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Assessment of Severity of Cerebellar Mutism in 4th Ventricular Tumors in Pediatric Age Group

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ABSTRACT

Background: Cerebellar mutism syndrome (CMS) is a neurological condition following surgery that generally manifests 1-2 days after removal of a midline posterior fossa tumor.

Aim of work: To evaluate and compare the severity and occurrence of CMS in pediatric patients with 4th-ventricular tumors after surgery by two different appraches (telovelar&transvermian) and two different positions (sitting&prone) and to assess predisposing factors for the severity and occurrence of CMS.

Methods: This prospective study has been conducted on forty-four pediatric patients with age range of 1-12 years old. Patients were subdivided into two groups and prepared for surgery, 22 patients on sitting position where half of the patients were operated by transvermian approach, which the other half by telovelar approach. The other 22 patients were operating on prone position and subdivided equally to be operated by the two approaches.

Results: Results revealed that 71.4% of patients with CMS were operated on in prone position, while 28.6% of on sitting position had mutism. An insignificant variation has been observed among both groups. Mutism was detected in 57.1% patients with transvermian and telovelar approaches. Out of 25 patients with epidymomas, 20% developed mutism, 20% with medulloblastoma suffered from CMS. The severity of cerebellar mutism was categorized into two major groups: complete profound (neurological and speech abnormalities) and partial (emotional lability).

Conclusion: The sitting position offers advantages like clean surgical field, good access to tumors, minimal retraction, and reduced edema in cerebellar tissue. Prone position offers bloody field, reduced retraction, and increased incidence of CMS.

Keywords: *CMS; Pediatric; Tumor*

1. INTRODUCTION

Fourth ventricular tumors are brain tumors that occur in the fourth ventricle in the posterior fossa between the brainstem and the cerebellum (pons and medulla) most often it obstructs the flow of cerebrospinal fluid (CSF), leading to various complications (1,2).

Most likely the management of these tumors involves surgery and depending on the tumor type and location in most cases chemotherapy or radiation are used (1,3).

Cerebellar Mutism Syndrome (CMS) is a postoperative neurological condition that often arises after the surgical removal of tumors in the posterior fossa, particularly in children. It is mainly characterized by mutism (sudden onset of speech loss), emotional lability, ataxia, hypotonia, and neurocognitive impairments (4-6).

The prevalence of CMS in adults is rare and less studied, however in children it affects approximately 25-30% of pediatric patients under 12 years of age with posterior fossa tumor resections (5,7).

The assessing of CMS severity in children with fourth ventricular tumors involves clinical evaluation and imaging studies. Improvements in imaging and surgical methodologies, together with evidence demonstrating the significance of macroradical resection for the survival of pediatric patients with ependymoma and medulloblastoma, have enabled surgeons to undertake larger resections than previously (8).

The most common surgical approaches are transvermian and telovelar in which as well patient positioning during surgery plays a crucial role in outcomes. The transvermian approach involves splitting the cerebellar vermis to access the tumor. In contrast, the telovelar approach avoids splitting the vermis by accessing the fourth ventricle through the cerebellomedullary fissure (2,9,10).

The primary purpose of this study is to compare the severity and occurrence of cerebellar mutism and assess predisposing factors for the severity and occurrence of CMS in prediatric patients with two different approaches and two different positions during the surgery.

1. Subjects and Methods

This prospective study was conducted in accordance with the Declaration of Helsinki (as revised in 2013) and was approved by the institutional review board of faculty of medicine, Cairo University Research Ethics committee, CMDRF132701; date: January 21, 2019. Informed consent was obtained from all individuals' parents or legal guardians as participants are under 18 years old.

Study design

This research was conducted between June 2018 and June 2020. A total number of forty-four pediatric patients with fourth ventricular tumors were enrolled in the study. The study was conducted at Cairo University hospitals, Abu El-Reesh Children's Hospital, Egypt.

Inclusion criteria: Pediatric patients with age ranged between 1 and 12 years old having 4th ventricular tumors, cases subjected to preoperative C.S.F. diversion (shunt or ETV) or non-hydrocephalic cases at presentation, and non-metastatic cases.

Exclusion criteria: Patients with preoperative neurobehavioral abnormalities, speech abnormalities, and manifestations of the three arms of mutism (ataxia, dysphasia, and emotional lability), cerebellar or CPA tumors, and previously operated cases were excluded.

For all patients a full historical and clinical assessment were performed including a general examination; neurological examination as well as laboratory investigations and radiological investigations. Figure 1 shows a workflow diagram for the present study.

Surgical management

Anesthetic considerations during the surgical management of obstructive hydrocephalus included monitoring for air embolism using capnography to estimate PCO_2. Hemodynamic stability was prioritized, especially in young children, with prompt management of blood loss. Standard practices involved invasive arterial pressure and central venous monitoring, placement of urinary catheters, administration of perioperative antibiotics, and the use of dexamethasone. Mannitol was not routinely utilized. Blood preparedness was emphasized with the availability of two to three units of packed red blood cells (PRBCs) preoperatively for each patient. In terms of hydrocephalus management, all 44 patients had obstructive hydrocephalus identified on preoperative imaging, and cerebrospinal fluid (CSF) diversion procedures were performed to effectively manage the condition. Surgical steps involved the careful positioning of patients either prone or sitting, followed by shaving and marking the incision line from the external occipital protuberance to C2. Hemostasis was achieved using local anesthetic and diluted epinephrine, along with monopolar cauterization to control bleeding. An initial Y-shaped fascial incision was made to expose the occipital bone and C1 posterior arch, with control of emissary vein bleeding through the application of bone wax. The creation of a bone flap included drilling burr holes on either side of the occipital plate and using a high-speed craniotome to elevate the flap. Dural management was performed with a Y-shaped dural incision, ensuring careful avoidance of major sinuses. Various techniques for managing bleeding included the use of surgical clips, bipolar coagulation, or Vicryl™ 4/0 sutures. In most cases, the cisterna magna was opened to drain CSF and alleviate pressure in the posterior fossa. To prevent venous air embolism, copious saline irrigation and bone wax were used, complemented by early detection and management strategies.

Tumor Excision: In 22 patients with ventricular tumors, the telovelar approach was used, which involved dissection of the arachnoid membrane and division of filamentous arachnoidal attachment bilaterally along the tonsillo-medullary and uvulo-tonsillar fissures. This allowed for the separation and elevation of cerebellar tonsils and exposure of the tela choroidea. The tela choridea was then incised, allowing for total tumor excision. In extensive ventricular tumors, central debulking has been carried out, subsequently followed by the incision of the attenuated inferior medullary velum and tela choroidea bilaterally, utilizing multidirectional uvular retraction. The 1ry goal of surgery was total tumor excision, leaving only a thin sheet in cases with brainstem invasion. At the end of the operation, the craniotomy flap was replaced to prevent postoperative headaches. **Postoperative Assessment:** Postoperatively, patients were assessed for conscious level and posterior fossa syndromes, cranial nerve deficits, long tract affection, and CSF collection or leak. Non-contrast CT brain scans were performed within 24 hours to exclude hematomas and pneumocephalus, while MRI brain scans were done within 48 hours to assess resection extent. Pathological examination of the excisional biopsy material was performed. Adjuvant therapy was

addressed based on patient risk and tumor grade. **Outcome:** The outcome for the patients was assessed and estimated on the following occasions: On admission, immediately following surgery, on discharge, and every three weeks till the end of six months postoperatively. Patients were categorized as having a good outcome if they have only emotional lability, a fair outcome if they have dysphasia alone or with emotional lability, and a worse outcome if they have neurological affection (ataxia, apraxia, or cranial nerve disorders). **Treatment:** The extent of resection has been detected by following surgery MRI results and the surgeon's opinion, with adjuvant radio and/or chemotherapy given to patients except those with pilocytic astrocytoma GI.

Data Statistical Analysis

Data was organized and analyzed using statistical package of social science (SPSS 17.0) on windows 8.1. Data were subjected to the Kolmogorov-Smirnov test to determine the distribution and method of analysis. Chi-square test was used for categorical variables. Student t-test was used for quantitative parametric data. Kolmogorov-Smirnov test was used for non-parametric data. Mann-Whitney U test was used to compare outcomes between two independent groups. P-value≤0.05 was considered for significance.

2. RESULTS

Demographic and clinical assessment

According to the demographic data, t**he patient's age ranged between** 2 and 12 years old.

The number of females was 11 which is considered 50% of the patients while the number of males was 11 (50%). There was no statistically significant difference as regards to the gender with p-value>0.05 (Table 1).

All patients had undergone surgery for excision of their lesions through midline suboccipital craniotomy and evaluation of the incidence, severity and outcome of cerebellar mutism. Individuals were subdivided equally into two groups to be operated and approached at sitting and prone positions:

Sitting Position (N=22)

Prone Position (N=22)

Each group were operated by both approches to be assessed and compared accordingly:

Transvermian approach at sitting position (N=11)

Telovelar way at sitting position (N=11)

Transvermian approach at prone position (N=11)

Telovelar way at prone position (N=11)

Table 2 shows the presenting symptoms and signs of the pre-operation findings. Results revealed that the main presenting symptoms detected include headache, vomiting, ataxia, DCL, diplopia, Gait disturbance and papilledema. Some patients had combination of symptoms where 2(4.5%) of the patients had headache and vomiting preoperatively , 3(6.8%) had ataxia and 2(4.5%) had diplopia and headache. Papilledema was the constant sign in all patients with cerebellar mutism (Table 2).

Based on the pathologogical findings, 25 (56.8%) had ependymomas where 14(31.8%) of the patients were diagnosed as grade 1, 5(11.4%) were grade 2 and 6(13.6%) were grade 3. Medulloblastoma was detected 10(22.7%) and 9(20.5%) pilocytic astrocytoma.

Multivariate analysis of prognostic factors affecting the severity of mutism

We reported that all patients had obstructive hydrocephalus in which VP shunts were inserted. Gross total tumor resection could be safely achieved in 35(79.5%) of the patients whome tumors were not found invading/ attached to floor of brain stem. The rest of the patients 9(20.5%) were subjected to subtotal resection due to brain stem involvement to avoid deleterious effects of brain stem injury.

Our findings showed that there were composite factors affecting the incidence and the severity of mutism among the patients group such as gender; position of the operation (sitting or prone); operation approach (Transvermian or Telovelar); pathology (ependymoma, medulloblastoma or pilocytic astrocytoma) and pre-operative symptoms (increased ICP, Cerebellar affection or Brain stem affection& Cranial nerve deficits). Based on these factors the severity of the patients were recorded and patients were categorized according into two groups:

Complete profound with neurological and speech abnormalities (N=2)

Partial with emotional lability (N=5)

Pe-operative findings and outcomes

Symptoms of increased the intracranial pressure (headache, vomiting) were reported for two weeks preoperatively in four

cases of mutism,symptoms of cerebellar affection were reported in two cases for one week and symptoms of brain stem affection, cranial nerve dificits were reported in one patients for two weeks. So, cerebellar mutism was obvious in patients presenting with increase of intracranial pressure in contrast to patients presenting with cerebellar or brainstem affection.Incidence of mutism was higher in patients with long period of pre-operative symptoms.

In addition, we evaluated the incidence of cerebellar mutism among individuals with mutism. Crying, irritability, ataxia as well as dysphasia had been reported (Table 3).

Table 4 shows a detailed analysis of the prognostic factors that affect the incidence of mutism.

After evaluating patients regarding different positioning and approaches, results revealed that 5(71.4%) operated the prone position and had cerebellar mutism. While 2(28.6%) of the sitting group had mutism with insignificant statistical variance among the 2 groups. There was a significant difference between the two groups as regards to the approach with p=0.014 (Table 5).

Regarding the approach variable, 4(57.1%) had mutism of those operated via the transversal approach, and 3(42.9%) operated via the telovelar approach, with insignificant statistical difference between both groups with p>0.05 (Table 5).

The outcome of the patients was assessed and estimated on the subsequent occasions: on admission, immediately following surgery, on discharge, as well as every three weeks till the end of six months postoperatively.

Fair, good and worse were the evaluation criteria for the operations inwhich a fair evaluation if patients had only dysphasia or with emotional lability; good evaluation if they had only emotional lability and worse if they had neurological affection (ataxia, apraxia, and cranial nerve disabilities). Accordingly, 5 patients had good outcomes and 2 were with worse evaluation. However, all patients improved during the period of follow-up (six months) except for one patient who left with a major deficit which is dysphasia.

Figure 2 shows pre and post operative CT brain for random selections of patients with cerebellar mutism.

Tables

Table 1: Demographic and clinical characteristics for studied group

Parameters	**Cerebellar Mutism patients (N=44)**	**p-value**
Age (years)	7.44±2.98	-
Gender		
Female	22 (50%)	1.0a
Male	22 (50%)	
Pathology		
Ependymoma	25 (56.8%)	>0.05
Grade 1	14 (31.8%)	
Grade 2	5 (11.4%)	
Grade 3	6 (13.6%)	
Medulloblastoma	10 (22.7%)	
Pilocytic astrocytoma	9 (20.5%)	

Age is shown as mean ±SD. Gender and Pathology are presented by n (%) p-value a Chi-squared test. * Significant (p≤0.05)

Table 2: Presenting Symptoms and Signs for Cerebellar Mutism patients

Parameters	**Cerebellar Mutism patients**	
	N	**%**
Headache	10	22.7%

Vomiting	15	35%
DCL	4	9%
Diplopia	5	11.3%
Gait disturbance	17	38.6%
Papilledema	35	80.2%

Table 3: Analysis of Incidence of cerebellar mutism patients

Parameters	**Cerebellar Mutism patients (N=7)**	
	N	**%**
Crying + Irritability	5	11.4%
Ataxia	1	2.3%
Ataxia + Dysphasia + Crying + irritability	1	2.3%

Table 4: Multivariate analysis of prognostic factors that affect the incidence of mutism.

Parameters	**Cerebellar Mutism patients N(%)**		**p-value**
	Positive	**Negative**	
Gender			
Female	5 (71.4%)	17 (45.9%)	0.412
Male	2 (28.6%)	20 (54.1%)	
Position			
Prone	5 (71.4%)	17 (45.9%)	0.412
Sitting	2 (28.6%)	20 (54.1%)	
Approach			
Telovelar	3 (42.9%)	19 (51.4%)	1.0
Transvermian	4 (57.1%)	18 (48.6%)	
Pathology			
Ependymoma	5 (71.4%)	20 (54.1%)	0.461
Medulloblastoma	2 (28.6%)	8 (21.6%)	
Pilocytic astrocytoma	0	9 (24.3%)	
Extent of resection			
Gross total resection (GTR)	4 (57.1%)	31 (83.8%)	0.11
Subtotal resection (STR)	3 (42.9%)	6 (16.2%)	

Data presented by n (%) p-value a Chi-squared test. * Significant ($p \leq 0.05$)

Table 5: Variables affecting the severity of cerebellar mutism patients

Parameters	Severity of Cerebellar Mutism patients N=7		p-value
	Profound N=2	Partial N=5	
Gender			
Female	1 (50%)	1 (20%)	0.327
Male	1 (50%)	4 (80%)	
Position			
Prone	2 (100%)	0	**0.014***
Sitting	0	5 (100%)	
Approach			
Telovelar	1 (50%)	2 (40%)	0.82
Transvermian	1 (50%)	3 (60%)	
Pathology			
Ependymoma	1 (50%)	4 (80%)	0.46
Medulloblastoma	1 (50%)	1 (20%)	
Pilocytic astrocytoma	0	0	
Pre-operative symptoms			
Increased ICP	1 (50%)	3 (60%)	1.0
Cerebellar affection	1 (50%)	1 (20%)	
Brain stem affection&Cranial nerve deficits	0	1 (20%)	
Pre-operative symptoms	0	0	
Extent of resection			
Gross total resection (GTR)	1 (50%)	3 (60%)	0.82
Subtotal resection (STR)	1 (50%)	2 (40%)	

Data presented by n (%) p-value a Chi-squared test.For significance Mann-Whitney Test is used at significant ($p \leq 0.05$)

3. DISCUSSION

Tumors of the the 4th ventricle represent almost 1-5% of all intracranial lesions. According to the standards, the treatment of the 4th ventricle tumor is the microsurgical removal however neurosurgeons may face challenges during the surgery. There are several surgical approaches for the removal of tumor including telovelar approach, unilateral approach, bilateral approach, shunting procedures intraop and others (11-13).

In the present study, pediatric patients with the 4th ventricle tumor were subdivided into two equal groups operated at sitting and prone positions to detect the mutism incidences. The two groups were subjected into two approaches, the telovelar approach and transvemian technique by which the tumor has been removal surgically. Generally, for all patients no problems regarding the tumor's size or its position in the superior part of the ventricle were reported. Most tumors have been completely resected.

Cerebellar mutism incidences were analyzed among all patients. Predicting the prognosis for an individual case is difficult, and the recovery trajectory is extremely varied. Of the studied group, some of the patients recovered completely, while others had a long-term sequela such as ataxia, dysarthria, diminished IQ, and persistent psychosocial problems.

In the present study the main presenting symptoms detected include headache, vomiting, ataxia, DCL, diplopia, Gait disturbance and papilledema.

Based on the pathologogical findings, results revealed that ependymomas, Medulloblastoma and pilocytic astrocytoma were reported. Our findings showed that the risk of CM was higher among Epedymoma patients.

Agreeing to our findings, several studies reported that incidence of CM was higher among medulloblastoma patients. In addition, researches showed that risk factors recognized were location of tumor in the vermis, medulloblastoma, and tumor invading the brainstem. Factors that were not associated with cerebellar mutism: tumor size, gender, and following surgery, central nervous system aseptic meningitis or infection. Factors that were not associated with cerebellar mutism: tumor size, gender, and following surgery, central nervous system aseptic meningitis or infection (5,14,15).

Disagreeing to our findings, a study reported that ependymoma exhibited a statistically significant superior progression-free survival compared to medulloblastoma and pilocytic astrocytomas, which had the worse prognosis (16).

Among the studied patients, gross total tumor resection was safely achieved in the majority of the patients and the rest were subjected to subtotal resection due to brain stem involvement to avoid deleterious effects of brain stem injury. Regarding surgical approach, CMS was reported in 3(42.9%) patients of the telovelar group, and 4(57.1%) patients were operated on through the transvermian approach.

Our findings showed that there were composite factors affecting the incidence and the severity of mutism among the patients group such as gender; position of the operation; operation approach; pathology and pre-operative symptoms. As for the severity of mutism, 5 patients were classified into partial with emotional lability and 2 were complete profound with neurological and speech abnormalities.

Agreeing to the classification of severity we indicated, a study showed that among 450 children, 107 individuals had CM where according to the symptoms intensity patients were classified into mild, moderate and severe patients. Mutism and ataxia were the features most frequently judged as severe (17).

While regarding the symptoms, in the present study it has been recorded that symptoms of increased the intracranial pressure including headache and vomiting were reported for two weeks preoperatively in four cases of mutism and symptoms of cerebellar affection were reported in two other cases for one week and symptoms of brain stem affection, in addition cranial nerve dificits were reported in one patients for two weeks.

It can be concluded that cerebellar mutism incideces was noticeable in those with increase of intracranial pressure in contrast to patients presenting with cerebellar or brainstem affection.

Our research indicated that the telovelar method allowed enhanced and broader access to the tumor within the ventricle, allowing for early observation of the ventricular floor.

Our findings showed that mutism typically occurs twelve to 96 hours following operation, with speech regained within a few weeks or months. In our research, cerebellar mutism syndrome occurred 48–96 h following the operation, and 7 cases had been recovered. Recovery was associated with residual dysarthria in one case.

Cerebellar mutism as a rare neurological condition often clearly observed after the surgery of posterior fossa. It can be detected using difference appraches ubcluding the Telovar approach and the Transvermain method. Those two distinct strategies often utilized in advanced technological systems (4,18).

The Telovar approach emphasizes automation and scalability making it the most suitable technique used to analyze neuroimaging data and identify incidences for mutism. However, most of the literature supports the evidence that the incidence of mutism is higher when the tumor is operated on through the transversal approach that matches with our study. Recently, MBs have been separated into 4 molecular subtypes: WNT, SHH, type C/3, and type D/4 (19-21).

The prone and sitting positions provide adequate access to midline tissues, precautions must be taken to prevent abdominal compression in the prone position to reduce surgical hemorrhage. The seated position enhances surgical access to the posterior fossa by promoting gravity-assisted drainage of blood and cerebrospinal fluid, hence reducing intracranial pressure. It enhances surgical orientation, facilitates access to midline structures, and reduces the amount of surgical retraction required to reach deeper structures (22).

To the best of our knoweledge, there is a lack literature addressing all variables affecting the incidence of mutism composite together putting in consideration the position and the approach as well. Thus overall, the choice of approach and position depends on various factors like tumor characteristics, surgeon expertise, and the patient's general condition. While the telovelar approach is gaining popularity for minimizing complications, both methods remain viable, with no definitive evidence favoring one over the other in all cases. Future studies could explore the combined influence of surgical approach and position on outcomes more comprehensively.

4. CONCLUSION

The sitting position offers potential advantages in surgery but it has few complications like venous air embolism, which can be fixed intraoperatively with saline irrigation. It also consumes time to adjust the head up and exhausts the surgeon. However, the sitting position provides a clean surgical field and good access to the tumor, allowing for radical resection. It also offers minimal retraction, reducing edema in cerebellar tissue and nuclei, especially dentate nuclei, and achieving the integrity of the dentato-thalamocortical pathway. This decreases the incidence and severity of cerebellar mutism. Venous air embolism is a fatal complication that can be fixed with copious saline irrigation and bone wax at the embolism site. Older surgeons may face issues with the sitting position, as it exhausts them and makes them easily fatigable. On the other hand, the prone position creates a bloody surgical field, restricting initial visibility of the tumor interface and the floor of the fourth ventricle. A broad incision of the cerebellomedullary fissure and careful retraction of the tonsils via the telovelar technique mitigate the possibility of cerebellar mutism and other significant cerebellar dysfunctions.

5. FIGURES LEGENDS

Figure 1: A workflow diagram for the present study.

Figure 2: Pre and post operative CT brain for random selections of patients with cerebellar mutism: (a) Case 1: M (4yrs) , vomiting for three days prior to admission. Obstructive hydrocephalus with placement of a VP shunt. Transvermian approach at prone position. Developed ataxia, dysphasia, crying, and irritability two days post-operatively. Histopathological type was classic medulloblastoma (WHO grade IV). The patient received adjuvant radiation therapy and chemotherapy. He had a follow-up for 6 months, and the patient improved through this period except for dysphasia. (b) Case 2: M (3yrs), ataxia for two weeks prior to admission. Obstructive hydrocephalus with placement of a VP shunt. Telovelar approach at prone position. Developed ataxia one day post-operatively. Histopathological type was ependymoma (WHO grade II). The patient received adjuvant radiation therapy and chemotherapy. He had a follow-up for 6 months, and the patient had complete recovery.

6. ETHICS APPROVAL AND CONSENT TO PARTICIPATE

The study was reviewed and approved by the institutional review board of faculty of medicine, Cairo University Research Ethics committee, CMDRF132701; date: January 21, 2019.

A written informed was obtained from all individuals' parents or legal guardians as participants are under 18 years old.

7. CONSENT FOR PUBLICATION

Not applicable.

8. AVAILABILITY OF DATA AND MATERIALS

The data that support the findings are available upon reasonable request from the corresponding author, Amr Hashad [email: amr.hashad@hotmail.com].

9. FUNDING

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