where possible) during the removal of tumors. The use of aggressive CSF drainage, gravity assistance facilitated by patient positioning, and the telovelar approach has greatly facilitated minimizing or avoiding retraction. Methods of tumor removal also deserve scrutiny. Elective *avoidance of the CUSA®* in this delicate region also appeared to decrease the incidence of CMS in our series. While not statistically significant, there was a strong suggestion of a trend in this regard, which, together with the work of Avula et al. [30], may be suggestive of the role of thermal injury due to the CUSA®. When possible, we avoid using any high-frequency ultrasonic instruments when removing tumor from the region of the 4th ventricle/brainstem.

The use of *intraoperative imaging* has brought near-time ability to assess precise localization during surgery as well as extent of resection. The use of iMRI to assess DTI tractography and evidence of early edema [38] also offers improved capability to avoid causing additional injury in addition to navigating perilous neuroanatomical territories.

Careful management of *postoperative* factors, including the *avoidance of fever or hydrocephalus*, use of vasoactive medications to *maximize perfusion and avoid vasospasm*, and careful monitoring and treatment of *oxygen saturation* may help to avoid exacerbation of any surgical injury or predisposing factor(s) that may already be present. Subsequently, when CMS does occur, improved definitions and early recognition of the syndrome may provide an opportunity to quickly treat the etiologic causes and direct the patient to early and intensive neurocognitive rehabilitation.

Even in the wake of ongoing advances in the treatment of posterior fossa tumors—including a guarded optimism that molecular stratification and "knife-less" neurosurgery are in the not too distant future—surgeons have been unable to fully and effectively combat postoperative CMS. Significant progress has been made through the identification of likely anatomic and etiologic factors, as well as methods of risk stratification and strategies for prevention and treatment. Although some aspects remain unclear, the adoption of evidence-based risk-reducing practices should be undertaken whenever possible to suppress the impact of this highly morbid complication. It is our hope that continued implementation and investigation of the measures outlined here will help surgeons to define a strategy to minimize CMS in their own patients.

Compliance with ethical standards

Conflict of interest The above authors have no conflict of interest in any of the data or information presented in this paper.

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