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REVIEW ARTICLE

Cerebellar mutism syndrome caused by bilateral cerebellar hemorrhage in adults: a case report and review of the literature

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Abstract

Cerebellar mutism syndrome (CMS) is a frequent complication of surgical intervention on posterior fossa in children. It has been only occasionally reported in adults and its features have not been fully characterized. In children and in young adults, medulloblastoma is the main reason for neurosurgery. A single case of postsurgical CMS is presented in an adult patient with a cerebellar hemorrhage and a systematic review of the published individual cases of CMS in adults was done. Literature review of individual cases found 30 patients, 18/30 (60%) males, from 20 to 71 years at diagnosis. All but one case was post-surgical, but in one of the post-surgical cases iatrogenic basilar artery occlusion was proposed as cause for CMS. The causes were: primary tumors of the posterior fossa in 16/22 (72.7%) metastasis in 3/30 (10%), ischemia in 3/30 (10%) cerebellar hemorrhage in 3/30 (10%), and benign lesions in 2/30 (6.7%) patients. 8/30 patients (26.7%) were reported as having persistent or incomplete resolution of CMS within 12 months. CMS is a rare occurrence in adults and spontaneous cerebellar hemorrhage has been reported in 3/30 (10%) adult patients. The generally accepted hypothesis is that CMS results from bilateral damage to the dentate nucleus or the dentate-rubro-thalamic tract, leading to cerebro–cerebellar diaschisis. Several causes might contribute in adults. The prognosis of CMS is slightly worse in adults than in children, but two thirds of cases show a complete resolution within 6 months.

Keywords Cerebellar mutism syndrome · Dural artero-venous fistula · DAVF · Hemorrhage · Adult · Cerebellum

Introduction

Cerebellar mutism syndrome (CMS) is a relatively common complication following surgical resection of posterior fossa tumors in children, occurring in about ~ 1 in 3 children undergoing posterior fossa surgery [1–3], in particular after fourth ventricular or midline cerebellar tumor resection [2, 4, 5]. CMS was first described in 1939 [6]. The main features of CMS are the occurrence of alteration of language production, up to its abolition (mutism) and many accompanying cognitive and emotional complaints in the post-surgical course starting from 24 h after the intervention. In addition, there are several associated cerebellar signs (hypotonia and other cerebellar motor signs, cerebellar cognitive-affective syndrome or CCAS), motor deficits from the involvement of the long pathways, and cranial neuropathies. The mean duration in children is 6 months, but most cases with permanent deficit have been reported [7]. In particular, most studies considered mutism as the main solved clinical manifestation, because recovery from mutism occurs in almost all cases within 6 months. The other deficits in language, speech, and communication and some motor issues were reported as improving but not disappearing in most patients [7]. The main hypothesis about its pathogenesis is the damage of the

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proximal efferent cerebellar pathway, including the dentate nucleus, the superior cerebellar peduncle, and its decussation in the mesencephalic tegmentum. Indeed, the cerebellum plays a crucial role in the control and regulation of motor functions, including the articulatory phase of language, but only 20% of cerebellar functions are related to motion. The role of cerebellum in cognitive and emotional behavior (e.g. attention, memory, and language) is much more subtle [8, 9]. The most evident feature of CMS is mutism and it sounds expected, because the cerebellum is believed to be engaged in lexical selection and in the coordinator of motor functions for articulation of speech.

In 2016, an international group met to formulate a new definition of CMS and standardized methods for diagnosis and follow-up [10]. Post-operative CMS is now defined as a syndrome characterized by delayed onset mutism/reduced speech and emotional lability after posterior fossa tumor surgery in children. Hypotonia and oropharyngeal dysfunction/dysphagia are further common features. It may frequently be accompanied by cerebellar motor syndrome, CCAS, and brain stem dysfunction as long tract signs and cranial neuropathies. The mutism is always transient, but recovery from CMS may be prolonged. Speech and language may not return to normal as well as other deficits of cognitive, affective, and motor functions often persist.

The pathophysiology behind CMS is still poorly understood. The putative cause might be a surgical disruption of the cerebellar input to the supratentorial brain, resulting in a cerebello-cerebral diaschisis [11]. CMS occurs more frequently after a midline tumor resection [12]. Other risk factors include tumor type and size, and brainstem compression [5, 12–14]. Medulloblastoma is the most common type of tumor associated with PFS in the pediatric population, and even its molecular subtype has recently emerged as a predictor of the syndrome's onset [15]. In an observational single-center prospective study enrolling 52 adults with posterior fossa tumors undergoing surgery [16], none was found to have CMS.

At least 400 cases of CMS have been described in reported studies, but it has been only occasionally reported in adults [17, 18] and the spontaneous occurrence is anecdotal. Then, information about its natural course, prognosis and treatment is lacking in adults. In this review, we are presenting a clinical case of an adult patient with CMS from bilateral cerebellar hemorrhage and the literature review about the features of CMS in adults.

Methods

A single case of postsurgical CMS is presented in an adult patient with a bilateral cerebellar hemorrhage due to a dural artero-venous fistula (DAVF) and a systematic review of the published individual cases of CMS in adults (> 18 years old persons) was conducted in order to better describe this phenomenon. This systematic review follows the Meta-Analyses and Systematic Reviews of Observational Studies (MOOSE) group guidelines [19]. We searched PubMed and EMBASE databases for studies addressing CMS or posterior fossa syndrome in adults from 1969 and 31 December 2023. We used the following keywords respectively for PubMed and EMBASE: "cerebellar mutism" OR "posterior fossa syndrome" AND (adult*). In addition, we applied forward and backward citation tracking to improve the results. All studies presenting original data that reported CMS in patients ≥ 18 years old were included. We limited the selection to English and French-language studies and excluded case reports and studies on nonhuman subjects. Abstracts presented at relevant scientific meetings were excluded because of the lack of relevant information. We avoided including duplicated datasets. We relied on the definition, diagnostics and prognosis provided in the original studies for CMS. We considered resolved the CMS when the original studies declared it (considering not only mutism but all the associated clinical manifestation as per definition of CMS) and partially resolved when the individual studies reported an improvement of the clinical manifestations but not a complete resolution within the reported follow-up time. Two investigators (MZ, RP) independently screened the papers retrieved in the literature search and performed them accordingly to the previously detailed criteria. Case series where adult patients are described as aggregate cohorts were excluded because of the impossibility to retrieve individual information. The NIH Quality Assessment Tool for Observational Cohort and Cross-Sectional Studies [20] was used to evaluate each eligible publication. The following information was extracted: authors, year publication, country, and number of adult patients, main demographic and diagnostic features. In case of missing values, we tried to derive them whenever it is possible [20]. Disagreements between the two reviewers were addressed and resolved by consensus.

Results

Case description

We present the case of a 60 years old, right-handed man with a previous history of binaural hypoacusis, admitted to the hospital because of the abrupt onset of headache and unsteadiness. The non-contrast computed tomography (NCCT) at admission revealed an acute intracerebral hemorrhage in the deep cerebellar hemisphere on both sides (Fig. 1) and a posterior fossa subarachnoid hemorrhage with intraventricular extension. The patient underwent CT angiography, showing a tentorial DAVF and in the same day Digital Subtraction Angiography (DSA)

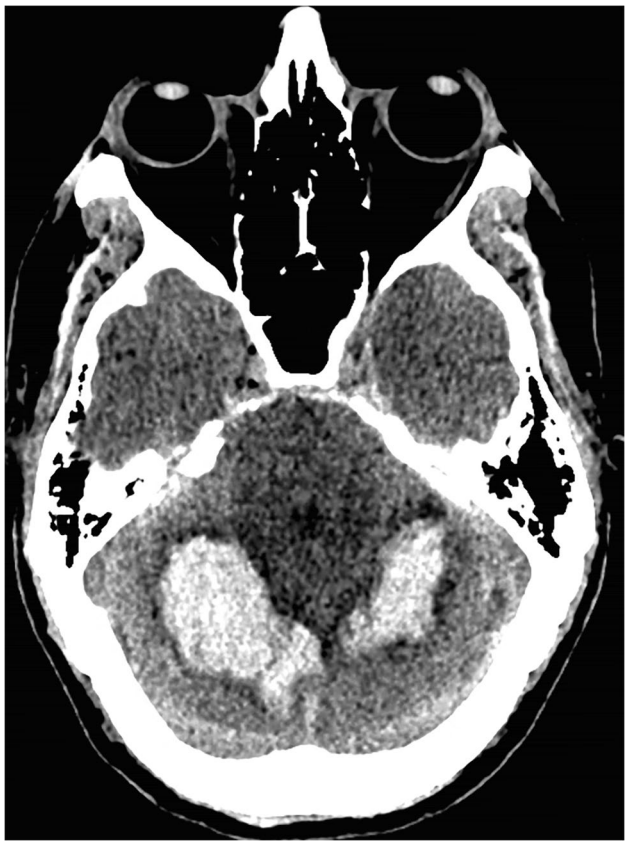


Fig. 1 Baseline brain CT at the level of the middle cerebellar peduncles, showing a deep located hyperdense hemorrhagic lesion on both cerebellar hemispheres

(Fig. 2) was performed, confirming and detailing the presence of a medial tentorial DAVF with subtorcular location (Cognard grade IV) [21], fed by transoxeous branches of the occipital artery from both sides and by the right lateral tentorial branch (receiving from mastoid branch of the occipital artery and from the petrosal-squamous branch of the middle meningeal artery). The venous efflux was characterized by a venous aneurysm proximal to the point of fistula and extensive involvement of the superficial cerebellar veins and median occipital sinus with a severe congestive venopathy. Because of the sudden worsening of the patient and enlargement of the cerebellar hemorrhages in the following hours, the patient underwent an emergent neurosurgical intervention, excluding the DAVF and draining the right cerebellar hemorrhage. In the following days, a complete mutism was noted with spared comprehension of the spoken language, and a severe hypotonia both axial and in the four limbs. Brain Magnetic Resonance Imaging (MRI) (Fig. 3) confirmed the bilateral cerebellar damage from the known hemorrhages, encircling both the dentate nuclei. The clinical diagnosis was CMS, considering the site of the hemorrhagic lesions and the clinical phenomenology of the patient. In order to achieve more information from the

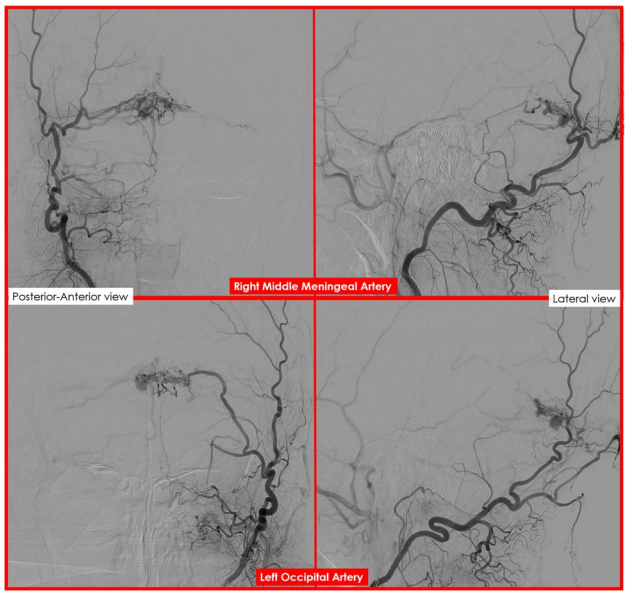


Fig. 2 DSA, showing two of the feeders of the DAVF in posterior-anterior and lateral view. In the upper half of the figure the right external carotid artery (ECA) injection allowed to image the feeding of the lateral tentorial branch from the middle meningeal artery. In the lower half of the figure, the injection of the left ECA showed the feeding from the left occipital artery. The venous aneurysm near the point of fistula is well evident (red arrow)

pathophysiological point of view a Fluoro Deoxy Glucose Positron Emission Tomograhy (FDG PET) was performed at 14 days from the admission (Fig. 4, upper half), showing, in the automatic quantification of Z score through a commercially available software, approved for medical use (CortexID Suite, GE), a pattern supporting the role of cerebellar damage in a diaschisis model. A complete neuropsychological battery

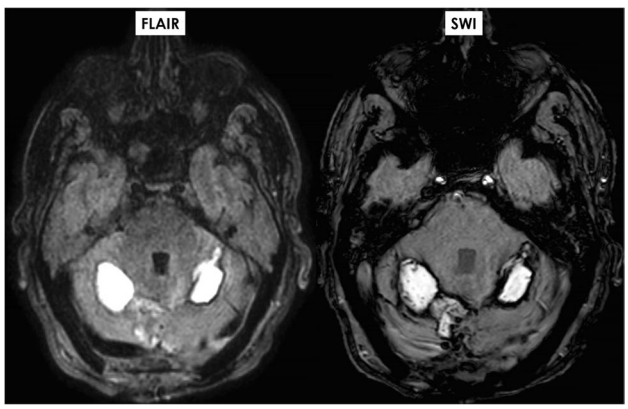
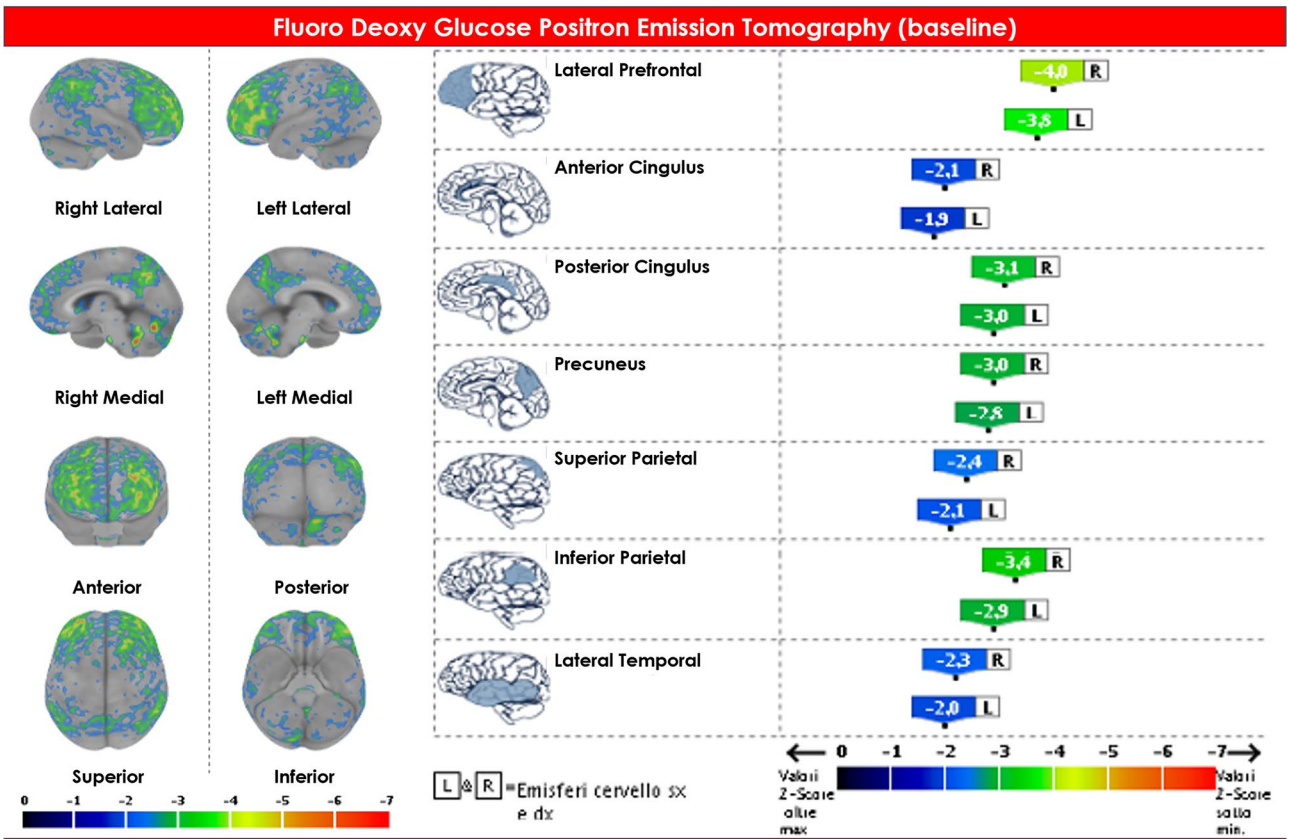


Fig. 3 Brain MRI at 10 days from the hospital admission, showing in Fluid Attenuated Inversion Recovery (FLAIR) axial section and in the corresponding Susceptibility Weighted Imaging (SWI) section reconstructed in Minimum Intensity Projection/Multiplanar Reconstruction (MinIP/MPR) the hyperintense hemorrhage in the deep portion of both cerebellar hemispheres


Fluoro Deoxy Glucose Positron Emission Tomography (baseline)
Right Lateral
Left Lateral
Right Medial
Left Medial
Anterior
Posterior
Superior
Inferior
0 -1 -2 -3 -4 -5 -6 -7
Lateral Prefrontal
-4,0 R
-3,8 L
Anterior Cingulus
-2,1 R
-1,9 L
Posterior Cingulus
-3,1 R
-3,0 L
Precuneus
-3,0 R
-2,8 L
Superior Parietal
-2,4 R
-2,1 L
Inferior Parietal
-3,4 R
-2,9 L
Lateral Temporal
-2,3 R
-2,0 L
L & R = Emisferi cervello sx e dx
0 -1 -2 -3 -4 -5 -6 -7
Valori Z-Score alte max
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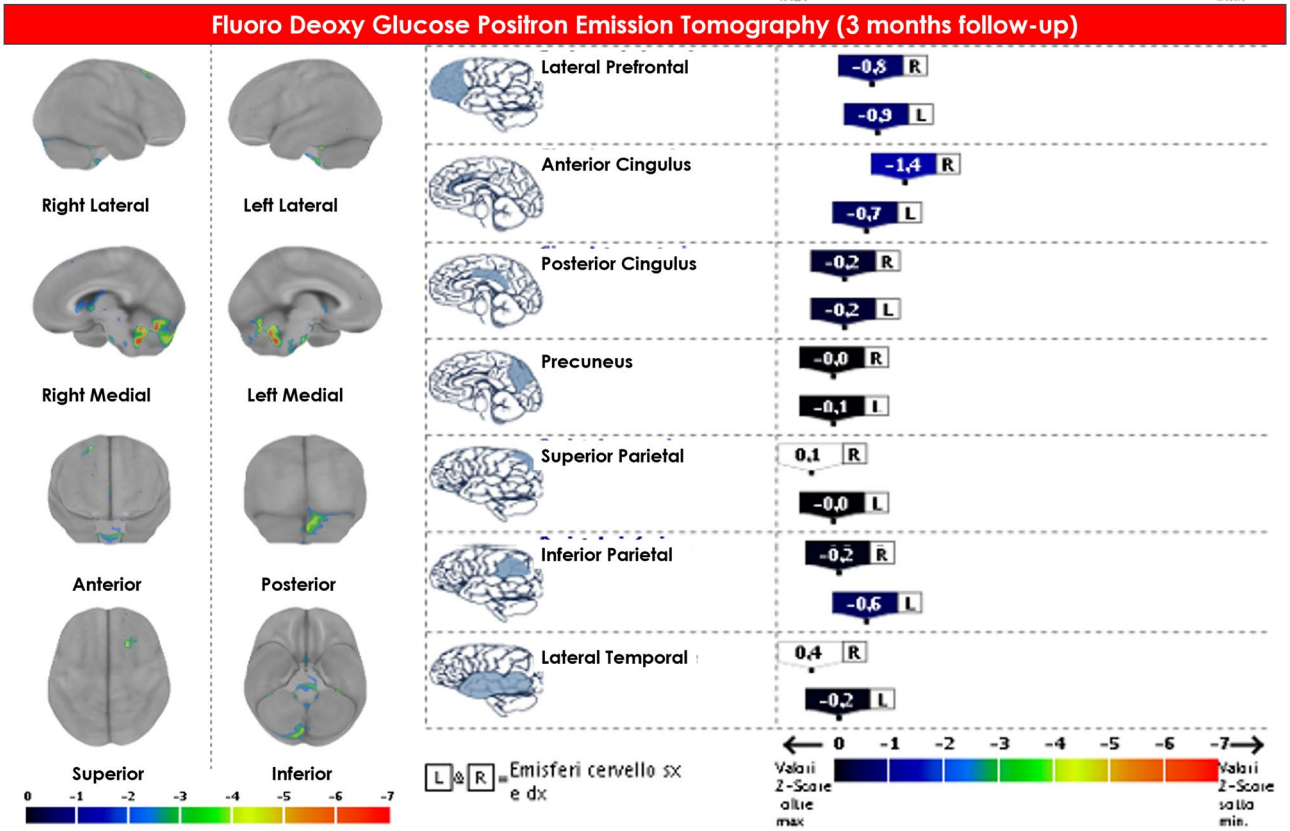
Fluoro Deoxy Glucose Positron Emission Tomography (3 months follow-up)
Right Lateral
Left Lateral
Right Medial
Left Medial
Anterior
Posterior
Superior
Inferior
0 -1 -2 -3 -4 -5 -6 -7
Lateral Prefrontal
-0,8 R
-0,9 L
Anterior Cingulus
-1,4 R
-0,7 L
Posterior Cingulus
-0,2 R
-0,2 L
Precuneus
-0,0 R
-0,1 L
Superior Parietal
0,1 R
-0,0 L
Inferior Parietal
-0,2 R
-0,6 L
Lateral Temporal
0,4 R
-0,2 L
L & R = Emisferi cervello sx e dx
0 -1 -2 -3 -4 -5 -6 -7
Valori Z-Score alte max
Valori Z-Score salla min.

◂**Fig. 4** FDG PET at baseline (upper half) and after 6 months (lower half). At baseline a marked decreased glucose captation was evident in the frontal and prefrontal cortical regions on both hemisheres, in the precuneus, cuneus and cingulus and in the inferior parietal regions. A marked glucose hypometabolism is evident in the cerebellum and in the thalamus and basal ganglia on both sides. IN the follow-up FGD PET a marked improvement of the glucose capitation was showed in all examined regions with a minimal persistent hypometabolism in the left anterior cingulate cortex

confirmed the clinical hypothesis and supported the diagnosis of CMS. The patient was transferred in an inpatients' rehabilitation pathway with rapid improvement up to the resolution of all deficit and complete restoration of the speech and motor initiative at 6 months. The FDG PET at this time-point (Fig. 4, lower half) showed a near complete normalization of the glucose hypocaptation in comparison with the previous study.

Systematic review

The systematic review of the available literature was performed accordingly with the Methods section. The selection of the studies is summarized in the PRISMA diagram [22] (Fig. 5).

A total of 22 case descriptions were retried, providing information on 30 patients, whose data are summarized in Table 1.

A male prevalence was evident, being 18/30 (60%) males with an age range at diagnosis 20–71 years. All but one case was post-surgical, but in one of the post-surgical cases a iatrogenic basilar artery occlusion was proposed as cause for CMS [30]. The distribution of causes was more variable than in the child cases, being primary tumors of the posterior fossa in 16/22 (72.7%) (5 medulloblastomas, 3 hemangioblatomas, 1 pinealoblastoma, 2 astrocytomas, 2 gangliocytomas, 1 choroid plexus papilloma, 1 ependymoma, 1 swannoma) more prevalent, followed by metastasis in 3/30 (10%), ischemia in 3/30 (10%) cerebellar hemorrhage in 3/30 (10%), and benign lesions (1 dermoid, 1 epidermoid) in 2/30 (6.7%) patients. 8/30 patients (26.7%) were reported as having persistent or incomplete resolution of CMS within 12 months. All patients undergoing surgery stayed in Intensive Care Unit (ICU) for some days and some of them needed a respiratory support, but CMS or other neurological deficits were not reported as triggered or worsened by the need of respiratory support or ICU staying and the potentially related complications.

Discussion

CMS is characterized by the onset of mutism or severely poor speech associated with emotional lability usually occurring within the first 24–48 h after surgical resection [44–46]. Complete, albeit transient, speech loss then evolves into dysarthria, but without the features of ataxic dysarthria, such as irregular articulatory breakdown and scanning speech [7], suggesting that a higher-level motor planning disorder (apraxia) may underlie the speech disorder [47]. Hypotonia and ataxia are the most common accompanying symptoms, followed by cranial nerve deficit and brainstem station damage. Dysphagia is also very common, due to lesions of the truncal centers or cranial nerves. The postoperative CMS is also characterized by a broad spectrum of emotional and behavioral disorders that include states of profound irritability, communication disorders, and a tendency to isolate up to an autistic-like framework. These behavioral aspects are associated with agrammatic language disorders and verbal stereotypies.

CMS is a rare occurrence in adults and spontaneous cerebellar hemorrhage has been reported in 3/22 (4.1%) adult patients. No previous descriptions of cerebellar hemorrhage due to DAVF are retrievable in the literature, as in the presented case. Since CMS is mostly found in pediatric patients who undergo surgery for a cerebellar tumor [48], much of the current knowledge regarding the pathogenetic mechanisms comes from studies of children with medulloblastoma [11]. In an Italian retrospective multicentric study [49] aiming to assess the preoperative radiological and surgical risk factors for the onset of CMS in a histologically homogeneous population of children with medulloblastoma (N = 109), and compare it to a similar population of young adults (N = 27), among children, 29 (27%) developed CMS, and all of them had tumors at midline site with invasion of the fourth ventricle. Radiological evidence of involvement of the right superior (39% versus 12%; p = 0.011) or middle cerebellar peduncles (52% versus 18%; p = 0.002) seemed more common in children who developed CMS. Young adults showed an expected lower incidence of CMS (4 out of 27; 15%), that may be due to anatomical, physiological and oncological elements. Post-operative CMS is currently believed to occur due to the surgical injury of anatomical structures that connect the cerebellum to the brainstem, in particular the proximal efferent cerebellar pathway (ECP), which includes the dentate nucleus, the superior cerebellar peduncle, and its decussation in the mesencephalic tegmentum, while its fibers travel towards the red nucleus and the thalamus (dentato-rubro-thalamic tract, DRTT) [50]. In a study on 28 children with medulloblastoma who underwent resective surgery [2], 11/28 (39%) developed CMS and the first neuroimaging study obtained immediately after surgery showed cerebellar edema in 92% of all patients, with a greater tendency to localization in the middle and upper cerebellar peduncle in patients with CMS (p = 0.05 and 0.07, respectively). In a retrospective cohort study [51] on 56 children diagnosed with medulloblastoma, 12/56 (21.4%) developed post-operative CMS and both early and follow-up

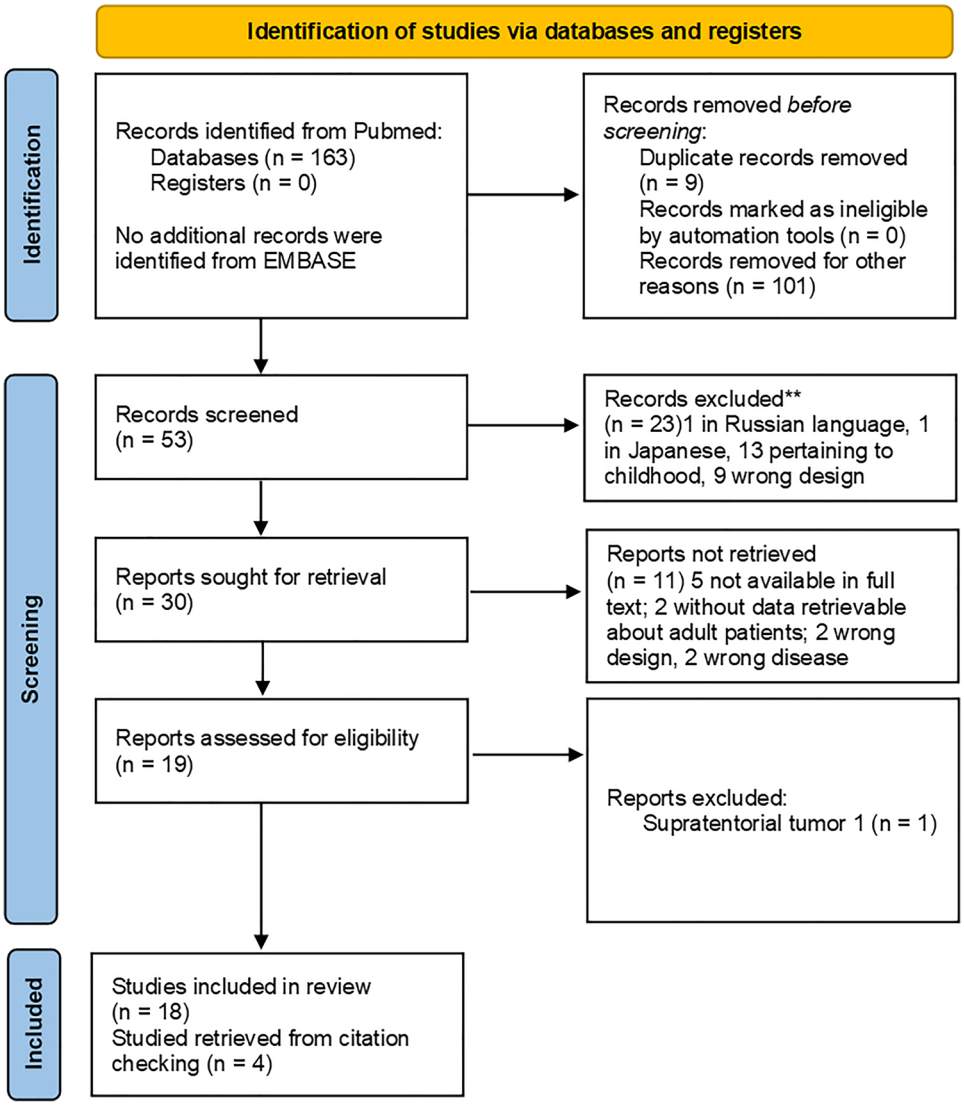

Fig. 5 PRISMA flow diagram

MRI found that T2-weighted change in superior cerebellar peduncle was more common in the group of patients diagnosed with postoperative CMS ($p = 0.040$ and 0.046 respectively), flanked by a statistically significant signal alteration in the dentate nuclei ($p = 0.024$). One of the suggested mechanisms is cerebral-cerebellar diaschisis [52]. According with this hypothesis, a DRTT lesion causes loss of excitatory impulses from the cerebellum to areas of the cerebral cortex such as the motor, premotor, and prefrontal regions, resulting in their loss of function; all these areas are involved in both motor and cognitive functions impaired in CMS [52]. Hypoperfusion, reduced oxygen consumption, and hypometabolism of the cerebral cortex due to the lack of cerebellar input are the hallmarks of cerebral cerebellar diaschisis [52, 53]. It appears that bilateral injury to the dentate nuclei or to the outflow from the cerebellum in the brainstem can lead to CMS. The dentate nucleus is located at the superolateral wall of the fourth ventricle and the vermis bilaterally [54, 55] and has major projections to the ventrolateral thalamus, which feeds signals from the cerebellum to the motor cortex. The dentate nucleus is involved in the execution and planning of voluntary movement and in higher cognitive function and sensory processing [56–58]. The dentate nucleus has been proposed to have anatomically separate domains for motor and nonmotor functions. These domains receive afferents from the cerebrum via the cortico-ponto-cerebellar pathway and also send efferent signals back up to the cortex via the dentate-thalamo-cortical (DTC) pathway [59].

Currently, the generally accepted hypothesis is that mutism results from bilateral damage to the dentate nucleus or the dentate-rubro-thalamic (DRT) tract within the superior cerebellar peduncle (SCP) [60–62], leading to cerebro–cerebellar diaschisis [52] and lower volumes of frontocerebellar white matter tracts [63]. Interestingly, some elements of the pathogenesis were provided in the eighties by Fraioli [64], attempting to provoke bilateral stereotactic lesion of

Table 1 Summary of the main features of adult patients CMS

Reference	Patient	Sex	Age	Disease	Extension	CMS after surgery	Investigations	Course
Moore 1969 [23]	1	M	68	Cerebellar hemangioblastoma	Not reported	yes	Pneumoencephalography	Progressive worsening
Coplin 1997 [24]	1	M	47	Cerebellar hemorrhage	Large superior vermis, extending symmetrically and anteriorly to the brachium pontis	yes	NCCT, CTA, DSA, MRI	Persistent deficit
Salvati, 1991 [25]	1	M	20	Medulloblastoma	Vermis, IV ventricle	yes	NCCT, MRI	Resolution at 4 weeks
D'Avanzo, 1993 [26]	1	F	20	Medulloblastoma	IV ventricle	yes	NCCT, MRI	Resolution at 6 weeks
D'Avanzo, 1993 [26]	2	M	45	Medulloblastoma	Vermis, R hemisphere, IV ventricle	yes	NCCT, MRI	Resolution at 8 weeks
D'Avanzo, 1993 [26]	3	M	22	Pinealoblastoma	R mesencephalon, vermis	yes	NCCT, MRI	Resolution at 16 weeks
D'Avanzo, 1993 [26]	4	M	48	Ischemia	R ponto-mesencephalic	yes	NCCT, MRI	Not reported
Cakir, 1994 [27]	1	M	61	Metastasis	R cerebellar hemishere	Yes	NCCT, MRI	Resolution at 4 days
Silveri, 1994 [28]	1	M	67	Ischemia	R cerebellar hemishere	Yes	NCCT, MRI	Not reported
Dailey, 1995 [29]	1	F	20	Astrocytoma	Vermis	Yes	NCCT, MRI	Resolution at 8 weeks
Nishiokawa 1998 [30]	1	F	30	Iatrogenic BA occlusion	Bilateral cerebellar infarction, bilateral thalamic infarction	Surgery for neurinoma in the upper thoracic paravertebral region	NCCT, DSA, MRI, 99mTc-HMPAO SPECT	Improvement at 3 months
Sherman 2005 [31]	1	F	33	Recurrent dermoid tumor	Pineal region	Yes	MRI	Improvement at 3.5 months
Sherman 2005 [31]	2	F	56	Cerebellar hemorrhage + metastasis from renal carcinoma	Left cerebellar hemispheric hemorrhage + adjacent ring-enhancing lesion	Yes	MRI	Resolution at 12 months
Ildan 2002 [32]	1	M	32	Medulloblatoma	Vermian mass with an extension to the R cerebellar hemisphere	Yes	MRI	Resolution at 4 months
Ildan 2002 [32]	2	M	44	Astrocytoma	Posterior fossa	Yes	MRI	Improvement at 9 months
Bhatoe 1997 [33]	1	M	28	Hemangioblastoma	Cerebellar hemisphere	Yes	MRI	Resolution at 4 weeks
Dunwoody et al., 1997 [34]	1	M	54	ArteroVenous Malformation	Vermis	Yes	MRI, DSA, EEG	Resolution at 4 weeks
Kai et al. 1997 [35]	1	M	71	Hemangioblastoma	Superior cerebellar hemisphere	Yes	NCCT, MRI	Resolution at 4 weeks
Kai et al. 1997 [35]	2	F	74	Metastasis of adenocarcinoma	Vermis	Yes	NCCT, MRI	Resolution at 3 weeks
Caner et al., 1999 [36]	1	F	18	Choroid plexus papilloma	IV ventricle	Yes	MRI	Resolution at 4 weeks
Akil 2006 [37]	1	M	49	Haemangioblastoma	L cerebellar hemisphere	Yes	MRI	Non stated
Marien 2013 [17]	1	F	38	Grade II ependymoma	IV ventricle	Yes	NCCT, MRI, (Tc-99m-ECD) SPECT	Not remission at 1 year
Marien 2013 [38]	1	M	71	Cerebellar hemorrhage	R cerebellar hemisphere, vermis, IV ventricle	No	NCCT, Tc-99m-ECD SPECT	No change at 6 months

Table 1 (continued)

Reference	Patient	Sex	Age	Disease	Extension	CMS after surgery	Investigations	Course
van Baarsen 2013 [18]	1	F	55	Epidermoid cyst	L cerebellopontine area	Yes (pontine ischemia by basilar perforator occlusion)	NCCT, MRI, DTI	Resolution at 2 Months
Shamov 2019 [39]	1	F	25	Medulloblatoma	IV ventricle	Yes	NCCT, MRI	Resolution in 5 days
Muthappan 2012 [40]	1	F	55	Swannoma	Vagus nerve	No	MRI	Not reported
De Smet 2012 [41]	1	M	60	Cerebellar hemorrhage	L cerebellar haematoma and obstructive hydrocephalus	Yes	MRI, Tc-99m-ECD brain SPECT	Persistent deficit at 3.5 months
Oromieh 2010 [42]	1	M	36	Lhermitte-Duclos disease (LDD; dysplastic gangliocytoma)	Space-occupying lesion with a perifocal edema in the L cerebellar hemisphere with hydrocephalus and beginning vermal herniation into the foramen magnum	Yes	NCCT, MRI	Resolution at 6 Months
Oromieh 2010 [42]	2	F	31	Lhermitte-Duclos disease (LDD; dysplastic gangliocytoma)	Bilateral lesion predominantly involving nodulus and uvula vermis of the cerebellum and infiltrating the IV ventricle	Yes	NCCT, MRI	Resolution at 4 Months
Akhaddar et al. [43]	1	M	22	Medulloblastoma	Vermis	Yes	NCCT, MRI	Resolution at 4 weeks

Abbreviations: *NCCT* Non-contrast Computed Tomography, *CTA* CT Angiography, *DSA* Digital Subtraction Angiography, *MRI* Magnetic Resonance Imaging, *ECD* Brain perfusion scintigraphy, *R* right, *L* left

nn. dentati for treating dystonias. The main basis of CMS is the lesion of the proximal segments of the efferent cerebellar pathways, passing through the superior cerebellar peduncle and including mostly fibers originating from n. dentatus, but also projection fibers from the other cerebellar nuclei (n. fastigii, n. globosus et n. emboliformis) and crossing in the ponto-mesencephalic tegmentum (Guillain-Mollaret decussation), before projecting to the thalamic nuclei and from the thalamus to different cortical areas.

However, the exact mechanisms underlying cerebellar mutism are unknown. Starting from the identification of the location of damage, several pathophysiological hypotheses were proposed. Lesions of the dentate nuclei, the dento-thalamic tracts, the brachium pontis, hydrocephalus as well as splitting the inferior vermis [1, 65] have all been reported to cause the problem. Based on the onset of cerebellar mutism several days after the initial trauma, edema may be proposed as the primary cause [52]. However, the natural course of neurological deterioration caused by edema is much shorter than seen in cerebellar mutism. Another hypothesis is the transient decrease in cerebellar blood flow due to reversible vasoconstriction of small vessels [32]. As previously said, the information provided by metabolic and functional investigations support cerebro–cerebellar diaschisis as main mechanism. Cerebellar output is primarily through the inferior cerebellar peduncle (ICP) and the superior cerebellar peduncle (SCP). ICP efferents are primary vestibulospinal, whereas the SCP carries efferents from the dentate, which then decussate sharply within the posterior brainstem and then ascend to the thalamus. Subsequent pathways relay this information to neocortex including sensorimotor cortex and wide areas of pre-motor frontal cortex. A study on a subset of children with posterior fossa brain tumors using Diffusion Tensor Imaging (DTI)-MRI [66], patients with midline tumors that still had observable SCP did not develop posterior fossa syndrome. SCPs were absent, on either preoperative or postoperative studies, in the five patients who developed PFS. Another DTI study in a single case report [18] supports the general hypothesis that cerebellar mutism is caused by functional disruption of the dentate-rubro-thalamic tract. DTI studies supported the hypothesis of diaschisis as main mechanism for CMS, documenting microstructural alterations in the white matter of the superior cerebellar peduncle and the thalamic projections to the cortex [67]. In addition, the same authors have proven that the edema and degeneration of the fibers of the superior cerebellar peduncle could lead to edema of the contralateral oliva in the medulla oblongata and degeneration of the fibers originating in the inferior olivary nucleus. Such changes can be explained by the topical distribution of the fibers in the Guillain-Mollaret decussation.

In the presented case, the hypothesis of diaschisis could receive support, because the bilateral deep cerebellar lesion disrupted the cerebellar afferents to the nn. Dentate, triggering the loss of inhibitory signaling leading to thalamic and frontal and prefrontal cortical decreased projections, as inferable from the FDG PET study (Fig. 4). Indeed, during the follow-up, the complete resolution of CMS corresponded to the near complete restoration of metabolic activity in these regions. Then, this mechanism might be involved not only in children but also in adults. Serial DTI studies are not available in adults, mainly due to the clinical conditions of the patients in the postsurgical phase, sometimes requiring prolonger staying in Intensive Care Units. The identification of CMS in adults, considering causes and diseases not largely described in the literature, might help to define the prognosis and start a dedicated rehabilitation pathway, with a complete resolution of the deficit in 63.7% of cases.

Conclusions

CMS is seldom reported in adults and cerebellar hemorrhage is a rare cause. The prognosis in adults is slightly worse than in children, but two thirds of cases show a complete resolution within months, if addressed in a dedicated rehabilitation pathway.

Author contributions All authors contributed to the study conception and design. Material preparation, data collection and analysis were performed by Marialuisa Zedde, Rosario Pascarella, Manuela Napoli and Claudio Moratti. The neuroimaging data were reviewed by Rosario Pascarella, Manuela Napoli, Claudio Moratti, Giovanna Di Cecco, Claudio Pavone, Lara Bonacini, Serena D'Aniello. The clinical data were reviewed by Ilaria Grisendi, Federica Assenza and Franco Valzania. Antonio Romano and Giacomo Pavesi reviewed surgical data. Marialuisa Zedde, Francesca Romana Pezzella and Rosario Pascarella performed the literature search and the screening of papers. Ilaria Grisendi, Federica Assenza, Manuela Napoli, and Antonio Romano performed the data extraction. The first draft of the manuscript was written by Marialuisa Zedde and Rosario Pascarella. All authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

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Declarations

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