Posterior Fossa Society Consensus Meeting 2018 : a synopsis

Query Details

1. **Please check if the presentation and sequence (i.e., extended given name, middle name/initial, family name) of author names are accurate. Also, kindly confirm correctness of details in the metadata.**

2. **Please check and confirm if the authors and their respective affiliations are correctly identified and amend if necessary.**

Posterior Fossa Society Consensus Meeting 2018: a synopsis

Emanuela AQ1 Molinari, [1,2]

Barry Pizer, [3,4]

Coriene Catsman-Berrevoets, [5]

Shivaram Avula, [6]

Robert Keating, [7]

Philippe Paquier, [8,9,10]

Jeffrey H. Wisoff, [11]

Karin S. Walsh, [12]✉,13

Phone +1 202-476-3923
Email kwalsh@childrensnational.org

on behalf of the Posterior Fossa Society

[1] Department of Neurology AQ2 , The Queen Elizabeth University Hospital, Glasgow, UK

[2] College of Medical Veterinary & Life Sciences, School of Medicine, Dentistry & Nursing, University of Glasgow, Glasgow, UK

[3] Department of Pediatric Oncology, Alder Hey Children's Hospital, Liverpool, UK

[4] Institute of Translational Medicine, University of Liverpool, Liverpool, UK

[5] Department of Paediatric Neurology, Erasmus Medical Centre, Rotterdam, The Netherlands

[6] Department of Radiology, Alder Hey Children's Hospital, Liverpool, UK

[7] Division of Neurosurgery, Children's National Health System, Washington, DC, USA

[8] Department of Linguistics, Vrije Universiteit Brussel, Brussels, Belgium

[9] Department of Neurology, Hôpital Universitaire Erasme ULB, Brussels, Belgium

[10] Unit of Translational Neurosciences, Universiteit Antwerpen, Antwerp, Belgium

[11] Division of Pediatric Neurosurgery, New York University Langone Medical Center, New York, USA

[12] Division of Pediatric Neuropsychology, Children's National Health System, 111 Michigan Ave NW, Washington, DC, 20010 USA

[13] Departments of Pediatrics and Psychiatry, The George Washington University Medical Center, Washington, DC, USA

Received: 13 May 2019 / Accepted: 23 May 2019

Abstract

Purpose

The Posterior Fossa Society (PFS) was founded 4 years ago to systematically gather and exchange information on the post-operative (CMS) and cerebellar cognitive affective syndrome (CCAS). With its consensus meetings, the PFS orchestrates research studies in the field of cerebellar injury and progresses the knowledge of post-operative pediatric cerebellar mutism syndrome (CMS). In this article, we captured the 3-day program of presentations, group discussions, interactive workshops, and dialogue, highlighting the key topic areas of CMS and its research advances.

Methods

This synopsis is based on the third consensus meeting which was held in Reykjavik, Iceland, in August 2018.

Results

Three working groups have been defined to drive the future research priorities on post-surgical CMS: (i) refining definition and symptoms scoring of CMS; (ii) understanding the pathogenesis and enhancing risk-stratification strategies; and (iii) developing rehabilitation approaches and protocols.

Conclusions

The third consensus meeting highlighted a unanimous desire for data-driven information to advance the knowledge and guide future research efforts. The PFS constitutes an established and expanding network of multi-disciplinary expertise that can facilitate the development of collaborative studies and produce official guidelines on the topic.

Keywords

Posterior fossa tumors
Cerebellar mutism syndrome
Rehabilitation
Pathogenesis
Cerebellar cognitive affective syndrome

Background

Brain tumors (BTs) constitute around 25% of neoplasms in children and young people and around half of these tumors arise in the posterior fossa with an incidence rate of approximately 5.13 cases per 100,000 children [7]. Posterior fossa tumors include cerebellar astrocytoma, medulloblastoma, ependymoma, atypical teratoid rhabdoid tumor, and both malignant and benign tumors arising from the brain stem. Most types of tumors require surgical excision, the malignant types requiring adjuvant chemotherapy plus/minus radiotherapy with generally increasing survival rates [5, 12, 20]. Although surgery has a key role in improving outcomes, injury to the cerebellum and its supratentorial connections may result in significant acute and long-term morbidity for pediatric survivors.

Cerebellar mutism syndrome (CMS) is a known adverse effect of cerebellar injury and posterior fossa surgery particularly in children and increasingly recognized since the 1970s [24]. The rate of CMS is variable but reports suggest that it occurs in between 20 and 30% of the children undergoing posterior fossa surgery with highest rates reported in very young children [15, 30] and those with medulloblastoma [6]. CMS usually emerges within 1 to 6 days after surgery and is manifest by mutism usually associated with emotional lability. A range of neurological (e.g. cranial nerve palsies and long tract signs) and neuropsychological abnormalities may accompany these manifestations [11]. The presence of post-operative CMS is independently linked to poorer cognitive outcomes later in life [21, 22], with implications on the survivor's quality of life. Despite an increased awareness of CMS over the last 50 years, attempts to identify pathogenesis and predictive risk factors have provided conflicting results for tumor size, type, location, and radiological features [6, 8, 16, 26]. Thus, the incidence of CMS has remained fairly stable over time. There is a paucity of systematic prospective trials examining this common post-surgical complication [33] that affects the quality of life of children living with, and surviving a brain tumor diagnosis. There is, therefore, a clear need to better refine the formal definitions and standard assessment criteria of CMS across the ages. Further clarification on the relationship between CMS and the Cerebellar Cognitive Affective Syndrome (CCAS) [18, 27, 32] is also important in developing future research. Many key questions remain unanswered on the mechanisms and pathophysiology of injury, the predictors of occurrence and recovery, the timing and most effective rehabilitation therapy, as well as the role of pharmacological and other therapies.

The Posterior Fossa Society (PFS) was formed in 2014 by Thora Gudrunardottir, together with Elizabeth Wells and Karin Walsh, and has brought together a multidisciplinary and international group of committed researchers and clinicians with a shared interest in post-surgical CMS. The society has achieved advances on the topic through collaborative research networks. Two previous meetings set the stage for the 2018 consensus meeting. The first consensus meeting held in Reykjavik, Iceland in 2015, focused on finalizing a consensus on the definition and diagnosis of CMS, based on results of the Delphi process carried out during the previous year, which lead to our initial consensus paper [13]. A follow-up, topic-specific meeting was held in conjunction with the International Symposium on Pediatric Neuro-Oncology (ISPNO) in 2016, with a focus on prevention and intervention.

The third PFS consensus meeting was held on August 2–5, 2018 at the Harpa Conference Center in Reykjavik, Iceland. The conference was attended by 28 members of the Society (Appendix), representing seven countries in three continents. The primary aim of this third consensus meeting was on the pathogenesis of CMS and the management/rehabilitation of post-operative pediatric CMS. Conference delegates were given the opportunity to compare and contrast different practices across the world, highlight key messages of practical importance, and suggest topics for future research direction. We provide a synopsis of the 3-day meeting to promote awareness and collaborative

research efforts, thus harmonizing the approaches world-wide.

Conference sessions

Delegates from several institutions presented their research. Conference attendees took part in four facilitated discussions on “take-home messages” that could identify and facilitate the next stage of research. Two facilitated group sessions were arranged to discuss practical scenarios and define working groups to prioritize research areas through live votes. Results of these interdisciplinary group discussions highlighted that more compelling future research will be driven by working groups focusing on: CMS symptom scoring (refining definitions and scales), surgery and radiology (pathogenesis and risk prediction), and rehabilitation (intervention and management). The key messages of each working group are described below. To ensure transparency and pass a unanimous message that could harmonize the approach and management of the post-surgical CMS and related conditions, we sent out the summary of the presentations and discussions and asked delegates to provide a feedback on the relevant key points.

CMS scoring

The initial effort of the Society was to develop a rating/scoring system based on the consensus definition established through the Delphi process and agreed upon at the initial PFS consensus meeting. By developing a standard measurement tool, clinicians and scientists could better define and capture the post-surgical occurrence of CMS. The Iceland Delphi result [18] aimed at resolving terminology conflicts and provided a solid foundation for future work in both clinical and research fields.

A review of a proposed CMS rating scale was performed in Rotterdam by Dr. Catsman-Berrevoets who applied the scoring system as initially drafted at the PFS Consensus in 2015 to a historical cohort of children. Her work emphasized that symptoms such as severe axial ataxia and swallowing difficulties may need further evaluation, as they are possibly strong predictors of long-term outcomes, and they may better predict the duration of CMS, independently of the degree of speech impairment (i.e. mutism versus reduced speech). It also highlighted some of the challenges with implementing a potential CMS scale. Use of the scale at the earliest possible time-point after surgery in order to capture the real delay in symptom presentation was presented as an important factor. Also, formulating a user-friendly format to detect CMS severity considering the changing needs of the patient during the post-surgical period, and one that could be used interchangeably by different staff (e.g. nurses, doctors, and speech/language pathologists) that can test it multiple times during the day is also imperative in adequately capturing the data.

The interactive discussion also included the use and weight of the primary and supporting criteria, with particular focus whether emotional lability should be a core (in addition to mutism) or a supporting feature. There is the increasing suggestion that the same disease spectrum manifests with different predominance of symptoms during different stages of brain development and that its variants may well extend into adulthood. The latency, duration, and severity of symptoms may all be important factors to better define prognostic groups and guide specific interventions on acute and chronic symptoms. Following discussion, there was a perceived need to further develop a feasible, valid, and reliable assessment tool by:

1. Establishing a PFS working group to develop a novel scale, which can then be paired with the previous one for correlation and comparison in future clinical and research application

2. Supporting an envisaged multi-center collaboration for the validation and use of specific children

scales especially on ataxia and cognitive affective symptoms. The development of such scales from adult versions is under the lead of Dr. Schmahmann.

The group also recognized that the ongoing multi-center trial "Nordic Study of the Cerebellar Mutism Syndrome in Children with Brain Tumors of the Posterior Fossa" [33] will further inform on the CMS definition, and scoring system.

Surgery and radiology

The pathogenesis of post-surgical CMS remains elusive. Several studies have suggested the involvement of the dentato-thalamo-cortical (DTC) pathway through a cerebellar-cortical diaschisis effect. Additionally, previous evidence has shown the development of hypertrophic olivary degeneration (HOD) in children with CMS, which indirectly indicates the disruption of the dentato-rubro-olivary pathway [23]. Specific imaging abnormalities in the inferior olivary nuclei (ION) are deemed to capture HOD [9]. Dr. Avula presented a review of a single-center data that further supports the described neuroanatomical evidence, with emphasis of new magnetic resonance imaging (MRI) and analysis techniques highlighting signal changes in the left or bilateral ION as a very relevant neuroradiological feature of for CMS in the period following surgery [2, 3]. Dr. Patay presented how other modalities of MRI, such as resting state functional MRI, could add further value in the knowledge of processes underpinning the development of CMS.

Dr. Avula presented an audit on the incidence of CMS in a single center highlighting potential for reducing the occurrence of post-surgical CMS and again focused attention on the role of surgical tools and techniques. Since 2015, the Liverpool group report a decrease in the incidence of CMS at their site from around 31 to 3%. Dr. Avula presented that factors associated with this decrease in incidence that may include a combination of increased awareness of the anatomical structures involved in CMS, awareness that total resection of tumor in order to have a good survival is not always necessary in all cases, and the avoidance of surgical equipment that may cause thermal injury (e.g. cavitron ultrasonic surgical aspirator - "CUSA"). The thermal injury hypothesis has been raised by the apparent convergence of data from the heat stroke literature, which highlights a selective vulnerability of the dentate nuclei [17] and Purkinjee cells [4] to heat, and data suggesting elevated temperature in patients post-surgically in the absence of infection, which seems to be highly predictive of CMS [25]. Thus, the change in CMS incidence recorded by Alder Hey Children's Hospital in Liverpool seemed to coincide with the abandon of CUSA devices and ultrasonic aspiration near the cerebellum may further support the contribution of "thermal damage" in CMS. Dr. Keating further supported the possibility of achieving a decreased incidence of CMS, again partially linked with the avoidance of CUSA. Dr. Keating's experience at the Children's National, Washington, USA, extended the possible factors associated with a decrease in CMS to the surgical approach (e.g. telovelar) and the degree of surgical retraction.

Additional discussion focused on the role of aggressive steroid regimes pre-operatively, with evidence-based data expected to come from the Nordic Study [33]. The experience of Liverpool and Washington should be confirmed by other groups and a multi-center trial looking at the comparison of different neurosurgical equipment was considered.

Drs. Walker and Dineen presented the findings from the 2017 International Workshop hosted in Nottingham, UK. The main aim of this workshop was to generate a pre-operative scoring system that could predict the risk of post-operative pediatric CMS. The stratification of patients to risk-groups based on pre-surgical imaging could guide treatment-decisions, thus potentially reducing the incidence of CMS, and better informing patients and families. The criteria for neuroimaging scoring

were developed through a retrospective review of neuroimaging data [19]. During the workshop, participants (including neuroradiologists, neurosurgeons, and neurologists) rated the pre-surgical magnetic resonance imaging (MRI) blinded to the clinical outcome. The delegates worked in small groups to test the effects of such pre-surgical information on clinical decision-making (e.g. low-risk and high-risk patient). The Nottingham group is leading a future prospective validation study that could produce a model for risk-stratification of children with posterior fossa tumors. The ability to stratify the individual patient-risk enhances the opportunity to achieving a better comparison across centers and harmonizing the approaches and outcomes. The Nordic study may provide a wide source of neuroimaging to further testing and refining the current scoring system.

The outcomes and goals envisaged by the PFS are the following:

1. Multi-center collaboration to develop protocols to evaluate the effects of altering surgical techniques and tools with the aim of reproducing or confuting the preliminary data from the Liverpool and Washington groups

2. Supporting neuroimaging studies that could potentiate the discovery of biomarkers, thus better informing on the individual risk, quantifying the injury of the proximal efferent cerebellar pathway (pECP), and evaluating the functional and anatomical correlates of cerebellar injury

3. Multi-center collaboration for the prospective validation of the pre-surgical predictive scoring system, for which Nottingham and Liverpool neuroradiology groups are developing web-based tools with CMS-specific training modules that would harmonize the scoring of neuroimaging data across participating centers

Rehabilitation

Rehabilitation strategies that could minimize the consequences of a cerebellar injury received significant attention during the consensus meeting. There is an increasing interest in CMS research studies and in the quality of life of survivors. Despite this, there have not been rehabilitation trials focused on reducing or eliminating the consequences of post-operative CMS. The main challenges identified relate to the difficulties in defining the key elements of management guidelines and standardizing the programs of speech, physical, and cognitive rehabilitative therapies. There has been a lack of knowledge and experience in the management of neurobehavioral symptoms that could negatively impact in the success of rehabilitative programs. Additionally, there are challenges in the use of techniques that may have the potential to boost the neuroplasticity and thus the brain recovery.

The Liverpool group has reviewed the natural history of ataxia evaluation in children with posterior fossa tumors. Scales such as Scale for the Assessment and Rating of Ataxia (SARA) [29] and Brief Ataxia Rating Scales (BARS) [28] showed a drop in scores (decreased problems) at 3 months, which reflects an improved function, followed by a plateau. It was noted that the recovery trend changes around the same time that the intense physiotherapy program ends. It raises the question whether prolonged rehabilitation beyond the initial 3-month program would result into a further gain in functional recovery. We see the opportunity to investigate the optimal window for functional improvement post-surgery, the role of prolonged intense physiotherapy, the optimal time period during which other interventions (i.e. pharmacological or non-invasive clinical interventions) are most effective in enhancing the recovery based on neuroplasticity principles.

The 2018 meeting saw the invaluable contribution of psychiatry colleagues who provided added value to the area of management, rehabilitation, and quality of life. Dr. Abrams presented her experience of emotional and behavioral symptoms that widen the spectrum of pediatric post-operative CMS.

Emphasis was placed on the fluidity and variability of the presentation of emotional and behavioral symptoms in CMS, including positive (e.g. irritability) and/or negative (e.g. withdrawn) features. Drugs targeting different mood symptoms at different times during the acute and long-term presentation of CMS-associated symptoms may result in symptom relief and improved quality of life. Some limited literature, mostly based on case studies, has been published on pharmacologic treatment approaches e.g. fluoxetine for CMS [1]. More notably, for cerebellar neuropsychiatry symptoms in children, carbamazepine has been used for severe dysphoria and irritability [31] and ariprazole for agitation and related mental status changes [35]. Dr. Abrams suggested that low doses of atypical antipsychotics and benzodiazepines may prove beneficial for short-term treatment in the post-surgical periods and allow for greater engagement in therapies (physical, occupational, speech/language, etc.) thus maximizing potential benefit. The long-term emotional, behavioral, and social consequences of CMS will likely need to be addressed with drugs appropriate for the individual specific clinical presentation [34].

Dr. Samargia presented on non-invasive techniques by that may be promising in enhancing recovery by acting on developmental neuroplasticity. Transcranial Direct Current Stimulation (tDCS) and transcranial magnetic stimulation (TMS) have been deemed safe for use in children [14]. Dr. Samargia showed the proof of concept that the DTC tract is susceptible to neuroplasticity and that both tDCS and TMS modulate the connectivity between the cerebellum and supratentorial areas [10]. This theoretical basis represents the first step in testing the hypothesis that non-invasive cerebellar stimulation may have a positive effect on recovery associated with cerebellar injury and specifically post-operative CMS. These approaches are gaining popularity, and there is an increased need for randomized controlled clinical trials to clarify the role of non-invasive neurostimulation for cerebellar injury. Further questions to be resolved should address the role of neuroplasticity in shifting maladaptive recovery, compensation versus true recovery, the standardization of methodology, and the relationship between restoration of connectivity and true functional recovery.

As a way forward, the PFS will envisage the following:

1. Development of a survey aimed at collecting information on rehabilitation guidelines and practices across countries which would determine what specific and relevant interventions are most useful to the CMS population

2. The harmonization of rehabilitation therapy approaches based on survey results around common themes. Future goals would be to establish feasibility studies using virtual training

3. The identification and monitoring of emotional, behavioral, and cognitive morbidities to intervene on these and improve the quality of life

Other key-points

The Posterior Fossa Society is expanding its focus beyond the post-surgical CMS in children to encompass variants and related conditions across the age spectrum (e.g. Cerebellum Cognitive Affective Syndrome). The Society has moved from an international multidisciplinary collaboration aimed at defining the post-operative pediatric CMS, thus raising awareness and improving its recognition, to a working group that aims to provide guidance on the prevention and management of pediatric CMS, set the direction of research in cerebellar injury, and provide a collaborative, scientific environment to encourage and support collaborative studies in the field.

The Society foresees further fertile contribution that could be achieved by broadening the involvement of countries and continents that have been under-represented to date such as Australia and Asia.

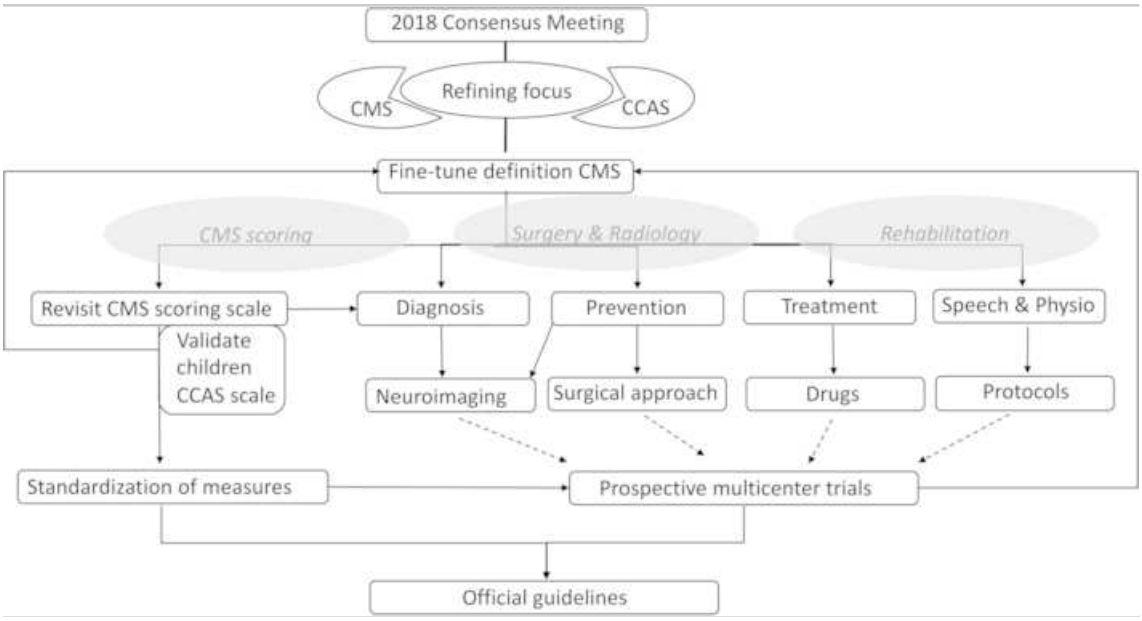
Additionally, it was strongly felt that the Society needs increased participation from specialties such as psychiatry that have expertise in areas that are invaluable in learning more about the spectrum of neuro-behavioral symptoms and potential pharmacologic interventions targeting symptoms. The importance of recruiting allied health professionals, specifically nurses, was also highlighted during discussions, as these professionals often have the best opportunity to closely and regularly observe the patients in the acute and longer-term phases of CMS. In particular, nurses and other allied health professionals can help advance the utility and implementation of symptom scales, thus better capturing and recording the symptoms.

Future directions

Discussions clearly and unanimously highlighted the desire and need for data-driven information and the development and implementation of multi-center collaborative studies to advance this field (Fig. 1). It is anticipated that such approaches and work will refine the definition of the syndrome, enhance risk-stratification strategies, and lead to effective rehabilitation approaches.

Fig. 1

Work plan agreed at the 2018 PFS Consensus Meeting. Three working groups (oval grey areas) prioritizing future research efforts. PFS, Posterior Fossa Society; CMS, cerebellar mutism syndrome; CCAS, cerebellar cognitive affective syndrome; Physio, physiotherapy



Conclusions

The third Posterior Fossa Society consensus meeting proved highly successful, with results of the meeting setting the stage for a paradigm shift in the field of CMS and its associated conditions. Positive feedback was received from all delegates for the advances achieved by the Society over the years and in the established future directions. Each delegate renewed a strong commitment in driving future research advances as reflected by the working groups. Increasing and differentiated membership to the Society is advocated and desired by the group. Variability in the awareness of CMS across medical centers was highlighted, as was the need to produce evidence-based knowledge that could harmonize the definition, measurement, and interventions. Our joint efforts aim to produce guidance and collaboration on various aspects of post-surgical CMS that could help clinicians and patients in tailoring the decision-making process. We strongly support international collaborations to

undertake future prospective research, and our established network may facilitate the access to multi-disciplinary expertise as well overcoming recruitment limitation. Future meetings are being planned, and the new Posterior Fossa Society website, currently under construction, will provide updated information and links (we invite the readers to contact the corresponding author for website address and status).

Publisher's note

Compliance with ethical standards

Conflict of interest Author Dr. E Molinari has received Travel Grant from Children with Cancer UK to cover the expenses for attending the Posterior Fossa Consensus Meeting 2018. Authors Prof. B Pizer, Dr. C Catsman-Berrevoets, Dr. S Avula, Dr. R Keating, Dr. P Paquier, Dr. J Wisoff and Dr. K S Walsh are Board Members of the Posterior Fossa Society with Dr. C Catsman-Berrevoets, Prof B Pizer, and Dr. K Walsh, currently holding the position of President, Treasurer, and Secretary respectively.

The authors declare that there are no financial or non-financial interests, including personal relationships or competing interests directly or indirectly tied to this paper, or professional interests or personal beliefs that may influence the content of the paper.

Appendix

Participants in the third Posterior Fossa Consensus Meeting 2018

Abrams Annah, Child Psychiatrist. USA.

Shivaram Avula, Radiologist. UK.

Andrea Carai, Pediatric Neurosurgeon. Italy.

Coriene Catsman-Berrevoets, Pediatric Neurologist. The Netherlands.

Robert Dineen, Radiologist. UK.

Thora Gudrunardottir, MD, Researcher. Denmark.

William Gump, Neurosurgeon. USA.

Robert F. Keating, Pediatric Neurosurgeon. USA.

Ram Kumar, Pediatric Neurologist. UK.

Helen Hartley, Pediatric Physiotherpaist. UK.

Annette Kingma, Neuropsychologist. The Netherlands.

Jurgen Lemiere, Neuropsychologist. Belgium.

Marteen Lequin, Radiologist. The Netherlands.

Jo-Fen Liu, Research Center Coordinator. UK.

References

1. Akhaddar A, Salami M, El Asri AC, Boucetta M (2012) Treatment of postoperative cerebellar mutism with fluoxetine. Childs Nerv Syst 28(4):507–508

2. Avula S, Spiteri M, Kumar R, Lewis E, Harave S, Windridge D, Ong C, Pizer B (2016) Post-operative pediatric cerebellar mutism syndrome and its association with hypertrophic olivary degeneration. Quant Imaging Med Surg 6(5):535–544

3. Avula S, Spiteri M, Guillemaut JY, Windridge D, Kumar R, Pizer B, Mallucci C, Lewis E (2018) Postoperative pediatric cerebellar mutism syndrome-identifying quantitative biomarkers on longitudinal follow-up MRI. Neuro-Oncol 20(Suppl_2):i171

4. Bazille C, Megarbane B, Bensimhon D, Lavergne-Slove A, Baglin AC, Loirat P, Woimant F, Mikol J, Gray F (2005) Brain damage after heat stroke. J Neuropathol Exp Neurol 64(11):970–975

5. Bonfield CM, Steinbok P (2015) Pediatric cerebellar astrocytoma: a review. Childs Nerv Syst 31:1677–1685

6. Catsman-Berrevoet CE, Van Dongen HR, Mulder PG, Paz y Geuze D et al (1999) Tumour type and size are high risk factors for the syndrome of “cerebellar” mutism and subsequent dysarthria. J Neurol Neurosurg Psychiatry 67(6):755–757

7. Dolecek TA, Propp JM, Stroup NE, Kruchko C (2012) CBTRUS statistical report: primary brain

and central nervous system tumors diagnosed in the United States in 2005–2009. Neuro-Onc 15:v1–v49

8. Gelabert-González M, Fernández-Villa J (2001) Mutism after posterior fossa surgery. Review of the literature. Clin Neurol Neurosurg 103(2):111–114

9. Goyal M, Versnick E, Tuite P, Cyr JS, Kucharczyk W, Montanera W, Willinsky R, Mikulis D (2000) Hypertrophic olivary degeneration: metaanalysis of the temporal evolution of MR findings. AJNR 21(6):1073–1077

10. Grimaldi G, Argyropoulos GP, Boehringer A, Celnik P, Edwards MJ, Ferrucci R, Galea JM, Groiss SJ, Hiraoka K, Kassavetis P, Lesage E, Manto M, Miall RC, Priori A, Sadnicka A, Ugawa Y, Ziemann U (2014) Non-invasive cerebellar stimulation--a consensus paper. Cerebellum 13(1):121–138

11. Gudrunardottir T, Sehested A, Juhler M, Schmiegelow K (2011) Cerebellar mutism: review of the literature. Childs Nerv Syst 27(3):355–363

12. Gudrunardottir T, Lannering B, Remke M, Taylor MD, Wells EM, Keating RF, Packer RJ (2014) Treatment developments and the unfolding of the quality of life discussion in childhood medulloblastoma: a review. Childs Nerv Syst 30:979–990

13. Gudrunardottir T, Morgan AT, Lux AL, Walker DA et al (2016) Consensus paper on post-operative pediatric cerebellar mutism syndrome: the Iceland Delphi results. Childs Nerv Syst 32(7):1195–1203

14. Hameed MQ, Dhamne SC, Gersner R, Harper L et al (2017) Transcranial magnetic and direct current stimulation in children. Curr Neurol Neurosci Rep 17(2):11

15. Korah MP, Esiashvili N, Mazewski CM, Hudgins RJ, Tighiouart M, Janss AJ, Schwaibold FP, Crocker IR, Curran WJ Jr, Marcus RB Jr (2010) Incidence, risks, and sequelae of posterior fossa syndrome in pediatric medulloblastoma. Int J Radiat Oncol Biol Phys 77(1):106–112

16. Law N, Greenberg M, Bouffet E, Taylor MD, Laughlin S, Strother D, Fryer C, McConnell D, Hukin J, Kaise C, Wang F, Mabbott DJ (2012) Clinical and neuroanatomical predictors of cerebellar mutism syndrome. Neuro-Oncology 14(10):1294–1303

17. Lee JS, Choi JC, Kang S-K, Kang J-H, Park J-K (2009) Heat stroke: increased signal intensity in the bilateral cerebellar dentate nuclei and splenium on diffusion-weighted MR imaging. Am J Neuroradiol 30(4):e58

18. Levisohn L, Cronin-Golomb A, Schmahmann JD (2000) Neuropsychological consequences of cerebellar tumour resection in children: cerebellar cognitive affective syndrome in a paediatric population. Brain 123(5):1041–1050

19. Liu JF, Dineen RA, Avula S, Chambers T, Dutta M, Jaspan T, MacArthur DC, Howarth S, Soria D, Quinlan P, Harave S, Ong CC, Mallucci CL, Kumar R, Pizer B, Walker DA (2018) Development of a pre-operative scoring system for predicting risk of post-operative pediatric cerebellar mutism syndrome. Br J Neurosurg 32(1):18–27

20. Michiels EM, Schouten-Van Meeteren AY, Doz F, Janssens GO, van Dalen EC (2015) Chemotherapy for children with medulloblastoma. Cochrane Database Syst Rev 1:CD006678

21. Moxon-Emre I, Bouffet E, Taylor MD, Laperriere N, Scantlebury N, Law N, Spiegler BJ, Malkin D, Janzen L, Mabbott D (2014) Impact of craniospinal dose, boost volume, and neurologic complications on intellectual outcome in patients with medulloblastoma. J Clin Oncol 32(17):1760–1780

22. Palmer SL, Hassal T, Evankovich K, Mabbott DJ et al (2010) Neurocognitive outcome 12 months following cerebellar mutism syndrome in pediatric patients with medulloblastoma. Neuro-Onc 12(12):1311–1317

23. Patay Z, Enterkin J, Harreld JH, Yuan Y, Löbel U et al (2014) MR imaging evaluation of inferior olivary nuclei: comparison of postoperative subjects with and without posterior fossa syndrome. Am J Neuroradiol 35(4):797–802

24. Pitsika M, Tsitouras V (2013) Cerebellum Mutism. J Neurosurg Pediatr 12(6):604–614

25. Pols SYCV, van Veelen ML, Aarsen FK, Gonzalez Candel A, Catsman-Berrevoets CE (2017) Risk factors for development of postoperative cerebellar mutism syndrome in children after medulloblastoma surgery. J Neurosurg Pediatr 20(1):35–41

26. Robertson PL, Muraszko KM, Holmes EJ, Sposto R et al (2006) Incidence and severity of postoperative cerebellar mutism syndrome in children with medulloblastoma: a prospective study by the Children's Oncology Group. J Neurosurg 105(6):444–451

27. Schmahmann JD, Sherman JC (1998) The cerebellar cognitive affective syndrome. Brain 121 (Pt 4:561–579

28. Schmahmann JD, Gardner R, MacMore J, Vangel MG (2009) Development of a brief ataxia rating scale (BARS) based on a modified form of the ICARS. Mov Disord 24(12):1820–1828

29. Schmitz-Hübsch T, Tezenas du Montcel S, Baliko L, Berciano J, Boesch S et al (2006) Scale for the assessment and rating of ataxia: development of a new clinical scale. Neurology 66:1717–1720

30. Toescu SM, Hettige S, Phipps K et al (2018) Childs Nerv Syst. https://doi.org/10.1007 /s00381-018-3867-x

31. Turkel SB, Chen LS, Nelson MD et al (2004) Case series: acute mood symptoms associated with posterior fossa lesions in children. J Neuropsychiatr Clin Neurosci 16(4):443–445

32. Wells EM, Walsh KS, Khademian ZP, Keating RF, Packer RJ (2008) The cerebellar mutism syndrome and its relation to cerebellar cognitive function and the cerebellar cognitive affective disorder. Dev Disabil Res Rev 14(3):221–228

33. Wibroe M, Cappelen J, Castor C, Clausen N, Grillner P, Gudrunardottir T, Gupta R, Gustavsson B, Heyman M, Holm S, Karppinen A, Klausen C, Lönnqvist T, Mathiasen R, Nilsson P, Nysom K, Persson K, Rask O, Schmiegelow K, Sehested A, Thomassen H, Tonning-Olsson I, Zetterqvist B, Juhler M (2017) Cerebellar mutism syndrome in children with brain tumors of the

posterior fossa. BMC Cancer 17(1):439

34. Wolfe-Christensen C, Mullins LL, Scott JG, McNall-Knapp RY (2007) Persistent psychosocial problems in children who develop posterior fossa syndrome after medulloblastoma resection. Pediatr Blood Cancer 49(5):723–726

35. Yap JL, Wachtel LE, Ahn ES, Sanz JH, Slomine BS, Pidcock FS (2012) Treatment of cerebellar cognitive affective syndrome with aripiprazole. J Pediatr Rehabil Med 5(3):233–238