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ORIGINAL PAPER

Brainstem compression: a predictor of postoperative cerebellar mutism

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Abstract
Purpose Cerebellar mutism is a common complication of posterior fossa tumor resection. We observed marked, preoperative brainstem compression on MR imaging, among patients who developed postoperative mutism. This study was designed to investigate if an association was indeed present.
Materials and methods Patients (18 months–18 years) undergoing resection of a midline, posterior fossa tumor were retrospectively reviewed. Demographic data, tumor pathology, mutism onset and duration, and postoperative complications were obtained from hospital records. Pre- and postoperative MR images were studied to assess tumor size and the severity of pons compression (an estimate of the mechanical and distortional forces imparted by the tumor).
Results Patients with mutism showed greater preoperative pons compression and a greater increase in postoperative pons diameter.
Conclusion We predict that brainstem compression may represent white-matter injury from (1) surgical manipulation and traction, and (2) axonal damage caused by the release of the tumor's compressive force and ensuing axon distortion and dysfunction. The results provide support that mutism may be largely caused by white-matter damage disrupted axon integrity and function.

Keywords Mutism · Posterior fossa tumors · Cerebellum · Dysarthria · Cerebellar neoplasm

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Introduction

Mutism is the complete absence of speech in a conscious patient who demonstrates intact comprehension and no evidence of oromotor apraxia [1]. Cerebellar mutism is a well-described complication of posterior fossa tumor resection. It may occur at any age, but is far more common among children (91% of the reported cases) [2], reflecting the higher incidence of posterior fossa tumors in this age group. Clinically, it may coexist with a number of clinical features including; pseudobulbar-type of emotional lability, agitation, swallowing dysfunction, marked truncal or axial hypotonia and weakness. Cranial nerve palsies (typically CN VI and/or VII) may also be seen [3, 4]. Mutism occurrence was initially estimated in 8–8.5% of children undergoing posterior fossa tumor resection [5–7]. However, prospective studies suggest that the risk may in fact be threefold higher, with up to 24–29% of children developing postoperative mutism [8, 9]. Increased risk for mutism is seen with vermian or midline tumors [5], particularly large tumors (>5 cm) and medulloblastomas [8]. Brainstem or fourth ventricle involvement may further increase the risk of postoperative mutism [10].

Lesions at several anatomical locations, from a wide range of causes, may cause mutism. Holmes [11] provided one of the earliest observations that traumatic injury to the cerebellum results in profound impairment of speech production. Since that time, the role of the cerebellum in speech initiation

has become better understood. Crutchfield [12] proposed a dentate–thalamus–cortical connection as the efferent cerebellar pathway affected in mutism, based upon evidence from prior case reports. Bilateral, stereotactic lesions of the dentate and interpositus nuclei (with attempts to surgically manage spasticity) have caused mutism [13]. Similarly, surgical resection of a pontine cavernous malformation (via a supratentorial approach) has also been a cause of mutism [14], presumably injuring cerebellar efferents as they decussate from the dentate nucleus to the contralateral thalamus. Pollack [4, 5] has provided detailed reviews suggesting mutism may result from excessive paravermian manipulation or tissue retraction injuring any portion of the afferent and/or efferent pathways of the dentate nuclei. Lesions involving some supratentorial structures; the dominant paramedian thalamus, bilateral ventrolateral thalamus, corpus callosum, and supplemental motor cortex [12, 15] have also been implicated in mutism.

The precise cause of mutism after posterior fossa surgery remains unclear. The early theory of vermian incision as a cause of postoperative mutism [6] has fallen out of favor having failed to explain; (1) the delayed onset of mutism (typically, days 1–3 postoperatively [4]) and (2) the observation that many patients with complete vermian incision show no evidence of postoperative language dysfunction [7].

We have observed a much greater degree of brainstem compression among patients with posterior fossa tumors who developed postoperative mutism, relative to those who did not. This observation led to our hypothesis that the amount of preoperative pons compression might be predictive of postoperative language dysfunction. The numerous white-matter tracts in that region; inferior, middle, and superior cerebellar peduncles may be more vulnerable to the effects of tissue manipulation, retraction, and saline irrigation compared to adjacent grey-matter structures. It has been argued that the increased rate of mutism may reflect increased pressure to achieve gross total tumor resection due to its more favorable long-term survival rates [9]. A link between brainstem compression and postoperative mutism raises the question of other mechanisms of injury including; (1) axonal distortion and injury as white-matter tracts are released from the compressive force of the tumor and (2) excessive bending or relaxation of white-matter tracts as they "relax" into the newly formed cavity created by tumor resection.

Materials and methods

Patients

Patients were eligible for inclusion in this retrospective study if: (1) diagnosed with a midline posterior fossa tumor (1990–2007); (2) aged 18 months–18 years old at diagnosis and; (3) surgical resection of the posterior fossa tumor was performed at the Children's Hospital of Eastern Ontario. Patients were excluded if: (1) known to have severe, preexisting language or cognitive impairment or (2) were presenting with symptoms due to disease relapse. Children <18 months old were excluded as reliable language assessment, and surveillance for postoperative mutism was more difficult for infants with little expressive language development. Pre- and postoperative MRI studies were reviewed with the researcher blinded as to which patients did or did not develop mutism.

Institutional research ethics board approval was obtained prior to starting this review. Hospital charts were reviewed for the following information: (1) patient demographic information (gender, age at surgery, presenting symptoms); (2) surgical notes (surgical approach, vermis incised/intact, placement of extraventricular drains and/or ventriculoperitoneal shunts); (3) postoperative complications (mutism, hemorrhage, meningitis, hydrocephalus); (4) pre- and postoperative MR measurements.

MRI measurements

In order to quantify the degree of tumor-derived pontine compression, two MR measurements were obtained from axial T1-weighted (T1W) or T2-weighted (T2W) images at the level of the cerebellar peduncles:

1. Pons, antero-posterior (AP) distance (see Fig. 1a). This measurement was taken at midline, immediately posterior to the basilar artery to most anterior portion of the tumor or cystic component of the tumor. Preoperative, postoperative measurements were recorded.
2. Angle of tumor (see Fig. 1b). This measurement was obtained by placing the vertex of the angle immediately posterior to the basilar artery. Lines were placed from the vertex, making contact with the most lateral portion of the tumor or cystic component of the tumor. Edema may have been present within the middle cerebellar peduncles but was not included in the measurement.

Tumor volume was measured using axial T1W or T2W images to obtain the maximal antero-posterior and lateral diameter of the tumor or cystic component of the tumor. Sagittal T1W images were used (midline section) to measure the maximum rostral–caudal distance of tumor or cystic component of tumor. Edema, if present, was not included in this measurement.

Statistics

Statistical analysis was completed with SPSS, using independent sample *t* tests to compare means for mutism

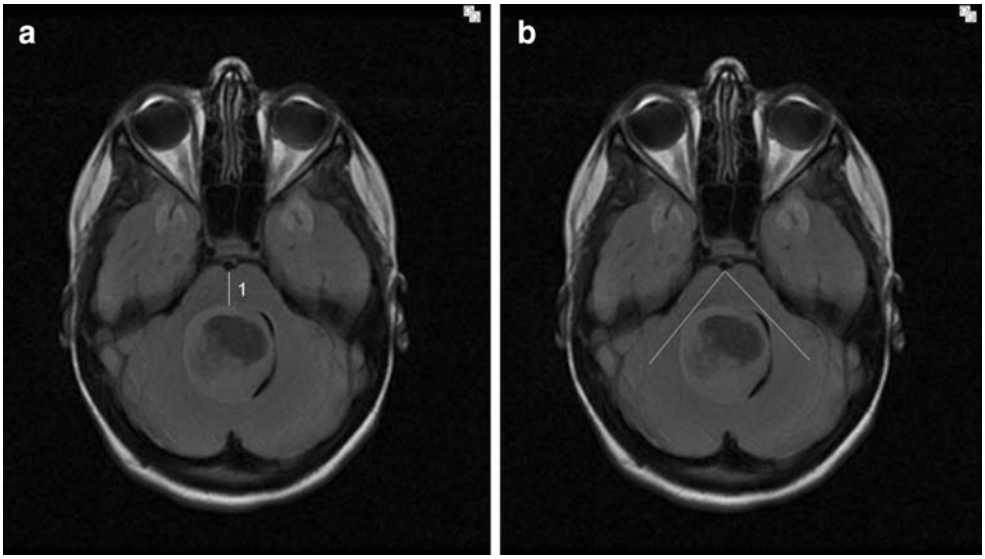

Fig. 1 Pontine AP diameter and tumor angle measurement (see text for detailed description)

versus non-mutism groups. Standard error values are reported for calculated means. The level of statistical significance was <0.05.

Results

Fifty-one patients with midline, posterior fossa tumors met inclusion criteria. Postoperative cerebellar mutism occurred in 13 (25%) patients. Demographic comparison (Table 1) noted a male predominance for both mutism and non-mutism groups. The mean patient age for the mutism group was 8.32 years and did not differ from the non-mutism group (6.72 years; p=NS). Compared to non-mute patients, those who developed postoperative mutism had a higher incidence of medulloblastoma (70% vs 50%). The two groups did not differ in rates of: (1) vermian incision, (2) surgical approach taken, or (3) whether an intraoperative extraventricular drain or ventriculo-peritoneal shunt was placed. None of the three patients requiring preoperative VP shunts (due to clinical complications from hydrocephalus) developed postoperative mutism. Complete, gross total tumor resection was more common among the mutism group (92% vs 79%). The mean time for mutism onset was 2.1 days postoperatively (range 0–5 days). Onset was unclear only in one patient, who required reintubation (postoperative, day 1) for increasing somnolence from hydrocephalus. An extraventricular drain was placed, and the patient was found to be mute when extubated, again, on postoperative day 8. Patients with mutism also demonstrated pseudobulbar-like emotional lability (54%), truncal and/or axial hypotonia (54%), and swallowing dysfunction (30%). The median time before the onset of speech recovery was 21 days (range 6–120 days) with 62% patients demonstrating complete recovery of speech.

Pre- and postoperative MR measurements were available for 36 patients (nine out of 13 mutism and 27out of 38 non-mutism patients). Patients were excluded from MR analysis if both pre- and/or postoperative MR imaging was not available (patients in the early 1990s received only CT brain imaging). MR studies were performed 1–7 days postoperatively (median=4 days), with half (18 out of 36) patients receiving repeat MR imaging on postoperative day 1. Demographic information was reexamined for the subgroup with postoperative MR imaging (data not shown) and found to be in representative of the overall group of midline, posterior fossa tumor patients.

Maximum tumor dimensions and calculated volume did not differ between mutism and non-mutism groups (Table 2). Tumor angle also showed no difference between mutism (75.5±4.2°) and non-mutism groups (65.5±3.2°; p=NS).

Preoperative pons AP diameter was significantly less in patients who developed postoperative mutism (1.42± 0.05 cm) compared to those patients who did not (1.65± 0.05 cm; p<0.05). Postoperative pontine A-P distance did not differ between mutism (1.83±0.07 cm) and non-mutism group (1.91±0.06 cm; NS).

Comparing the change in pons *A–P* distance for each patient (postoperative minus preoperative distance), there was a greater increase in pons measurement for mutism (0.43±0.06 cm) compared to non-mutism patients (0.24± 0.03 cm; p<0.005).

Discussion

These results suggest that the presence of preoperative brainstem compression associated with posterior fossa tumors may have predictive value for the development of postoperative, cerebellar mutism.

Table 1 Demographic data: mutism and non-mutism patients

	Mutism	Non-mutism
Total patients (N=51)	13 (25.5%)	38 (74.5%)
Gender: Male	9 (70%)	21 (55%)
Female	4 (30%)	17 (45%)
Age (at surgery):	8.32 years (3.3–13.8 year)	6.72 yearrs (1.8–15.8 yearr)
Tumor pathology		
Medulloblastoma/PNET	9 (70%)	19 (50%)
Astrocytoma	2 (15%)	15 (40%)
Ependymoma	2 (15%)	3 (8%)
Other	–	1 (2%) 'ependymo-astrocytoma'
Resection		
Gross total	12 (92%)	30 (79%)
Subtotal	1 (8%)	8 (21%)
Surgical approach		
Suboccipital craniotomy	5 (38%)	9 (24%)
Suboccipital craniectomy	8 (62%)	29 (76%)
Vermian incision		
Yes	11 (85%)	30 (79%)
No	–	3 (8%)
Not stated	2 (15%)	5 (13%)
Intraoperative shunt/EVD		
No shunt/EVD	7 (54%)	18 (47%)
Intraoperative EVD placed	6 (46%)	17 (45%)
Preoperative VP shunt placed	–	3 (8%)
Time of postoperative extubation		
Immediately postoperatively	13 (100%)	35 (92%)
Delayed extubation	–	3* (8%) *(1,2 & 15 h postoperative)
Postoperative complications		
Hemorrhage	2 (15%) small (1=vermis; 1=IVH)	2 (5%) small (1=3rd; 1=4th vent)
Hydrocephalus (VP shunt required)	5 (38%)	11 (29%)
Meningitis	–	4 (10%)
CN palsy (new)	4 (31%)	5 (13%)

Experimentally, white matter tracts are exquisitely sensitive to focal, stretch injury, fluid percussion injury, or the application of shearing force from cortical impact injury, (see [16, 17] for review). Perhaps the best known and most common example is diffuse axonal injury (DAI) that occurs to white matter tracts after a traumatic head injury. Contrary to its name, diffuse axonal injury is not entirely uniform in its distribution. Certain regions of white-matter appear at increased risk of injury after head injury, particularly the corpus callosum, with brainstem, cerebellar, and cortical white matter tract involvement becoming apparent with the application of greater force [18]. Experimental studies indicate that the orientation and microstructural arrangements of axons may place some fiber tracts at greater risk of injury after head trauma [19]. We feel that the injury in cerebellar mutism may show some similarities to that described after head trauma. The application of force involved in surgical manipulation, traction, and saline irrigation may injure the vulnerable white-matter tracts in this region. Furthermore, the removal of the compressive force imparted by the posterior fossa tumor may impart additional injury to axons (particularly if tumor is aspirated or adherent to brainstem structures). Such intraoperative forces are much less intense than the rapid force imparted by head trauma. However, these intraoperative forces occur over longer periods of time (i.e., surgical retraction) and more frequently (i.e., saline irrigation, attempts to aspirate tumor). They are also associated with *release* of a tumor's compressive force and a *change* in local structures (i.e., creation of surgical cavity after tumor resection), both of which having the potential to distort the architecture of axons, neurofilaments and intra-axonal organelles causing injury and dysfunction [16]. The degree of preoperative brainstem compression makes such an argument plausible, as patients without the same degree of compression appear spared from the phenomenon of delayed onset, postoperative mutism.

Conventional MR imaging does not typically show any evidence for postoperative vasogenic edema that might implicate mechanical manipulation as the primary cause of injury. Regrettably, axonal injury resulting from the release of compressive force and axon distortion is not well identified by conventional MR technology. Emerging technology, such as diffusion tensor imaging (DTI) appears to be much better suited for this task. It has emerged as a sensitive technique for assessing the extent of white matter damage following traumatic brain injury [20]. It may have an emerging role in predicting clinical outcome after DAI [21] and may also aid in distinguishing between traumatic cytotoxic edema and broken fibers [22]. This imaging modality may aid in confirming and better identifying the predominant role of white-matter damage in postoperative mutism, since DTI appears to distinguish edema (from surgical manipulation) from axonal damage (from compressive force release and

Table 2 Pons and tumor measurements

	Mutism	No mutism	
Pons A-P diameter			
Preoperatively	1.42±0.05 cm	1.65±0.05	p<0.05
Postoperatively	1.83±0.07 cm	1.91±0.06	P=NS
Change (preoperatively–postoperatively):	0.43±0.06 cm	0.24±0.03	P<0.005
Tumor angle	75.5±4.2°	65.5±3.2°	P=NS

distortion). DTI may also have a role in confirming the specific pathways involved in mutism. Such clarification is critical given; (1) the relatively high incidence of mutism in 25–29% patients, (2) residual speech deficits in as many as 30–38% patients [23], and (3) increasing survival rate for children with posterior fossa tumors, particularly when complete resection has been achieved [9].

The delayed onset of mutism (typically 1–3 days postoperatively) and the potential for reversibility are both evidence that mutism is not a consequence of direct operative injury [7]. The time of symptom onset best corresponds with both the time of maximum postoperative edema and/or the time when axonal injury (from axonal, cytoskeleton, or organelle damage) would be likely to be clinically evident. The delayed onset has provided neurosurgeons only partial relief by providing support that mutism is not a direct consequence of surgery, but may nevertheless represent an indirect and potentially preventable cause from surgical intervention. Potential reversibility of symptoms may be expected with either postoperative edema or axonal damage. The slow, gradual return of function, however, favors the latter as a cause for the majority of mutism patients. Most patients with postoperative mutism patients demonstrate a slow, yet complete recovery of speech. Functional recovery remains incomplete; however, for one third of the patients even years after the surgery [23], presumably a reflection of the greater degree of axonal disruption and neuronal loss seen in this subset of patients.

The results of this study support Pollack's argument [5] that mutism results from injury to the afferent and/or efferent pathway of the dentate nucleus (i.e., dentatothalamocortical tract). We propose that the link between preoperative brainstem compression and postoperative cerebellar mutism may implicate white matter damage as the predominant cause of this relatively common surgical complication. We favor white matter damage associated with the forces from tumor resection and await additional data from DTI study in this population.

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