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ORIGINAL PAPER

Non-surgical transient cerebellar mutism—case report and systematic review

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Abstract
Introduction Transient cerebellar mutism has been well recognized in literature as a complication of posterior fossa tumor resection. It is marked by profound impairment of fluency, articulation, and modulation of speech, irritability and autistic features and typically resolves within days to months. Underlying pathophysiology is debated, but currently unknown.
Methods We present a case of a child with similar clinical findings after cerebellitis, demonstration of diffuse cerebellar signal changes, swelling, and protruding tonsils at the level of foramen magnum.
Discussion To support the hypothesis that this clinical syndrome may occur in a non-surgical context, we present a review of literature of non-surgical transient cerebellar mutism.

Keywords Cerebellar · Mutism · Transient · Cerebellitis

Introduction

The term "mutism" refers to the inability of an awake and conscious patient to produce verbal output [1]. It can reflect aphasia, anarthria, or aphonia, and has been attributed to damage to Broca's area, the supplementary motor cortex, the reticular activating system and can be seen in bilateral hemispheric lesions [1, 2]. Cerebellar mutism is a form of dysarthria characterized by a complete or transient disruption of speech following surgery for posterior fossa tumors [3]. It most frequently occurs in children, but occasionally in adults, and is often attributed to damage to the cerebellar vermis or hemispheres [2, 4]. It typically manifests as a profound impairment of fluency, articulation, and modulation of speech, irritability and autistic features and typically resolves within days to months [2].

The anatomical substrate of cerebellar mutism is not fully understood, but conventional hypotheses implicate the dentato-thalamo-cortical tract, the cerebellar cortex, and the dentate nuclei [1, 5]. The data on cerebellar representation of language control is still debated and uncertain [5]. While postoperative cerebellar mutism from posterior fossa surgery is well-documented in the literature, we define non-surgical cerebellar mutism as a similar syndrome that would occur following trauma, inflammatory diseases, and infections, in the absence of recent posterior fossa surgery. However, there is sparse literature regarding these causes [6]. It is suspected that the underlying pathologic mechanism for non-surgical cerebellar mutism is similar to that after posterior fossa tumor surgery.

We present the case of a young girl who developed anarthria and behavior mimicking a postoperative cerebellar mutism due to severe acute cerebellitis and cerebellar edema. We additionally review the literature with respect to development of non-surgical cerebellar mutism following cerebellitis.

Methods

Literature review

A systematic literature search was conducted using PubMed and Ovid. Search terms included "Cerebellar Mutism," "Cerebellar Mutism AND Cerebellitis," "Cerebellar

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Mutism AND Nonsurgical," "Cerebellar Mutism AND Inflammation," "Cerebellar Mutism AND Trauma," and "Cerebellar Mutism AND Infection" as the search criteria. Reported patients with a diagnosis of non-surgical cerebellar mutism fulfilled our inclusion criteria. Poster presentations, conference abstracts, and non-English articles were excluded.

Data extracted from eligible articles included the number of patients with non-surgical cerebellar mutism, age of presentation, sex, development of hydrocephalus, diagnosis, radiological imaging findings, extent of cerebellar involvement, duration of cerebellar mutism, surgical intervention (if any), and length of follow-up. Not all studies reported on all the above variables. Descriptive statistics were used to quantify the data extracted from studies that fulfilled our inclusion criteria.

Results

Case report

History

A nine-year-old girl presented with a two-week history of headache, intermittent vomiting, and verbal regression. Her symptoms began a few days after having had an orthodontic plate inserted into her upper jaw in preparation for reconstructive surgery on her palate. In the week prior to presentation, she stopped talking altogether. As no other cause for her symptoms was identified, the possibility of them being related to the orthodontic surgery was raised and the rod removed. Her symptoms however, did not improve. Her medical history was significant for a cleft palate repair in early childhood. She had no known allergies and took no regular medication. She was educationally and developmentally normal.

Examination

Neurological examination revealed anarthria, though she was able to comprehend commands and respond with "yes" and "no" non-verbal gestures. Otherwise, she was awake and alert, had a normal cranial nerve examination with no evidence of papilledema. She had full strength in her upper and lower extremities, and no obvious dysmetria. Systemic examination was normal. She was afebrile with no clinical suspicion of ongoing infection.

Laboratory findings

Serology for Lyme disease was non-reactive, and mycoplasma pneumoniae testing was negative. Virology was negative for active CMV, EBV, HSV, VZV, and HTLV I and II. Cerebrospinal fluid and blood cultures were negative as was the test for tuberculosis. We had performed cytology testing which showed no tumor cells in CSF on histopathological testing.

Radiology

Admission non-contrast CT imaging demonstrated posterior fossa edema with early hydrocephalus and no clear brain stem compression. An MRI scan demonstrated diffuse bilateral cerebellar hemispheric parenchymal T2 and FLAIR increased signal intensity in keeping with edema (Fig. 1). There was no evidence of contrast enhancement or diffusion restriction. This was consistent with cerebellitis. Additionally, there was compression of the fourth ventricle, tonsillar crowding of the foramen magnum, and obstructive hydrocephalus.

Clinical course

Forty-eight hours after admission, the patient's GCS suddenly dropped to 3, she developed fixed and dilated (7 mm) pupils and suffered a respiratory arrest. Following resuscitation, a right frontal external ventricular drain (EVD) was emergently placed. The patient was admitted to the pediatric intensive care and following a rapid improvement in level of consciousness, was extubated without event. The EVD was weaned over the course of a week and then removed. She ultimately regained limited verbal function with a vocabulary of 10–20 words, and is in the early recovery stages at a

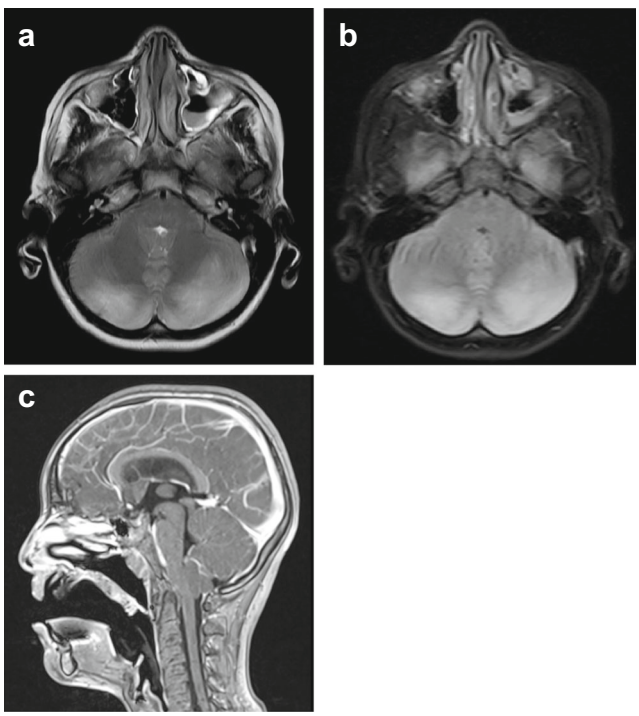

Fig. 1 Cerebellitis in MR imaging illustrated with **a** T2-weighted imaging **b** FLAIR and **c** without gadolinium enhancement

Table 1 Cases of non-surgical cerebellar mutism published in the English literature from 1980 to June 2017

Author	Year	Age (year)	Sex	Site/ cerebellar involvement	Hydrocephalus	Imaging	Pathology	Resolved mutism?	Surgical intervention
Ersahin [7]	1997	2.5	M	Vermis	No	CT – paravermian hematoma	Trauma	Resolved at 14 months f/u	None
Riva [6]	1998	4.2	F	Cortex	Yes	MR – increase T2 in cortex	Unknown	6 months persisting dysarthria	VP shunt
Miyakita [28]	1999	3.7	F	Tegmentum lower left midbrain	No	MR – increased T2 signal in brainstem	Infarct from traumatic vertebral artery dissection	Normal at 2 months	None
Drost [16]	2000	4	F	Cortex	No	T2 edema in cortex	Strep pneumoniae middle ear infection	2 months persisting dysarthria	None
Mewasingh [17]	2003	5	F	Cortex	No	MR – cerebellar edema	Pancolitis	Improving over 26 days, not to baseline	None
		4	F	Cortex	No	Cortical edema on MR	Unknown	Improving by 3 weeks, learning assistance 1 year	None
Fujisawa [8]	2004	7	M	Cortex	No	CT – acute subdural hematoma posterior fossa, traumatic subarachnoid hemorrhage, cerebellar cortical contusion	Trauma	Speech normal at 39 days following injury	Hematoma evacuation
Papavasiliou [18]	2004	3	F	Cortex	No	T2 signal increase	Unknown – gastrointestinal	6 months residual dysarthria, dysmetria, gait ataxia	None
Shiihara [11]	2007	2.6	F	Diffuse	No	MR – normal initially, day 180 widened cerebellar sulci, enlarged 4th ventricle	Rotavirus	Slow speech, dysarthria by day 180	None
		4.5	M	Diffuse	No	MR – normal initially, widened cerebellar sulci day 100	Rotavirus	Slow recovery day 100, still dysarthric, hand tremor, no more ataxia	None
Dimova [10]	2009	7.5	F	Diffuse	No	Diffuse FLAIR changes, cortical mainly	Unknown, URTI	Dysarthric at 6 months	None
Frassanito [29]	2009	7	F	Upper cerebellar vermis	No	MR – hemorrhage into Upper cerebellar vermis	Intratumoral hemorrhage	Moderate dysarthria 2 months after ictus, mild dysarthria postoperatively	Resection of upper vermian tumor
Takanashi (series of 10 patients) [13]	2010	2–4	3M, 7F	6/10 nuclear lesions, 10/10 vermis lesions, 10/10 atrophy	No	DWI changes, as above. Cerebellar atrophy in most	Rotavirus	Persisting dysarthria 7/10 patients	None
Kubota [12]	2011	1.5	M	Dentate	No	MRI – DWI changes in bilateral dentate nuclei	Rotavirus	Back to baseline 15 months	None
		3.2	M	Dentate, vermis, hemispheres	No	DWI changes in dentate nucleus	Rotavirus	6 months dysarthric	None

Table 1 (continued)

Author	Year	Age (year)	Sex	Site/ cerebellar involvement	Hydrocephalus	Imaging	Pathology	Resolved mutism?	Surgical intervention
		2.3	F	Dentate, vermis, hemispheres	No	DWI changes	Rotavirus	Persisting slurring 6 months onwards	None
Erol [14]	2013	7	F	Unknown	No	Normal	VZV	Normal at 2 months follow-up	None
Thabet [15]	2013	3	M	MCP and dentate nucleus	No	MR involvement of MCP and restrictive diffusion suggestive of cytotoxic edema	Influenza B	Normal at 6 weeks	None
Kariyattil [9]	2015	8	M	Cerebellar cortex	No	CT – cerebellar cortical hematoma	Trauma	Normal at 1 month	None

rehabilitation facility. Brainstem and lower cranial nerve function was normal.

Literature review

Since being first described by Rekate et al. in 1985, there have been 15 published reports in the English literature documenting 28 patients with cerebellar mutism which did not develop as a result of posterior fossa surgery [4]. Twenty three were secondary to cerebellitis, three followed a traumatic injury with a cerebellar contusion, one was due to a midbrain infarct from a vertebral artery dissection, and one was due to vermian intratumoral hemorrhage [7–11]. These results are summarized in Table 1. Patients had a median age at presentation of 4 years, with a male-to-female ratio of roughly 1:2. The most frequently encountered involvement was in cerebellar cortex (62%) and vermis (46%) regions on MRI. Dentate nuclei involvement was less frequent (35%). Three patients with diffuse cerebellar involvement have been reported, involving the cerebellar hemispheres, the vermis, as well as deep cerebellar nuclei [12, 13].

Of 23 patients with cerebellitis, in 15, the pathogen responsible was rotavirus, identified by PCR in cerebrospinal fluid [13–15]. In two patients, the agent was thought to be the cause of an upper respiratory tract infection; in one of the patients, the agent was varicella zoster virus (VZV); another one, it was influenza B [16, 17]. In six of the patients, no offending pathogen was identified [6, 12, 18–20].

The imaging modality most often used to characterize cerebellar injury in the event of mutism was computed tomography (CT), followed by magnetic resonance imaging (MRI) of the brain, with many (27/28) of the patients undergoing both imaging investigations. Given the low specificity of CT screening for posterior fossa lesions, the initial screening test may be negative, hence the need for MRI to better characterize the lesion. In nine patients, restriction was noted on diffusion-weighted imaging (DWI) at the site of cerebellitis.

The natural history has a similar course to postoperative mutism. Fluency returned within 2–6 months following the initial insult and in most cases, the patients returned to baseline at 6 months with persisting dysarthria. Interestingly, only three patients had no residual dysarthria at the time of the last follow-up. Only one of the patients presented with additional hydrocephalus due to cerebellar edema and tonsillar descent, and required an insertion of a ventriculoperitoneal shunt for hydrocephalus [6]. One patient with a traumatic posterior fossa injury required evacuation of their acute subdural hematoma.

Discussion

Prevailing theory identifies the dentato-thalamo-cortical tract, the cerebellar cortex, and the dentate nuclei as the structures

involved in the pathophysiology of cerebellar mutism, albeit the mechanism are still debated [1, 5]. Damage to vermis, superior cerebellar peduncle, edema of the dentate nucleus, and surgical injury to deep cerebellar structures have been implicated in the postoperative development cerebellar mutism [21–23]. Stereotactic ablation of the superior cerebellar peduncle and dentate nucleus has been shown to cause reversible mutism, suggesting bilateral dentato-thalamo-cortical tract involvement in its pathophysiology [6, 15, 24]. Furthermore, additional pathophysiology such as hydrocephalus, invasion of brainstem, histology of the lesion, and tumoral involvement of neural pathways pre-operatively have been associated [1, 25]. Advances in surgical technique such as the telovelar approach (spares the vermis), approaches through the cerebello-medullary fissure or a combined transventricular and supracerebellar approach may reduce the risk augmented by the use of intraoperative adjuncts such as ultrasonography [26–29].

In our case, the mutism dated back to a week prior to presentation, and thus is likely related to disruption of the dentate-thalamo-cortical tract visualized by the diffuse cerebellar edema seen on imaging. The pathophysiology of cerebellar mutism in cerebellitis is largely unclear and it may be multifactorial. While in a surgical resection, it may be clear which structures were manipulated, diffuse edema and cytotoxicity would indirectly disrupt communication for speech production in non-surgical cerebellar mutism.

In the cases where traumatic injury was the cause of cerebellar insult, the pathophysiology of cerebellar mutism seems akin to that of cases following posterior fossa surgery. The damage to the cerebellar cortex ultimately led to the disruption of speech pathways. The time until recovery certainly reflects a “stunned” state after the initial event, with all three patients in literature regaining their speech within 2 months.

In 19 of 23 patients with mutism and cerebellitis, MRI revealed transient lesions in several parts of the cerebellar anatomy. These lesions are associated with reduced white matter and nuclei diffusion between days 5 and 7 following the initial infection. These lesions disappeared afterward after 3–6 months, being followed by T2/FLAIR hyperintensity in the same regions, finally leading to cerebellar atrophy. Edema of the cerebellar cortex is also present. As expected, given limitation of CT imaging of the posterior fossa, these are often unremarkable. Cases of cerebellitis have been associated with rotavirus infection, with DWI changes in cerebellum [14]. These were thought to be associated with being a valuable predictor of cerebellar mutism. Additionally, some cases have reported the lesions disappearing by the time mutism is observed (between days 5 and 7), and this is unclear why [15]. Perhaps it is a delay in the biochemical response in nature, or perhaps the disturbance of consciousness in the acute stage lasts longer than the imaging abnormalities.

In the majority of cases, the mutism was observed following documented cerebellitis following rotavirus infection, with the largest portion of patients derived from Takanashi et al. [15]. This is often explained as direct CNS invasion by the rotavirus, despite lack of rotavirus antigen or positive detection by PCR of the CSF in some of the patients [15, 30]. It is suspected that this damage is responsible for the development of cerebellitis, which would then lead to cerebellar mutism. Ultimately, the resolution of the infection, and then subsequent development of cerebellar atrophy would explain to incomplete resolution of anarthria with residual difficulties in 17 of the patients (Table 1).

Conclusion

Non-surgical cerebellar mutism is an uncommon condition that should be included as part of clinical presentation in cerebellitis and following posterior fossa trauma. The clinical course characterized by irritability, autistic features, and anarthria is like that of those cases that develop following posterior fossa surgery. It is likely that the pathophysiology is similar between these two entities.

Compliance with ethical standards

Conflict of interest On behalf of all authors, the corresponding author states that there is no conflict of interest.

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