Cerebellar mutism

A review

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Mutism of cerebellar origin is a well-described clinical entity that complicates operations for posterior fossa tumors, especially in children. This review focuses on the current understanding of principal pathophysiological aspects and risk factors, epidemiology, clinical characteristics, treatment strategies, and outcome considerations. The PubMed database was searched using the term cerebellar mutism and relevant definitions to identify publications in the English-language literature. Pertinent publications were selected from the reference lists of the previously identified articles. Over the last few years an increasing number of prospective studies and reviews have provided valuable information regarding the cerebellar mutism syndrome. Importantly, the clarification of principal terminology that surrounds the wide clinical spectrum of the syndrome results in more focused research and more effective identification of this entity. In children who undergo surgery for medulloblastoma the incidence of cerebellar mutism syndrome was reported to be 24%, and significant risk factors so far are brainstem involvement and midline location of the tumor. The dentate-thalamo-cortical tracts and lesions that affect their integrity are considered significant pathophysiological issues, especially the tract that originates in the right cerebellar hemisphere. Moderate and severe forms of the cerebellar mutism syndrome are the most frequent types during the initial presentation, and the overall neurocognitive outcome is not as favorable as thought in the earlier publications. Advanced neuroimaging techniques could contribute to identification of high-risk patients preoperatively and allow for more effective surgical planning that should focus on maximal tumor resection with minimal risk to important neural structures. Properly designed multicenter trials are needed to provide stronger evidence regarding effective prevention of cerebellar mutism and the best therapeutic approaches for such patients with a combination of pharmacological agents and multidisciplinary speech and behavior augmentation.

KEY WORDS • cerebellum • mutism • children • tumor • posterior fossa surgery • cognitive

THE term cerebellar mutism (CM) is used to describe the lack of speech caused by lesions of the cerebellum, which is not associated with long tract signs, cranial nerve palsies, or alteration of consciousness. It usually appears as a consequence of posterior fossa surgery in children with cerebellar or fourth ventricle tumors.82,89 Other causes that have been reported are infections,15,19,24,26,72 posterior fossa hematomas (surgically removed31,89 or not60), arteriovenous malformations,33,51,82 a brainstem tumor,82 a pineal gland tumor,23 and traumatic cerebellar injury.15,82 Although this clinical entity is mainly seen in children, there are also reports of CM in adults.12,16,33,82,85

Abbreviations used in this paper: CM = cerebellar mutism; CMS = CM syndrome; DTC = dentato-thalamo-cortical; DTI = diffusion tensor imaging; FA = fractional anisotropy; fcMRI = functional connectivity MRI; MSD = mutism and subsequent dysarthria; PFS = posterior fossa syndrome.

Historical Overview

In 1917, Sir Gordon Holmes studied the disturbances of speech production in World War I soldiers who sustained gunshot wounds to the cerebellum. He observed that lesions in one hemisphere produced speech that was usually slow, drawling, and monotonous but at the same time tended to be staccato and scanning; a few of the patients showed additional behavioral disturbances. On the other hand, when the lesion included the vermis the main characteristics were phonation and articulation abnormalities.45,96 In 1949 Brown included dysarthria when describing cerebellar syndrome,69 while in 1972 Stein was the first to “incidentally” report CM.31 In 1975 Fraioli and Guidetti29 noted complete absence of speech in 2 of 43 patients who underwent bilateral stereotactic dentatolysis for the
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was lower in the past. This fact might have different explanations. First, the incidence seems to be lower in retrospective studies because of a lack of awareness of this syndrome or even because of difficulty in recalling past events. Moreover, there is evidence showing that there might be an actual increase in the incidence. More extensive tumor resection along with better overall outcome in children who undergo posterior fossa tumor resections can increase the rate of CMS. Korah et al. noted that in 2 different periods of time (1990–2000 and 2001–2007) the percentage of gross-total resection or near-total resection among children who underwent medulloblastoma resection was 83% and 93%, respectively, while the incidence of PFS was 17% and 39%, respectively. In addition, all patients with PFS underwent a gross-total resection and there was no radiological evidence of residual tumor.

It is known that CMS mainly appears after posterior fossa tumor resection in children and there are a few case reports of CMS in adults. A profound reason for this is that posterior fossa—and even more so midline—tumors appear more often in children than in adults. However, it seems that pathophysiological mechanisms contribute to the high incidence of CMS in children. The incomplete development of motor speech control and language is the first factor. Additionally, the immaturity and incomplete myelination of the reciprocal links in childhood, connecting the cerebellum to thalamus, sensory areas, motor, and supplementary motor area, makes the children more vulnerable. However, this can be considered an advantage for faster and more efficient redirection and recovery.

Cerebellum and Speech

In 1992 Turkstra and Bayles assumed that there are 5 stages in the production of speech and language: 1) arousal (ascending reticular system); 2) affect and drive (prefrontal and limbic areas); 3) cognition (dominant hemisphere speech areas); 4) initiation, planning, and coordination (Broca’s region, the supplemental motor area, the basal ganglia, the thalamus, and the cerebellum); and 5) execution (brainstem and cranial nerve nuclei). Studies in monkeys have shown that there is a direct neuronal connection between Brodmann’s area 46 (prefrontal area, involved in spatial working memory and planning) and the dentate nuclei, while major reciprocal neural pathways between the cerebellum and frontal areas of the language-dominant hemisphere, including Broca’s area and the supplementary motor area, have been discovered in humans as well. Today it is strongly believed that different fibers from the dentate nuclei leave the cerebellum through the superior cerebellar peduncle, decussate in the mesencephalic tegmentum, and synapse in the ventral lateral and ventral anterior nuclei of the thalamus. The corresponding postsynaptic neurons project to widespread cortical areas, including the primary motor, premotor, and prefrontal cortices (Fig. 1).
seems to contribute in sequential memory and language processing, whereas the left is more important for spatial and visual sequential memory.81 Recent advances in neuroimaging have allowed a further exploration of the cerebellum’s contribution to cognition and higher cortical functions. Traditional transneural tracing techniques (using virus strains) showed polysynaptic connections of cerebral motor areas and the anterior and posterior lobe of the cerebellum in monkeys.49 Task-based functional MRI confirmed such somatomotor representations within the cerebellum in humans.37 High and ultrahigh magnetic fields (> 3 T) are used to map brain systems in the human by detecting intrinsic, low-frequency functional correlations.41,42 These correlations were found to be anatomically selective, and the new tool was termed functional connectivity MRI (fcMRI).102 Using fcMRI, Krienen and Buckner54 discovered 4 segregated frontocerebellar circuits mainly between prefrontal regions and a large portion of the posterior cerebellar hemispheres. Similarly, Strick et al.95 found that closed-loop circuits represent the major architectural unit of cerebrocerebellar interactions and allow the cerebellum to influence the control of movement and cognition. Resting-state fcMRI was used by Buckner et al.7 to study 1000 young adults and establish an organization map of the cerebellum. It was found that the cerebellum possesses 3 distinct maps of the cerebral cortex (including somatomotor, premotor, and association cortices): a homotopic one that begins in the anterior lobe somatomotor representation and ends near Crus I/II, a mirror-image secondary map that begins in Crus I/II and ends with the second somatomotor representation near the paramedian lobule (HVIII), and finally a provisional map at the farthest extent of the posterior lobe. No representation was found only for the primary visual and auditory cortices.

Pathophysiology

The pathophysiology of CM has not been entirely established. There are many theories considering the responsible factors, but none of them provides an entirely satisfactory explanation.

The functional hypothesis supports that CM is a kind of negativism on the part of the child who feels betrayed by his parents and doctors (form of “elective mutism”).96 The fact that many patients recover as soon as they get home, in addition to the absence of cranial nerve deficits and the integrity of supratentorial speech centers, supports this theory. Moreover, most of the patients seem to understand spoken language, while some manage to communicate using gestures. However, it cannot be explained why mutism appears almost exclusively after posterior fossa surgery. The observance that in almost every case patients suffer from dysarthria during the recovery phase supports that there is as organic basis of this syndrome. It is widely accepted that stress and a long hospital stay are contributing factors for CMS.33 Damage to a specific anatomical substrate has been proposed as a pathogenetic factor. The dentate nucleus
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was the first region that was hypothesized to be involved. Fraioli and Guidetti\(^\text{26}\) reported on 2 patients with complete absence of speech after bilateral stereotactic lesioning of the dentate nuclei. Later on many authors proposed that bilateral damage of the dentate nuclei is a critical factor for CM.\(^\text{2,25,51,57,69}\) Asamoto et al.\(^\text{2}\) assumed that postoperative edema led to disturbance of the venous circulation, which was responsible for the dysfunction of the dentate nuclei. Dietze and Mickle\(^\text{69}\) observed that injury to the midportion of the cerebellum caused speech disorders and if a dentate lesion coexisted, CMS was present. Ozimek et al.\(^\text{5}0\) noted that a more frequent and more extensive involvement of the dentate nuclei was present in mutistic children, and evident dentate involvement was present in 73.5\% of patients with CM in the study by DiRocco et al.\(^\text{17}\) The authors also noted an even higher rate of dentate nucleus involvement among children with preoperative language impairment (90\% when preoperative language impairment existed vs 65.2\% when it did not exist). Neuroimaging studies have shown bilateral hypodense areas at the level of the dentate nuclei\(^\text{2,5}\) or abnormalities in T2 signal on MRI, within the dentate nuclei, mainly bilaterally.\(^\text{65}\) However, Dailey et al.\(^\text{14}\) reported on 9 patients with CM with no edema or infarction of the dentate nucleus postoperatively; in addition, most of the children with CM were still able to perform other functions that diffuse dentate destruction or swelling would render impossible. Moreover, Morris et al.\(^\text{65}\) suggested that neither unilateral nor bilateral dentate damage was required for CMS to appear.

The role of a lesion in the cerebellar hemisphere in CM has also been discussed. Robertson et al.\(^\text{82}\) noted that bilateral lesion involvement of the cerebellar hemisphere is necessary since CM rarely occurs after resection of tumors involving only one hemisphere. Erşahin et al.\(^\text{25}\) discovered an association of left cerebellar hemisphere hypoperfusion on SPECT scans in patients with CM. Blood flow returned to normal when mutism resolved. Later\(^\text{26}\) Erşahin and colleagues reported on 1 patient with right cerebellar hemisphere hypoperfusion. Sagiuchi et al.\(^\text{83}\) reported a case of CM in a 4-year-old boy with atrophy of both cerebellar hemispheres, predominately the right hemisphere, on MRI and circulatory disturbance in both hemispheres secondary to tumor resection in SPECT scans. Besides SPECT perfusion imaging, an alternative technique called arterial spin-labeling perfusion MRI was used on a girl with postoperative CM and showed bilateral hypoperfusion in the cerebellar hemisphere, thalamus, and frontal lobe. Watanabe et al. suggested that this technique was less invasive and more suitable for pediatric patients.\(^\text{87}\) Ozimek et al.\(^\text{70}\) reported 4 cases of CM with bilateral extension of the tumor into the cerebellar hemispheres. There have also been cases of CM with isolated hemispheric lesions such as contusion\(^\text{64}\) or metastasis.\(^\text{65}\) Neurophysiological studies have shown that the left cerebellar hemisphere is important for the executive functions. Lesions of the cerebellar hemisphere lead to deficits in complex mental activities.\(^\text{61}\) In addition, Ackermann et al.\(^\text{1}\) proposed that there is tight functional connectivity between the language-dominant frontal lobe and the contralateral cerebellar hemisphere, having a significant role in supporting motor speech function and in the temporal organization of a prearticular verbal code ("inner speech") as well. Riva and Giorgi\(^\text{61}\) found that children with right cerebellar tumors presented with disturbances of auditory sequential memory and language processing, whereas those with left cerebellar tumors showed deficits on tests of spatial and visual sequential memory. Similarly, linguistic processing was found to be impaired in patients with right cerebellar infarction,\(^\text{64}\) manifested as agrammatism in one case,\(^\text{68}\) and impaired error detection and practice-related learning of a verb-for-noun generation task in another.\(^\text{68}\) In a recent case report\(^\text{69}\) an adult developed PFS after a right cerebellar hemisphere stroke; SPECT imaging that followed demonstrated bilateral cerebroperfusion deficits suggesting a phenomenon of "transcallosal" or "transhemispheric diaschisis." Others have demonstrated that bilateral cerebellar involvement especially of the dentate nuclei is crucial for the development of cerebellar mutism.\(^\text{57}\) However, most authors believe that cerebellar hemisphere lesions do not play a significant role in CM. Van Dongen et al.\(^\text{103}\) believe that a lesion isolated in the cerebellar hemisphere is not able to cause CM. Pollack et al.\(^\text{77}\) reported that among patients with CM, the postoperative images showed no evidence of discrete areas of infarction, hypoperfusion, or decreased metabolic activity within the cerebellar hemisphere. Pollack later noted that CM was absent in cases of large cerebellar hemisphere tumors, resected without splitting the vermis,\(^\text{76}\) Robertson et al.\(^\text{82}\) reported a negative correlation between cerebellar hemisphere lesions and CM; they showed that the risk of developing CM was 6.7 times higher in one study\(^\text{53}\) and 8.2 in another one\(^\text{44}\) if tumor was located in the cerebellar midline versus the lateral cerebellar hemisphere.

The majority of case reports and studies support that CM can occur after the resection of a midline tumor and, as a rule, the vermis is involved.\(^\text{11,25,69,83}\) Dailey et al.\(^\text{14}\) were the first to officially suggest that the splitting of the vermis, especially the inferior part, is responsible for the development of CM and that, to avoid oropharyngeal apraxia, it must be preserved. Different studies have come to different conclusions since then. Incision of the vermis has been associated with a low performance IQ\(^\text{96}\) and neurophysiological and psychiatric problems.\(^\text{53}\) Riva and Giorgi\(^\text{61}\) supported that vermic lesions led to 2 different profiles: postsurgical CM, which evolved into speech disorders or language disturbances similar to agrammatism, and behavioral disturbances (ranging from irritability to autistic behavior) supporting the role of vermis as part of a "cerebellar limbic system."\(^\text{74}\) Sagiuchi et al.\(^\text{83}\) reported a case of CM that was associated with atrophy of the vermis on MRI and decreased blood flow in the same region on the SPECT scan, and proposed that CM resulted from damage to the vermis with or without a bilateral cerebellar hemisphere lesion. In addition, Frassanito et al.\(^\text{31}\) reported a case of CM after spontaneous intratumoral bleeding involving the upper cerebellar vermis and believed that the localization of bleeding provided confirmation of the role played by the upper vermis in speech control. Puget et al.\(^\text{77}\) found that persistent clinical cerebellar signs or fine motor dexterity impairment was significantly related
to the extent of injury (pre- or postsurgical) to both the inferior vermis and the dentate nuclei. Animal models were also used, and a recent study found that juvenile rats that had vermis splitting operations showed deficient social behavior and vocalization postoperatively, compared with sham-lesioned rats and healthy controls. However, other data showed that damage to the vermis is not as important as originally thought. Robertson et al. found no correlation between the vermian location of tumor and the development of CMS, although there was a negative association between cerebellar hemispheric lesions and CMS. Moreover, the authors noticed that the majority of children with posterior fossa tumors undergo radical resection through the vermis and do not develop CMS. Thus, the vermis and surgical approach cannot be the only determinants. Pollack et al. hypothesized that if the vermis were responsible for CMS then the condition would be more common and more persistent. The delayed onset of CMS after posterior fossa surgery is also a negative clue of the role of vermis in CMS.

One of the most famous theories about the pathophysiology of CMS involves the dentato-thalamo-cortical (DTC) tract. This pathway projects to and from the dentate nucleus of the cerebellum on either site, travels through the superior cerebellar peduncle, crosses the midline to the opposite side in the decussation of the superior cerebellar peduncle, continues through the brainstem to the contralateral ventrolateral nucleus of thalamus and then to the contralateral motor cerebral cortex (premotor and supplementary motor cortices). Mutism can occur after lesion anywhere along this tract, although after posterior fossa surgery, is more likely to involve proximal parts of the tract (dentate nucleus, cerebellar peduncles, and/or brainstem connections). Miller et al. using another perfusion imaging technique (dynamic susceptibility-weighted contrast-enhanced perfusion MRI), found that there is a strong (potentially predictive) relationship between bilateral damage to proximal efferent cerebellar pathways and the development of PFS. This finding was also supported by Kusano et al. and Morris et al., the first who used diffuse-tensor imaging (DTI). Authors of a recent study from Berlin also used DTI in a 3-T MRI suite and showed that volumes of frontocerebellar fibers had significantly diminished fractional anisotropy (FA) values in pediatric patients with CMS after surgery compared with patients without CMS and healthy peers. Diminished fiber signal intensities were localized at the level of the superior cerebellar peduncle and the midline cerebellar structures. Similarly, a case report of an adult who suffered from CMS after a left pontine infarction and was investigated using DTI exhibited asymmetry in FA values in the superior cerebellar peduncle. Law et al. used DTI to investigate the integrity of the cerebello-thalamic-cerebral pathways bilaterally in children who presented with CMS after posterior fossa tumor surgery, and the authors found that right cerebellar white matter within the cerebello-thalamic-cerebral pathway was significantly compromised in children with CMS compared with children without CMS and healthy children. They suggested that disruption of the connection between the right cerebellum and the left frontal cortex could contribute to the speech and language problems in children with CMS. As potential predictors, they distinguished left-handedness, medulloblastoma tumor type, and large tumor size. Diffusion-tensor imaging could be useful as a screening tool of high-risk patients preoperatively and further randomized large trials could focus on that. A high incidence of brainstem compression preoperatively in addition to edema in brainstem and superior cerebellar peduncle among patients with CMS postoperatively seems to confirm their role in CMS. Di Rocco et al. suggested that dominant-site DTC tract involvement was adequate enough for CMS to appear. Transient dysfunction of the neurons of the A9 to A10 dopaminergic cell group in the mesencephalon, which play a major role in the mesencephalofrontal activating system, has also been proposed as a possible anatomical substrate of CMS. Apart from a pure anatomical lesion along the DTC tract, cerebellocerebral diaschisis seems to be a possible mechanism explaining the pathophysiology of CMS. Diaschisis is traditionally defined as sudden inhibition of function in an area of the brain remote from, but anatomically connected through transsynaptic neural pathways, the site of primary injury. The most common form of diaschisis is crossed cerebellocerebral diaschisis. Multiple studies have supported the theory of cerebellocerebral diaschisis using different imaging techniques that revealed decreased blood flow, metabolic action, and function within supratentorial structures that play a crucial role in speech production, such as the thalami, frontal gyrus, and temporal lobe. In almost every case the abnormal findings returned to normal when mutism resolved.

The anatomical regions mentioned above can be damaged during the operation or later. Retraction during surgery might cause edema postoperatively, disturbing the venous circulation of the adjacent structures. However, the course of CMS outlasts the resolution of edema. Vasospasm plays a similar role. Coagulation of the perforators from the posterior inferior cerebellar artery to the brainstem results in the disturbance of blood supply to the pons. Alterations in neurotransmitter levels and synaptic or transsynaptic degeneration of connecting structures has also been proposed but not yet confirmed. Disturbances in CSF circulation and hydrocephalus as well as postoperative meningitis were considered to play a significant role in CMS, especially hydrocephalus as an exacerbating factor, but this significance has been questioned by many authors.

Risk Factors

Multiple factors have been studied regarding whether they predispose to the occurrence of CMS, and some seem to statistically increase the incidence of this syndrome (Fig. 2). Brainstem involvement seems to be the most important, including preoperative tumor invasion or postoperative edema. Moreover, McMillan et al. supported that brainstem compression could be used as a predictor of postoperative CMS. Some authors believe that midline location predisposes to the occurrence of CMS while others have found no significant difference. Tumor size had been considered as an indepen-
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dent risk factor, but later studies with larger populations showed that it maintains a significance but only in cases of medulloblastomas. Catsman-Berrevoets et al.\textsuperscript{9} reported that each increase in tumor size by 1 cm in the medulloblastoma group resulted in a multiplication of the odds to develop “mutism and subsequent dysarthria” (MSD) by 1.76 while Kotil et al.\textsuperscript{53} reported a multiplication by 1.53 and suggested that medulloblastoma is a risk factor for CM only when the tumor is larger than 5 cm. Küpeli et al.\textsuperscript{55} reported an increase of the odds by 7.2 if medulloblastoma occurred and by 5.7 if the family of the patient had a low socioeconomic level. In a multivariate analysis Korah et al.\textsuperscript{52} found that younger age and absence of radiographic evidence of residual tumor were significant risk factors for CM, while Robertson et al.\textsuperscript{52} found no significant difference regarding the extent of tumor resection. Di Rocco et al.\textsuperscript{17} concluded that preoperative language impairment can be considered as a subclinical state of CMS in some children and can be used as a predictor. By investigating the relationship between pre-surgical and clinical valuable and the incidence of CMS along with DTI, Law et al.\textsuperscript{58} found that left-handedness, medulloblastoma tumor type, and large tumor size were features that distinguished between patients with CMS and patients without CMS. Sex, meningitis, and preoperative hydrocephalus are generally considered as insignificant.\textsuperscript{26,36,82}

\textbf{Surgical Aspects}

The splitting of the vermis has been considered as an important factor for the occurrence of CM as already mentioned. As a result multiple efforts have been made to avoid the splitting or to minimize the extent of the incision. In their study Dailey et al.\textsuperscript{14} observed that postoperative mutism or oropharyngeal apraxia was only seen in children who had a vermian split that included the entire inferior portion of the vermis. Erşahin et al.\textsuperscript{26} reported that both superior and inferior vermic incisions have been associated with postoperative mutism. However, Siffert et al.\textsuperscript{87} reported that despite a change in the institutional practice to the non–vermis splitting technique, cases of PFS continued to emerge; the authors did not mention whether there was a decrease in the incidence of the syndrome. Moreover, Pollack\textsuperscript{76} tried to minimize the length of the vermic incision without eliminating the problem of CM. Thus, he recommended that surgeons make a conscious effort to avoid extensive paravermian manipulation.

In 1997 Kellogg and Piatt\textsuperscript{48} proposed that the cerebellomedullary fissure approach yields exposure comparable to what can be achieved by splitting the vermis and that the approach minimizes the risk of neurological complications, including MSD. The telovelar approach was originally thought to be a promising new technique for posterior cranial tumors. El-Bahy\textsuperscript{23} used this approach to the fourth ventricle in 16 patients, and CMS was not observed in any patient. However, among these patients only 3 harbored medulloblastomas while the remaining patients had low-grade tumors and nontumoral lesions; it is not clear how many of these patients were children.
Considering these facts together, we can assume that in general the risk of CMS in this group was low, and we cannot come to a conclusion whether this approach was beneficial. Rajesh et al.\(^{29}\) considered that to avoid the significant incidence of postoperative apraxia and mutism seen with this approach for large tumors, staged dissection of the uvulotonsillar cleft should be achieved with initial arachnoid release, followed by decompression of the tumor and subsequent complete dissection of the uvulotonsillar cleft. Frassanito and Massimi\(^{30}\) regarded that the telovelar approach cannot provide significant advantages in the prevention of CMS at tumors involving the cerebellar vermis or the brainstem, as both these structures are already damaged by the tumor itself. However, they agreed that it remains an elegant and effective way to reach tumors of the fourth ventricle. Lastly, Hermann et al.\(^{43}\) used a combined transventricular and supracerbellar approach to preserve the cerebellar vermis. No instances of akinetic mutism occurred postoperatively. However, since the semisitting position is required for this approach, there is skepticism with regard to the potential hazards,\(^{29}\) especially in young children and infants. Apart from the approaches, the neurosurgeon’s qualification was studied, and Robertson et al.\(^{82}\) found no difference between patients who underwent surgery performed by pediatric neurosurgeons and those who underwent surgery performed by general neurosurgeons. Centers with increased experience in pediatric neurosurgical service routinely use brain and cranial nerve electrophysiological monitoring, less aggressive retraction, and minimal ultrasonic aspiration during their procedures, although there is no significant evidence to support these precautions.\(^{108}\) A recent nonrandomized clinical study\(^{22}\) compared 60 children who underwent surgery for posterior fossa tumors. Thirty of these children underwent surgery with the aid of with navigated ultrasonography and 30 underwent conventional neurosurgical techniques. In the ultrasonography group only 1 patient with medulloblastoma suffered from CMS (3.3%) while in the conventional neurosurgery group, 6 patients were diagnosed with CMS (20%); 2 of these patients had medulloblastomas. The difference did not reach statistical significance.

**Clinical Presentation**

There are some core characteristics of the clinical presentation of CM. First, mutism in almost every case appears after 1–6 days of normal speech postoperatively (delayed onset). Second, the mutism has a limited duration (transient mutism). The CM usually lasts from a few weeks until 6 months, although there are reports of patients whose mutism lasted much longer. Finally, mutism is followed by severe dysarthria during the recovery phase, which might last even 2 years.\(^{14}\) Recent studies, however, imply that there are long-term, even permanent, cognitive abnormalities other than dysarthria.\(^{73,77}\)

Additional features have been described in the majority of the patients. Motor disorders include ataxia, axial hypotonia,\(^{69,104,109}\) flaccid hemiparesis,\(^{4,30,26}\) and decreased spontaneous movements or hypokinesia.\(^{62,87,109}\) Recovery of gait and coordination usually take longer than speech.\(^{57}\) Oropharyngeal apraxia is another common symptom that accompanies CM. The patients refuse to eat and have a difficulty in swallowing,\(^{10}\) although they have an intact gag response\(^ {44}\) and normal tongue movements on command. Visual disturbances are found in many cases and include persistent eye closure without any oculomotor nerve palsy, horizontal gaze paralysis, and lack of response to visual stimuli.\(^ {69}\) Vision loss without cranial nerve palsy has also been reported.\(^ {83,87}\) Patients with urinary incontinence and loss of bowel control have also been reported.\(^ {77}\) Von Hoff et al.\(^ {106}\) described the presence of ataxia, nystagmus, and dysmetria in patients after posterior fossa surgery as the “cerebellar syndrome.”

The spectrum of neurobehavioral abnormalities seen in CM is wide. Children can be seen lying curled in bed crying whenever asked to speak,\(^ {3,66,67}\) are emotionally labile,\(^ {2,8,70}\) and show either apathy or irritability.\(^ {2,52,65,103}\) Difficulty in eating and loss of bladder and bowel control might also be a form of behavioral disturbance. Behavior returns to normal earlier than speech.\(^ {5}\) A recent review\(^ {56}\) proposed that the clinical features can be explained as mutism itself mediated primarily by supratentorial dysfunction, and clinical findings following mutism are mediated by direct (surgical) injury of cerebellar and brainstem structures.

**Treatment**

There are quite a few suggestions for treatment interventions for CM. Apart from some individual reports, there are no clinical trials indicating possible beneficial options. Shyu et al.\(^ {96}\) reported a case of a 4-year-old boy with CM who was given daily 2.5 mg of zolpidem (a short acting nonbenzodiazepine hypnotic) starting from postoperative Day 21. There was obvious neurological and behavioral improvement, and after 14 days he started using single words and continued to improve steadily. Bromocriptine was used by another team in a 9-year-old girl without the desirable results.\(^ {25}\) Catsman-Berrevoets and et al. hypothesized that the lack of speech may be explained by transient dysfunction of the neurons of the A9 to A10 dopaminergic cell group into the mesencephalon,\(^ {10}\) and the administration of dopamine agonists could reverse this effect. However, neither van Dongen\(^ {103}\) nor Echiverri et al.\(^ {20}\) found significant results when using this kind of medication in patients with CM. Pretreatment with the calcium channel antagonist nimodipine has also been proposed to prevent postoperative vasospasm\(^ {99}\) but still more extensive studies need to take place. Gordon\(^ {43}\) has proposed the use of similar treatment for CM as for the elective type (when no organic causes for CM can be found), especially with drugs such as fluoxetine, bromocriptine, and phenelzine. There is a case report of the favorable results of fluoxetine (a selective serotonin reuptake inhibitor) on a child with CM,\(^ {3}\) but more clinical trials should take place for further information.

One of the most significant parts of the treatment of patients with CM is the counseling of the parents and the patient about the basis of CM, the duration, and the possible long-lasting speech and language deficits when the mutism resolves. Therapy to improve physiological func-
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tioning as well as compensatory strategies to improve intelligibility, and speech naturalness should be included. Thus far, there have been no clinical trials proving the contribution of speech therapy in the improvement of the neurocognitive status of these children.

Outcome

Cerebellar mutism was originally thought to be a benign self-limiting condition. Its short duration is actually part of the definition of CM. However, a significant number of reports have shown that some children are left with mild residual dysarthria, ataxia, or dysmetria after the resolution of mutism. As a result some scientists have tried to evaluate the long-term neurocognitive outcome in these patients. Children with cerebellar damage in general are considered to be at high risk for long-term neurophysiological dysfunction including problems of attention, memory, processing speed, verbal fluency, and behavioral deficits. Studies with children who had suffered CM showed that they had problems in solving novel situations; moderate difficulty in speed of speech, processing, and reasoning; decreased verbal initiation; and significantly poor performance in reading, spelling, math, and working memory. These children also seemed more dysfluent, speaking at a slower speech rate than children without CM. Considered that motor speech deficits persist for a long period of time (> 5 years), and similar findings were made by other authors. Lastly, Robertson et al. tried to analyze the neurological outcome of their patients, and they found that there is a significant relationship among the level of initial severity of the syndrome and the severity of ataxia and language dysfunction and global intellectual handicap after 1 year. It is worth mentioning than in a developing child such persistent symptoms have a lasting impact on global language and cognitive skills.

Conclusions

The clinical entity of cerebellar mutism after posterior fossa tumor surgery is currently well recognized, and significant clinical and research data have highlighted some basic features. An important issue remains the ambiguity regarding the current nomenclature, although some recent reports have provided very useful terminology. Advanced imaging techniques are used to identify possible preoperative risk factors (tumor location, size, type, and extension) and to provide a better understanding of the relationship between important anatomical structures and clinical findings. Selection of the less hazardous surgical approaches could be achieved by detailed study of sophisticated neuroimaging and solid knowledge of the surrounding anatomy. High-risk patients can be recognized, and proper counseling of the caregivers is essential in such cases for the potential sequelae and possible outcome. A variety of treatment options are under investigation, and a promising field of research could be that of early speech and behavioral rehabilitation. It should be emphasized that the overall cognitive outcome of this syndrome is not as favorable as previously thought and that periodical neurocognitive assessments of such patients—especially of younger age, with malignancy, and potentiality for radiation therapy—should be considered.

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The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

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